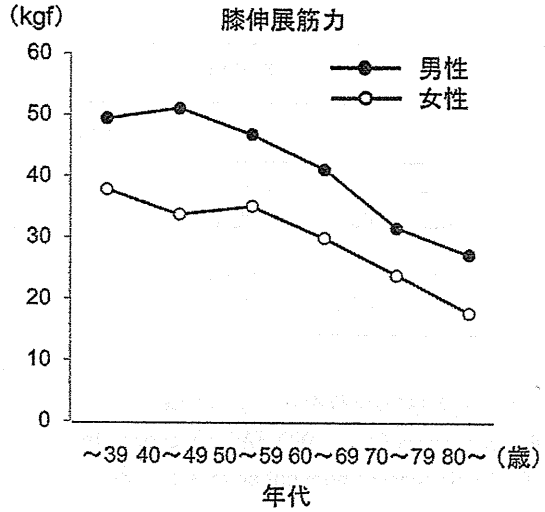

図 5　男女別年代別の膝伸展筋力

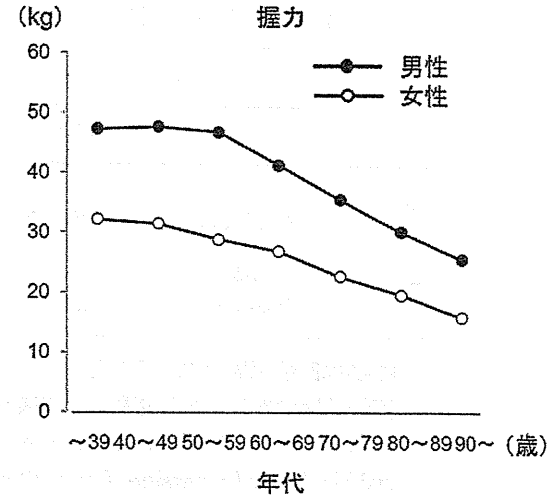

図 6　男女別年代別の握力

示す傾向がみられた。また男性のほうが中年以降年代とともに，筋量が低値を示す程度が女性に比べて大きいことが明らかとなった。一方，上肢筋量（図 4）においては，男性では年代とともに筋量が低値となる傾向を示したのに対して，女性では，中年以降は筋量がほぼ横ばい傾向であることが明らかとなった。

次に，アルケア社製簡易筋力測定・訓練器により測定した膝伸展筋力，および握力計により測定した握力の結果は，**図 5，6** に示すとおりとなった。膝伸展筋力は，50 歳代以降男女ともに，年代とともに筋力が低値となる傾向がみられた（**図 5**）。

しかし，39 歳未満と比較した場合の 80 歳以上における筋力の割合は，男性で 55.1%，女性で 46.8%であったのに対し，筋量は，男性で 67.6%，女性で 76.9%にとどまり，筋量に比べて筋力のほうが，男女ともにより低値を示す傾向となることが明らかとなった。

一方，握力は男性では 30 歳代から 50 歳代まではほとんど変わらず，60 歳代より年代が進むにつれ急激に低値となる傾向を示した（**図 6**）。女性では 50 歳代以降，年代とともに徐々に低値となり，その始まりとなる年代は男性よりも早かった。

次に，筋力と変形性膝関節症との関連を検討した。60 歳以上の対象者を膝伸展筋力の高値群（平均値以上）と低値群（平均値以下）とに分類し，変形性膝関節症の有病率を見たところ，男性では，高値群では 13.6%であったのに対し，低値群では 28.4%であった。また女性では，高値群で 14.5%，低値群で 36.1%となり，男女とも膝伸展筋力が低い群で有意に変形性膝関節症の有病率が高かった（chi square test，$p<0.0001$）。

さらに，年齢，体格指数調整済ロジスティック回帰分析を用いて検討したところ，男性では有意性は失われたが，女性では筋力の低値群では高値群より有意に変形性膝関節症の有病率が高かった（男性：オッズ比 1.6，95%信頼区間 0.6-4.3，女性：オッズ比 2.0，95%信頼区間 1.1-3.4）。

一方，下肢筋量と変形性膝関節症の有病率との関連を検討したところ，男性では筋量の高値群（平均値以上）で 14%，低値群（平均値以下）で 20%，女性では高値群で 23.1%，低値群で 26.7%であったが，男女とも有意な関連はみられなかった。以上より変形性関節症は，特に女性において，下肢筋量ではなく，膝伸展筋力が，関連していることが明らかになった。

さらにわれわれは，握力が疼痛や ADL，QOL にどのような影響を与えているかを明らかにするため，包括的 QOL 調査である Medical Outcomes Study Short Form 8（SF-8），EuroQOL（EQ-5D），および疾患特異的 QOL 調査で下肢の関節の疼痛，こわばり，身体機能を評価できる Western

表 1　握力と QOL との関連

	SF-8		EQ-5D	WOMAC		
	PCS	MCS		Pain	Stiffness	Function
男性	0.19 (0.12, 0.26)	−0.02 (−0.08, 0.03)	0.003 (0.001, 0.004)	−0.04 (−0.06, −0.02)	−0.01 (−0.02, 0.00)	−0.19 (−0.26, −0.12)
女性	0.20 (0.13, 0.27)	0.08 (0.01, 0.15)	0.004 (0.003, 0.006)	−0.04 (−0.07, −0.02)	−0.01 (−0.03, 0.00)	−0.21 (−0.30, −0.13)

数字は回帰係数（95%信頼区間）
回帰係数は年齢，体格指数および変形性膝関節症にて調整済重回帰分析により計算。
SF-8：Medical Outcomes Study Short Form-8，EQ-5D：EuroQOL，WOMAC：Western Ontario and McMaster Universities Osteoarthritis Index，PCS：physical component summary，MCS：mental component summary.
Muraki S, et al. Osteoarthritis Cartilage 2010 より一部改編

Ontario and McMaster Universities Osteoarthritis Index（WOMAC）を用いて，握力との関連を重回帰分析を用いて解析した。結果は，**表 1** のとおりで，握力はいずれの QOL 調査とも有意に相関していた（**表 1**）[5]。さらに，この結果は変形性関節症の有無で補正しても，有意性に変わりはなかった。すなわち，変形性関節症の有無とは独立して，握力は下肢の疼痛や身体機能，および QOL と関連していることが明らかになった。

さらに，問診調査による転倒回数と握力との関係を検討したところ，握力は特に女性において過去 1 年間の複数回転倒と有意に相関（＋1kg：オッズ比 0.92，95%信頼区間 0.88-0.97）していることが明らかとなった[6]。

3　考　　察

筋力の年代別データについては，文部科学省が毎年実施している体力・運動能力調査結果において，握力のデータが示されており，それによると，男女とも 20 歳ごろまで年齢とともに握力が高くなり，20 歳から 50 歳まではほとんど変化がなく，60 歳ごろから年代とともに低くなっている。しかし，高齢者についての筋力に関するまとまった報告はなかった。

今回，われわれの一般住民における疫学調査により，高齢者における上肢と下肢の筋量および筋力の年齢別推移が明らかとなり，中年以降における男女差，上肢と下肢における筋量・筋力の年代別傾向の相違が明らかとなった。

筋力の低下には運動単位の減少も関連していると考えられている。運動単位は，一つの運動ニューロンとこれによって支配されている筋繊維群の総称であり，筋活動が不活性になるとその部位の運動ニューロンは消滅し，運動単位および筋活動単位が減少する結果，発揮される最大筋力は低下することになる。

さらに，高齢者においては，高率に疼痛や関節の拘縮などが伴っており，筋肉が最大筋力を発揮できない一つの要因となっていると考えられる。また，大腿部筋量については，加齢に伴い屈筋群と伸筋群ともに減少するものの，伸筋群に比べて屈筋群は加齢による影響を受けにくいとされている[7,8]。タニタ体組成計では，下肢筋量を屈筋群と伸筋群の両方を含めて測定するため，加齢による低下が伸展筋力と比較して緩徐であった可能性もある。

一方，上肢筋量は，男性では加齢とともに緩徐な低下を示したが，女性では年齢による低下はみられなかった。過去の報告においても，MRI を用いた研究において，筋量における加齢の影響は上肢より下肢において顕著に表れると報告されており，加齢に伴う身体活動の低下が下肢優位の筋力低下の理由の一つであろうと推察されている[9]。

われわれの研究によると，高齢者では膝痛と変形性膝関節症の重症度は必ずしも相関せず，重度の変形性膝関節症でも，膝痛を持つ割合は男性で約50%，女性で約60%に過ぎず，一方，変形性膝関節症が無い者でも，男性で10%以上，女性では約20%が膝痛を訴えている[2]。これらは疼痛の要因としてレントゲン上の変化以外の要因があることを示唆していると考えられるが，その一つとして注目されているのが筋肉である。

今回，握力が疼痛やADL，QOLにどのような影響を与えているかを検討し，その結果，握力は，変形性膝関節症の有無とは独立して，下肢の疼痛や身体機能，QOLと関連していることが明らかになった。さらに，握力は特に女性において過去1年間の複数回転倒とも有意に相関していた[5]。握力は，全身筋力との関連が報告されており[10]，簡便な筋力の指標として有用であると思われる。

おわりに

高齢化に伴い，筋力の低下は非常に大きな問題である。筋力の低下は，運動器疾患のみならず，ADL，QOL，転倒などさまざまな事象と関連しており，筋力低下の予防対策の重要性が本研究により示された。現在，ロコモティブシンドローム対策として，ロコモティブトレーニング（ロコトレ）などの高齢者にとって安全かつ有効な運動法が推奨されているが，これらの有効性のエビデンスを更に積み重ねるとともに，地域の自治体で，専門設備や専門家を必要とせずに無理なく継続可能な運動介入システムを構築していくことにより，高齢者における筋力低下の予防対策をより充実させ，要介護者の低減をはかっていく必要がある。

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Osteoporosis Japan

ロコモティブシンドロームの基礎疾患である腰椎椎体骨折，変形性腰椎症，変形性膝関節症と運動機能との関連

阿久根 徹[1)]　村木重之[1)]　岡 敬之[2)]
川口 浩[3)]　中村耕三[3)]　吉村典子[2)]

はじめに

現在日本では65歳以上の高齢者が21％を超える超高齢社会に突入しており，少子高齢化による介護の問題が喫緊の課題となっている。厚生労働省国民生活基礎調査(平成19年)によると，変形性関節症や骨粗鬆症性骨折などの運動器疾患は，要支援の原因の約3分の1，要介護の原因の約2割を占め，その主要原因疾患となっており，運動器障害による日常生活機能の低下を予防するための対策の確立が社会的に焦眉の課題となっている。

運動器障害による要介護リスクの高い状態を表す概念として，ロコモティブシンドロームが日本整形外科学会により提唱されている。ロコモティブシンドロームの基礎疾患には，骨粗鬆症，変形性脊椎症，変形性関節症などが含まれ，これらの発生や進行の予防法の解明，ならびにこれらの疾患を含む運動器障害による生活機能低下の予防対策を確立することが，社会から強く求められている。

そのためには，まず運動器疾患の基本疫学指標を解明して日本人の基準値を明らかにし，その発生や進行に関わる危険因子を同定するとともに，発生や進行の予測に役立つ指標を明らかにして，簡便なスクリーニング方法を定め，有効かつ効率的な介入手段を開発することが必要であるが，それらのエビデンスの多くはいまだ解明されていないのが現状である。

本研究では，一般住民における片足立ち時間の男女別，年齢別推移を明らかにし，かつ，高齢者要介護度に強い影響を与えるロコモティブシンドロームの基礎疾患である腰椎椎体骨折，変形性腰椎症，変形性膝関節症と運動機能との関連を解明する目的で，一般住民集団の疫学調査研究を行った。

1 方　法

われわれは，2005年に変形性関節症などの運動器疾患をターゲットとする一般住民コホートを日本の3地域に設立し[1)]，2005年から2007年

Association of Lumbar Vertebral Fracture, Lumbar Spondylosis and Knee Osteoarthritis with Physical Function

Toru Akune：Department of Clinical Motor System Medicine, 22nd Century Medical and Research Center, Graduate School of Medicine, University of Tokyo, *et al.*

Key words：椎体骨折，変形性腰椎症，変形性膝関節症，運動機能

[1)] 東京大学大学院医学系研究科22世紀医療センター臨床運動器医学講座　[2)] 東京大学大学院医学系研究科22世紀医療センター関節疾患総合研究講座　[3)] 東京大学大学院医学系研究科整形外科

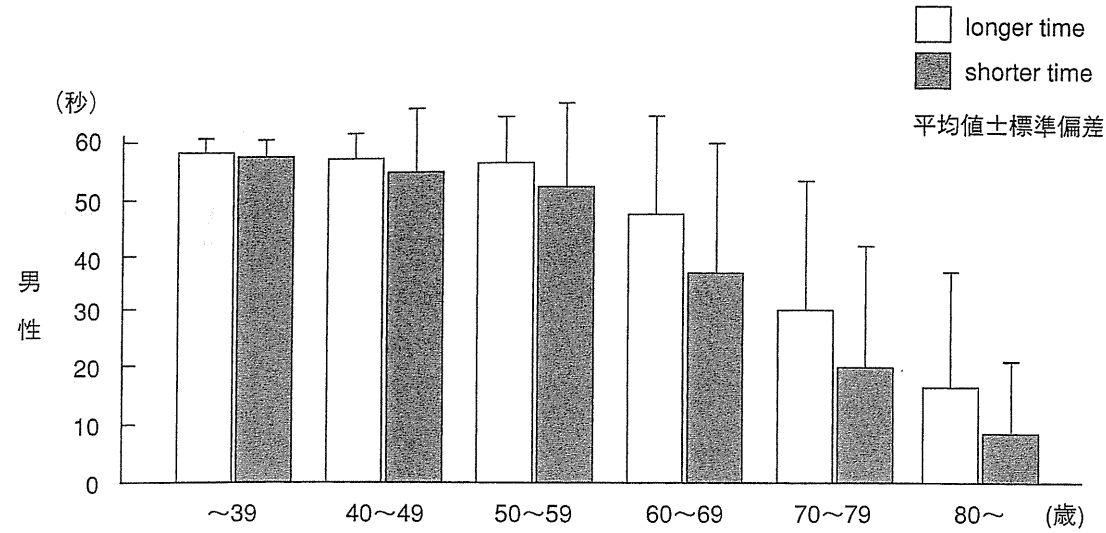

図1　年代別開眼片足立ち時間(男性)

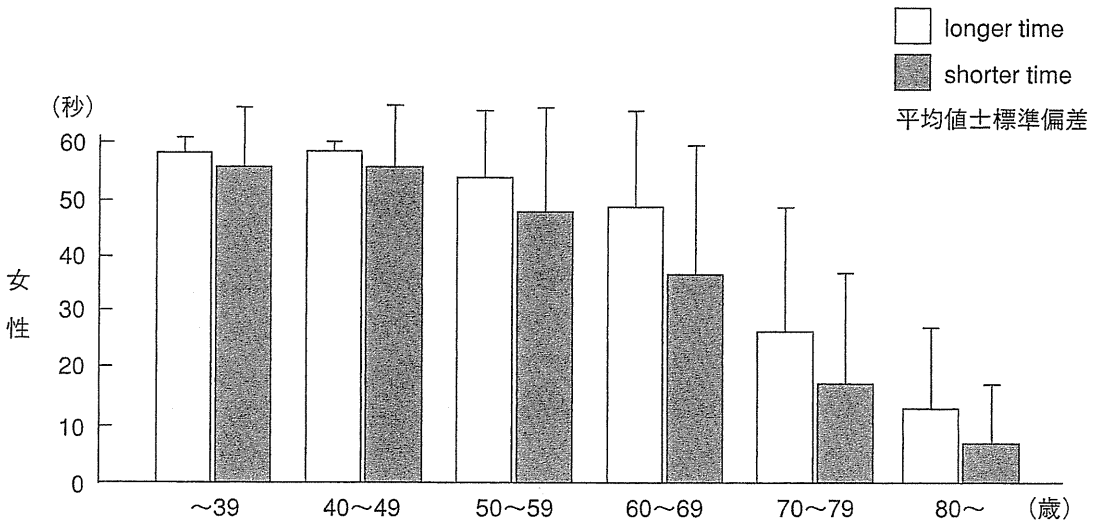

図2　年代別開眼片足立ち時間(女性)

にかけて総数3,040名のベースライン調査を実施した[2～4]。今回は，3地域のうち，山村型，漁村型の二つの地域コホートにおいて，2008年より2010年にかけて疫学調査を実施したデータを解析対象とした。対象者は，調査に参加した一般住民1,551名(男性514名，女性1,037名，平均65.8歳)である。問診調査，身体計測(身長，体重，握力)を行い，運動機能の指標として，開眼片足立ち時間を左右それぞれの足で測定し，計測時間の上限を60秒とした。測定時間の長短により各対象者の結果をlonger time，shorter timeに分類した。また，両膝正面，腰椎側面の立位単純レントゲン撮影を行い，読影により腰椎椎体骨折の有無を判定した。さらに，膝および腰椎において，最重症レベルがKellgren/Lawrence分類におけるgrade 3以上(関節裂隙の狭小化，椎間板高の狭小化が明らかなもの)を変形性膝関節症あり，変形性腰椎症ありと定義し，それらの有無を判定した。

開眼片足立ち時間の推移を男女別，年齢別に検討した。また，片足立ち時間を目的変数，上記各疾患を説明変数として，年齢，性，体格指数，握力を調整した重回帰分析を行い，関連を検討した。

2 結　　果

開眼片足立ち時間の測定結果を，男女別，年代別に示すと**図1，2**のとおりとなった。男女ともに40歳未満と40歳代では，ほぼ上限の60秒に近い結果となり差がみられなかった。それに対して，60歳代以降では，男女ともに年齢が高くなるにつれ，直線的に片足立ち時間が短くなる傾向を示した。

片足立ち時間と疾患の有無との関連を検討するために，片足立ち時間を目的変数，各疾患を説明変数として，年齢，性，体格指数，握力を調整した重回帰分析を行った結果，腰椎椎体骨折，変形性腰椎症，変形性膝関節症のいずれにおいても，疾患を有する者はない者に比べて片足立ち時間が有意に低値であった($p<0.05$)。この結果は，片足立ち時間がlonger time, shorter timeのいずれの場合も同様であった。また，被検者が有する上記疾患の個数(0～3個)を説明変数として，片足立ち時間を目的変数とする重回帰分析を同様に行った結果，疾患を多く保有している者ほど，片足立ち時間が低値となった($p<0.05$)。

考　　察

本研究では，地域代表性を有する一般住民集団を対象とした片足立ち時間の調査を実施しており，得られた結果は一般住民の基準値として用いることが可能と考えられる。ただし，片足立ち時間測定の上限を60秒としているので，60歳代以降では年齢とともに直線的に片足立ち時間が低値となる傾向を示したが，40歳未満，40歳代では，上限の60秒に近く差がみられなかった。これは天井効果により頭打ちの状態となったもので，若い世代については十分に評価できていないものと考えられる。

片足立ち時間の測定には，上限を3分とする方法や上限を定めないやり方もあり，一長一短がある。長時間測定する方法は，より若い年代についても正確に評価できる利点を有する反面，被検者一人あたりに要する検査時間が長くなり，多人数の集団に対して，効率良く多数の検診項目を実施する必要がある場合には支障になりやすい。本法は，若年者の片足立ち時間の評価には不十分であるが，高齢者を対象とする測定方法としては，効率的で有用な方法と考えられる。

ロコモティブシンドロームの基礎疾患である骨粗鬆症，変形性脊椎症や変形性関節症は，無症状のまま緩徐に進行する経過をたどることが多い運動器疾患であるため，早期の段階で発見して運動器障害の予防につなげるためには，医療機関を受診しない者も含めた一般住民健診などを実施して，簡便なツールにより効率的に高リスク者をスクリーニングすることが必要である。

運動器は，主に骨，関節，筋，神経より構成されており，筋力や神経系機能も反映する片足立ち時間測定検査は，運動器の評価指標として有用と思われる。片足立ち時間は，バランス能力などの運動機能を評価でき，体幹・下肢動作が中心となるような日常生活動作における運動器障害の評価に役立つ可能性がある。さらに本研究では，年齢などの因子を調整しても，椎体骨折，変形性腰椎症，変形性膝関節症を有する者のほうがない者より片足立ち時間が低値であり，また，それらの疾患数が多い者ほど片足立ち時間が低値であったことより，片足立ち時間という運動機能評価指標は，運動器疾患の構造学的な変性の有無やその重症度を反映する指標としても利用できる可能性が示唆される。

片足立ち時間の測定は，レントゲンや骨密度検査と異なり，特別な設備や検査資格を必要としないので，時計さえあれば誰でも簡単に検査できる方法で，また歩行速度測定のように検査のための広いスペースを確保する必要もないため，汎用性が非常に高い。たとえば屋外の検診所まで出かけることが困難な高齢者などに対しても，自宅訪問による検査で容易にデータ収集することができる。

本研究は横断的研究であり，因果関係について明らかにすることはできないが，今後の縦断調査データの検討により，運動器障害の発生や

進行の予測可能性に関する指標の有用性についても検討を行っていく予定である。

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Vertebral fracture status and the World Health Organization risk factors for predicting osteoporotic fracture risk in Japan

Saeko Fujiwara [a,*], Etsuro Hamaya [b], Wakana Goto [b], Naomi Masunari [a], Kyoji Furukawa [c], Masao Fukunaga [d], Toshitaka Nakamura [e], Akimitsu Miyauchi [f], Peiqi Chen [b]

[a] Dept. of Clinical Studies, Radiation Effects Research Foundation, 5-2 Hijiyama Park, Minami-ku, Hiroshima, 732-0815, Japan
[b] Lilly Research Laboratories Japan, Eli Lilly Japan KK, Sannomiya Plaza Bldg, 7-1-5, Isogamidori, Chuo-ku, Kobe, 651-0086, Japan
[c] Dept. of Statistics, Radiation Effects Research Foundation, 5-2 Hijiyama Park, Minami-ku, Hiroshima, 732-0815, Japan
[d] Kawasaki Medical School, 577, Matsushima, Kurashiki, Okayama, 701-0192, Japan
[e] Dept. of Orthopedics, University of Occupational and Environmental health in Japan, 1-1, Iseigaoka, Yahata-nishi-ku, Kitakyushu, Fukuoka, 807-8555, Japan
[f] Dept. of Internal Medicine, Omura City Municipal Hospital, 133-22, Kogashima-cho, Omura, Nagasaki, 865-8561, Japan

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ABSTRACT

Introduction: Vertebral fractures are the most common osteoporotic fracture and the prevalence of vertebral fracture is commonly assessed in clinical practice in Japan. The objective of this study was to evaluate potential risk factors for osteoporotic fractures, including morphometric spine fracture status and the WHO risk factors for predicting 4-year fracture risk.

Methods: A population-based community cohort, the Adult Health Study, consisting of 2613 men and women with mean age of 65 enrolled in Hiroshima was followed prospectively for 4 years. The prevalence and incidence of spine fractures were identified from lateral and posterior–anterior spine radiographs using a semiquantitative method. Information on incident nonvertebral fragility fractures (hip, proximal humeral, and forearm) was collected at interviews by trained nurses and physicians during biennial health examinations.

Results: A model, including spine fracture status in addition to the WHO risk factors, appeared to provide greater prognostic information regarding future fracture risk (gradient of risk/standard deviation: GR/SD = 2.73) than a model with the WHO risk factors alone (GR/SD = 2.54). In univariate analyses, age, bone mineral density (BMD), prior clinical fracture, and spine fracture status had the highest gradient of risk. The presence of multiple prevalent spine or non-spine fractures significantly increased fracture risk, but, their contributions to the gradient of risk were similar to those when fracture status was categorized as a binary variable. A model considering those four risk factors yielded GR/SD = 2.67, indicating that it could capture most of the predictive information provided by the model with spine fracture status plus the WHO risk factors.

Conclusion: The use of age, BMD, prior clinical fracture and spine fracture predicted future fracture risk with greater simplicity and higher prognostic accuracy than consideration of the risk factors included in the WHO tool.

Introduction

Prediction of future fracture risk can provide clinicians and patients with important information for their decisions on life style and treatments. Recently, a fracture risk assessment tool (FRAX) was developed by the World Health Organization (WHO) [1]. The WHO fracture risk assessment tool considers clinical risk factors for future fracture, including age, prior clinical fracture, current smoking, alcohol use, parental history of hip fracture, glucocorticoid use, rheumatoid arthritis, and bone mineral density (BMD) in order to assign a 10-year absolute fracture risk [2].

Vertebral fractures are the most common fragility fracture in postmenopausal women with osteoporosis [3–5]. Many studies have demonstrated that prevalent vertebral fractures increased the risk of new vertebral and nonvertebral fractures in postmenopausal women [6–11]. Cauley et al. [12] found that women with a prevalent vertebral fracture at baseline were greater than 4 times more likely to experience an incident vertebral fracture over 15 years of follow-up compared with women without a prevalent vertebral fracture. Furthermore, Siris et al. [13] demonstrated that, at any particular value

* Corresponding author. Fax: +81 82 263 7279.
E-mail address: fujiwara@rerf.or.jp (S. Fujiwara).

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for BMD, spine fracture status increased future vertebral or nonvertebral fragility fracture risk by up to 7-fold.

Vertebral fracture prevalence is higher among Japanese women than Caucasian women [14]. Fujiwara et al. reported that the risk of subsequent vertebral fracture increased 3 times for women with a prevalent vertebral fracture, which is similar to other findings [15]. Since X-ray is recommended to diagnose osteoporosis in Japanese guidelines, prevalent vertebral fracture status is commonly assessed in clinical practice in Japan. However, prevalent vertebral fractures are not identified as a distinct risk factor in the FRAX tool in Japan [16]. Recently, Chen et al. demonstrated the importance of prevalent vertebral fractures for predicting the future fracture risk in the Canadian Multicentre Osteoporosis Study (CaMos) which was one of nine cohorts used for the development and validation of the FRAX tool [17]. The results from CaMos used prevalent vertebral fracture status along with age and BMD to better predict future fracture risk than the WHO risk factors, with greater simplicity for Caucasians in the CaMos adult cohort [17]. Donaldson et al. reported that a combination of radiographic vertebral fracture, femoral neck BMD, and age could predict future vertebral fracture risk as well as the WHO risk factors for Caucasians in the Fracture Intervention Trial (FIT) [18]. Ensrud et al. also reported that simple models based on age and BMD alone or age and fracture history alone predicted 10-year risk of fracture as well as more complex FRAX models in the Study of Osteoporosis Fracture (SOF) [19].

It was acknowledged by the authors of the WHO tool [20] that a prior clinical vertebral fracture was an especially strong risk factor. It was also acknowledged that a fracture detected as a radiographic observation alone (a morphometric vertebral fracture) should be counted as a previous fracture [20]. However, most of the epidemiology studies from which this tool was developed did not include spine imaging, and so spine fracture status information was not available for study or for inclusion in the tool.

The objective of this analysis was to evaluate and compare potential risk factors, including morphometric vertebral fracture status and the WHO fracture risk factors for predicting 4-year fracture risk in a Japanese population-based cohort which was also used for the development and validation of the FRAX tool. Furthermore, because spine fracture status is an important determinant of future fracture risk, we hypothesized that consideration of morphometric vertebral fracture status would lead to a simple risk prediction tool.

Subjects and methods

Study participants and population

The study subjects were a total of 2613 Adult Health Study (AHS) subjects aged 47 to 95 years old who underwent physical examinations in Hiroshima in the 1994–95 examination cycle. The AHS was established in 1958 to document the late health effects of radiation exposure among atomic-bomb survivors in Hiroshima and Nagasaki. The initial AHS cohort consisted of about 15,000 survivors and approximately 5000 controls, all of whom were selected from residents of Hiroshima and Nagasaki on the basis of a questionnaire included in Japan's 1950 national census and survey of atomic-bomb survivors. AHS subjects have been followed through biennial medical examinations since 1 July 1958. The participation rate has been around 70% throughout this period. The details of the cohort have been previously described [21]. All participants provided written informed consent for BMD measurement, spine X-ray examination, and all other health examinations.

Bone mineral density

BMD at the spine (L2–L4, antero–posterior direction) and proximal femur were measured at each biennial health examination using dual X-ray absorptiometry (DXA, QDR-2000; Hologic Inc, Waltham, MA, USA). An anthropomorphic spine phantom was scanned daily to calibrate the instrument. Precision of the DXA was monitored over the study period using the anthropomorphic phantom, and fluctuation was found to be less than 1%.

Clinical risk factor measurement

Measurements of height and weight were made at each examination. Participants completed an extensive interviewer-administered questionnaire to assess for osteoporosis and fracture-related risk factors at baseline. All clinical risk factors were derived from the baseline interview. Subject responses were coded to indicate if they were current cigarette smokers, if they had used systemic glucocorticoid therapy, if they had sustained a prior clinical fracture, and if they were currently drinking alcohol. Information on glucocorticoid use and dosage was confirmed by a pharmacist to check medicine that the participants bring their medicine to their appointment. About 80% of the participants bring medicine. Diagnoses of rheumatoid arthritis were made by a physician based on interview of symptoms, health examination, and laboratory data. Parental history of hip fracture was unavailable in this study. Because there is no association between radiation dose and BMD, or vertebral and hip fracture incidence [14,15], we did not take account of radiation dose in the analyses.

Fracture diagnosis

Vertebral fracture was determined by semiquantitative assessment of T4–L4 vertebrae [22]. Incident vertebral fractures were diagnosed based on clinical reading of lateral thoracic and lumbar spine X-ray images by a radiologist at the health examinations. However, 7.7% (201 of 2613) subjects were evaluated by thoracic spine radiographs only because they refused to undergo lumbar spine X-ray twice. New vertebral fracture was defined as a decrease of at least 20% in height of any vertebral body. Information about nonvertebral fragility fractures (hip, forearm/wrist, humerus, and other) was collected at interview by trained nurses and physicians during the biennial health examinations. The WHO risk fracture assessment tool predicts the risk for hip fractures and of a major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture). In our study, the risk of any fragility fracture refers to the risk of a participant experiencing either an incident vertebral fracture detected by spine radiography and/or a nonvertebral fragility fracture.

Statistical analysis

A series of logistic regression analyses were performed to determine the importance of vertebral fracture status and the WHO risk factors for predicting the 4-year risk of any future vertebral or nonvertebral fragility fracture. Although the WHO fracture risk assessment tool provides a 10-year fracture risk, it is stated that, in individuals with low mortality, the one-year probability is up to 10% of the 10-year probability [1]. To test the significance of vertebral fracture status on the prediction of future fracture risk, a logistic regression model including the WHO risk factors only was compared with models including the WHO risk factors plus vertebral fracture status (yes/no). To pool the data from the genders, the models included the interaction effects of risk factors with gender at the 10% level of significance. As there were no statistically significant interactions, the relationship between all the risk factors and incident fracture risk was statistically consistent between the two genders. The performance of each model was assessed as the gradient of risk (GR), i.e., the increase in fracture risk per standard deviation (GR/SD); this assessment was used in the development of the WHO fracture risk tool [23].

After finding an improvement for the fracture risk prediction by adding the vertebral fracture status to the WHO risk factors, further analyses were conducted to determine the predictive ability of sequential addition of the most important WHO risk factors and vertebral fracture status. To do this, a series of univariate analyses were conducted to investigate the association between each of individual risk factors (age, BMD, prior fragility fractures, number of non-spine fracture, spine fracture status, number of spine fractures, current smoking, alcohol use, glucocorticoid use, and rheumatoid arthritis) and future fracture risk. The gradient of fracture risk was examined in different models by sequential addition of the most important risk factors determined from the univariate analyses. Four-year absolute fracture risk was estimated using the logistic regression model including the risk factors age, BMD T-score, spine fracture (yes/no), and prior fragility fractures (yes/no). All analyses are reported for pooled data using SAS version 8.2 (SAS Institute, Cary, NC, USA).

Results

Subject characteristics

In the Hiroshima cohort, 2613 subjects had spine radiographs both at baseline and 4 years later. The average observation period was 3.8 ± 0.8 (mean ± 1 standard deviation) years. The mean age of the sample population was 63.2 years for men (n = 794) and 65.9 years for women (n = 1819). Compared to men, women had significantly lower BMD values, a higher rate of prevalent morphometric vertebral fracture, and a higher proportion with prior clinical fracture (Table 1). Two hundred fifteen subjects experienced at least one incident vertebral fracture while seventy-five subjects had multiple incident vertebral fractures. Seventy-nine subjects experienced at least one nonvertebral fragility fracture (32 hip, 35 forearm/wrist, and 16 humerus). Two hundred eighty-one subjects experienced either an incident vertebral fracture and/or a nonvertebral fragility fracture during the follow-up period.

Comparison of models considering WHO risk factors alone versus WHO risk factors plus spine fracture status

Table 2 shows the performance characteristics of the model expressed as GR/SD change in the risk indicator. The GR for the WHO risk factors was 2.54 when lumbar spine BMD was used in the prediction model and 2.57 when femoral neck BMD was used. Inclusion of the vertebral fracture (yes/no) in the lumbar spine BMD model and femoral neck BMD model increased the GR to 2.73 and 2.77, respectively.

Table 1
Baseline demographics of the study population[a].

	Women (N = 1819)	Men (N = 794)	Total (N = 2613)
Age (years)[b]	65.9 ± 0.23	63.2 ± 0.35	65.1 ± 0.19
Prevalent morphometric vertebral fracture(s) (% yes)[b]	10.3	3.3	8.2
Prior clinical fracture (% yes)[b]	17.5	12.1	15.8
Lumbar spine BMD (g/cm^2)[b]	0.79 ± 0.004 (N = 1815)	0.96 ± 0.006 (N = 791)	0.84 ± 0.003 (N = 2606)
Femoral neck BMD (g/cm^2)[b]	0.62 ± 0.003 (N = 1804)	0.73 ± 0.004 (N = 792)	0.65 ± 0.002 (N = 2596)
Prior glucocorticoid use (% yes)	2.9	2.4	2.8
Current smoking (% yes)[b]	6.8	32.6	14.6
Alcohol use (% yes)[b]	6.9	39.2	16.7
Rheumatoid arthritis (% yes)	1.0	0.6	0.9

[a] Values are mean ± standard error (SE) unless otherwise stated.
[b] $P<0.01$ between women and men.

Table 2
Comparison of predictive ability of WHO clinical risk factors for new osteoporotic fracture.

	Model	GR/SD (95% CI)
Lumbar spine BMD	WHO clinical risk factors alone	2.54 (2.20–2.97)
	WHO clinical risk factors + spine fractures (yes/no)	2.73 (2.36–3.21)
Femoral neck BMD	WHO clinical risk factors alone	2.57 (2.22–3.01)
	WHO clinical risk factors + spine fractures (yes/no)	2.77 (2.39–3.26)

Univariate analyses for 4-year risk of new fractures

In univariate analyses, BMD provided the highest GR, followed by age, spine fracture status, and prior clinical fracture. Other risk factors provided relatively lower GRs. Further analyses showed that the gradient of risk for number of vertebral fractures and number of non-vertebral fractures was 1.53 (1.37, 1.66) and 1.29 (1.18, 1.42), respectively. However, their contributions to the gradient of risk were similar to those when fracture status was categorized as a binary variable (yes/no). The presence of multiple prevalent vertebral fractures significantly increased fracture risk 15-fold while the presence of single prevalent vertebral fracture was associated with a 4-fold increase in fracture risk. The presence of multiple non-vertebral fractures significantly increased fracture risk 7-fold while the presence of single non-prevalent vertebral fracture was associated with a 2-fold increase in fracture risk. The risk of incident fragility fractures increased with an increasing number of vertebral fractures as well as an increasing number of non-vertebral fractures. As the results were similar in men and women, multivariable analyses were performed on the combined set of men and women (data not shown).

Multivariable analyses for 4-year risk of new fractures

The performance characteristics of models with sequential addition of the most important risk factors are shown in Tables 3–4, expressed as GR/SD change in the risk indicator. For fracture prediction, a model that included age, lumbar spine BMD, presence or absence of spine fracture, and prior clinical fracture had a GR of 2.67. After those four risk factors were included in the model, the increment in the GR/SD by adding the four additional risk factors described in the WHO risk assessment tool was 0.06. Similarly, a model that included age, femoral neck BMD, presence or absence of spine fracture, and prior clinical fracture had a GR of 2.71. After those four risk factors were included in the model, the increment in the GR/SD by adding the four additional risk factors described in the WHO risk assessment tool was 0.06.

Absolute risk of fracture based on age, BMD T-score, spine fracture status, and prior clinical fracture

The 4-year absolute risk of incident fragility fracture in the Hiroshima cohort based on age, femoral neck T-score, spine fracture (yes/no), and prior clinical fracture (yes/no) is shown for women (Table 5) and men (Table 6). Results for lumbar spine BMD were similar to results for femoral neck BMD (data not shown). The fracture risk increased in both men and women with increasing age, more negative T-score, and presence of spine fracture.

Discussion

In this cohort of a Japanese population, we found that consideration of spine fracture status along with the WHO risk factors provided additional information compared with considering the WHO risk factors alone. In univariate analysis, we found that spine fracture

Table 3
GR/SD change in risk score for different models using lumbar spine BMD.

Model	Age	LS BMD	Spine fracture (yes/no)	Prior Clin Fx	Current smoking	Prior GC use	RA	Alcohol use	GR/SD (95% CI)
1	•								1.93 (1.68–2.24)
2	•	•							2.33 (2.02–2.72)
3	•	•	•						2.49 (2.15–2.91)
4	•	•	•	•					2.67 (2.31–3.13)
5	•	•	•	•	•				2.67 (2.31–3.14)
6	•	•	•	•	•	•			2.67 (2.31–3.14)
7	•	•	•	•	•	•	•		2.70 (2.33–3.17)
8	•	•	•	•	•	•	•	•	2.73 (2.36–3.21)

"•" Indicates that the factor is included in a model.
GR = gradient of risk; SD = standard deviation; LS BMD = Lu bone mineral density; Clin = clinical; Fx = fracture; GC = glucocorticoid; RA = rheumatoid arthritis; CI = confidence interval.

Table 4
GR/SD change in risk score for different models using femoral neck BMD.

Model	Age	FN BMD	Spine fracture (yes/no)	Prior Clin Fx	Current smoking	Prior GC use	RA	Alcohol use	GR/SD (95% CI)
1	•								1.93 (1.68–2.24)
2	•	•							2.34 (2.03–2.73)
3	•	•	•						2.50 (2.16–2.93)
4	•	•	•	•					2.71 (2.33–3.17)
5	•	•	•	•	•				2.71 (2.34–3.18)
6	•	•	•	•	•	•			2.71 (2.33–3.17)
7	•	•	•	•	•	•	•		2.71 (2.36–3.22)
8	•	•	•	•	•	•	•	•	2.77 (2.39–3.26)

"•" Indicates that the factor is included in a model.
GR = gradient of risk; SD = standard deviation; FN BMD = femoral neck bone mineral density; Clin = clinical; Fx = fracture; GC = glucocorticoid; RA = rheumatoid arthritis; CI = confidence interval.

status was one of the most significant predictors of 4-year fracture risk. In addition, we assessed models for predicting future fracture risk by sequentially adding the most important risk factors, and found that a model including age, BMD, presence or absence of spine fracture, and prior clinical fracture provided almost as much information as the WHO risk factors plus the spine fracture status could provide. Moreover, we found that this model provided more prognostic information than consideration of the WHO risk factors alone.

Table 5
Four-year risk of incident fragility fracture in the Hiroshima population of women based on age, femoral neck T-score, spine fracture (no/yes) and prior clinical fracture (no/yes).

Femoral neck T-score	Spine fracture	Prior clinical fracture	Age (years)							
			50	55	60	65	70	75	80	85
−1	No	No	3.6	4.5	5.5	6.7	8.2	10.0	12.1	14.6
		Yes	7.6	9.3	11.3	13.6	16.4	19.6	23.2	27.2
	Yes	No	9.9	12.0	14.4	17.3	20.6	24.4	28.5	33.1
		Yes	19.9	22.9	26.9	31.4	36.2	41.3	46.6	52.0
−1.5	No	No	4.3	5.2	6.4	7.8	9.6	11.6	14.0	16.8
		Yes	8.9	10.8	13.0	15.7	18.8	22.3	26.2	30.6
	Yes	No	11.4	13.8	16.6	19.8	23.4	27.5	32.0	36.9
		Yes	22.0	25.9	30.3	35.0	40.1	45.4	50.8	56.1
−2	No	No	5.0	6.1	7.5	9.1	11.1	13.4	16.1	19.2
		Yes	10.3	12.5	15.0	18.0	21.4	25.3	29.6	34.2
	Yes	No	13.2	15.9	19.0	22.5	26.5	30.9	35.7	40.8
		Yes	25.0	29.2	33.9	38.9	44.1	49.5	54.9	60.1
−2.5	No	No	5.8	7.1	8.7	10.6	12.8	15.4	18.4	21.9
		Yes	11.9	14.4	17.3	20.6	24.3	28.5	33.1	38.0
	Yes	No	15.2	18.2	21.6	25.5	29.8	34.5	39.6	44.8
		Yes	28.2	32.8	37.7	42.9	48.2	53.6	58.9	64.0
−3	No	No	6.8	8.3	10.1	12.2	14.8	17.7	21.1	24.9
		Yes	13.8	16.5	19.7	23.4	27.5	32.0	36.9	42.0
	Yes	No	17.5	20.8	24.6	28.8	33.4	38.4	43.6	48.9
		Yes	31.6	36.5	41.6	46.9	52.3	57.7	62.8	67.7
−3.5	No	No	7.9	9.7	11.7	14.1	17.0	20.2	23.9	28.1
		Yes	15.9	19.0	22.5	26.5	30.9	35.7	40.8	46.1
	Yes	No	20.0	23.6	27.8	32.3	37.2	42.3	47.7	53.1
		Yes	35.3	40.4	45.7	51.1	56.4	61.6	66.6	71.2
−4	No	No	9.2	11.2	13.5	16.3	19.4	23.0	27.1	31.5
		Yes	18.2	21.6	25.5	29.8	34.5	39.5	44.8	50.2
	Yes	No	22.7	26.7	31.2	36.0	41.1	46.4	51.8	57.1
		Yes	39.2	44.4	49.8	55.2	60.4	65.4	70.2	74.5

Table 6
Four-year risk of incident fragility fracture in the Hiroshima population of men based on age, femoral neck t-score, spine fracture (no/yes) and prior clinical fracture (no/yes).

Femoral neck T-score	Spine fracture	Prior clinical fracture	Age (years)							
			50	55	60	65	70	75	80	85
−1	No	No	4.2	4.3	4.5	4.6	4.8	5.0	5.2	5.3
		Yes	5.3	5.5	5.7	5.9	6.1	6.4	6.6	6.8
	Yes	No	17.5	18.0	18.6	19.2	19.8	20.4	21.0	21.6
		Yes	21.6	22.2	22.9	23.6	24.2	24.9	25.7	26.4
−1.5	No	No	4.9	5.1	5.3	5.5	5.7	5.9	6.1	6.3
		Yes	6.3	6.6	6.8	7.0	7.3	7.5	7.8	8.1
	Yes	No	20.3	20.9	21.5	22.2	22.8	23.5	24.2	24.9
		Yes	24.8	25.5	26.3	27.0	27.8	28.5	29.3	30.1
−2	No	No	5.9	6.1	6.3	6.5	6.8	7.0	7.3	7.5
		Yes	7.5	7.8	8.0	8.3	8.6	8.9	9.2	9.6
	Yes	No	23.4	24.1	24.8	25.5	26.2	27.0	27.7	28.5
		Yes	28.4	29.2	30.0	30.8	31.6	32.4	33.2	34.1
−2.5	No	No	7.0	7.2	7.5	7.8	8.0	8.3	8.6	8.9
		Yes	8.9	9.2	9.5	9.8	10.2	10.5	10.9	11.3
	Yes	No	26.9	27.6	28.4	29.1	29.9	30.7	31.5	32.4
		Yes	32.3	33.1	34.0	34.8	35.7	36.5	37.4	38.3
−3	No	No	8.3	8.6	8.9	9.2	9.5	9.8	10.2	10.5
		Yes	10.5	10.8	11.2	11.6	12.0	12.4	12.8	13.2
	Yes	No	30.6	31.4	32.2	33.1	33.9	34.8	35.6	36.5
		Yes	36.4	37.3	38.2	39.1	40.0	40.9	41.8	42.7
−3.5	No	No	9.8	10.1	10.5	10.8	11.2	11.6	12.0	12.4
		Yes	12.3	12.7	13.2	13.6	14.1	14.5	15.0	15.5
	Yes	No	34.6	35.5	36.4	37.2	38.1	39.0	39.9	40.8
		Yes	40.7	41.7	42.6	43.5	44.4	45.4	46.3	47.3
−4	No	No	11.5	11.9	12.3	12.7	13.1	13.6	14.0	14.5
		Yes	14.4	14.9	15.4	15.9	16.4	16.9	17.5	18.0
	Yes	No	38.9	39.8	40.7	41.6	42.5	43.5	44.4	45.3
		Yes	45.2	46.2	47.1	48.1	49.0	50.0	50.9	51.8

Our results are consistent with the findings in Caucasians from the CaMos cohort that showed a model considering age, BMD, and spine fracture status captured almost all of the predictive information provided by a model considering spine fracture status plus the WHO risk factors and provided greater predictive information than a model considering the WHO risk factors alone [17]. Similar findings have been reported in FIT where a combination of baseline radiographic vertebral fracture, femoral neck BMD, and age is the strongest predictor of future vertebral fracture [18]. Furthermore, baseline vertebral fracture status plus age and femoral neck BMD predicted incident radiographic vertebral fracture significantly better than FRAX with femoral neck BMD. The results of FIT indicate that once femoral neck BMD and age are known, the eight additional risk factors in FRAX do not significantly improve the prediction of vertebral fracture. Our findings are also consistent with reported findings in SOF where a simple model based on age and fracture history alone predicted 10-year risk of fracture as well as more complex FRAX models [19].

FRAX represents a major advance in the field of osteoporosis for several reasons. The tool is based on data collected from cohorts in the United States, Europe, Australia, and Asia and is applicable to both the developed and the developing world. Modeling techniques incorporated into the FRAX tool take into account country-specific fracture and death rates. Its aim to move forward risk assessment from a strategy based on BMD alone to an approach based on the absolute risk of fracture is appealing because absolute risk classification systems overcome several of the drawbacks posed by relative risk classification systems and may be more intuitive to both clinicians and patients [24]. However, despite those merits, findings from this study in a Japanese population suggest that one of the most important risk factors for predicting future risk – prevalent vertebral fracture detected by spine radiography – was not considered in the development and validation for the FRAX tool. In the absence of knowledge about prevalent spine fracture status, assessments based on the WHO risk factors may under- or over-estimate the true risk of an individual experiencing an incident fracture. This is similar to the experience of Siris et al. [13] who observed that in the absence of knowledge about spine fracture status, assessments based on BMD alone may under- or overestimate the true fracture risk.

The present analysis demonstrates that age, BMD, presence or absence of spine fracture, and prior clinical fracture were the most important risk factors for predicting future fracture in this population-based cohort. Consideration of those four risk factors alone provided greater predictive capacity than the risk factors included in the WHO tool. Furthermore, consideration of age, BMD, presence or absence of spine fracture, and prior clinical fracture was sufficient, and little more useful risk prediction was obtained by consideration of the other risk factors in the WHO model.

An advantage of including only four variables in the assessment of future fracture risk is that predicted absolute fracture risk can be reported in simple tables such as Table 5 for women and Table 6 for men. Those tables highlight the prognostic significance of spine fracture status. For example, in a 55-year old woman having a lumbar spine T-score of −1 and without a prior clinical fracture, fracture risk was 4.3% for subjects with no spine fractures and was 11.4% for subjects with spine fractures. For those patients with age or BMD between the intervals provided in the tables, the risk is intermediate. Practitioners assessing patients similar to those in our study for osteoporosis can therefore use age, BMD, presence or absence of spine fracture, and prior clinical fracture to predict 4-year fracture risk using the tables.

Several differences between these analyses and those performed to develop the WHO fracture risk assessment tool bear mentioning. Information on parental history of hip fracture was not available. However, according to a large meta-analysis [25], a parental history of fracture was slightly associated with risk of hip and fragility fracture. Furthermore, Plujim et al. demonstrated that family history of hip fracture was not associated with fragility fracture [26]. Our analyses included only one cohort of patients, whereas nine cohorts were used to develop the WHO fracture risk assessment tool [1]. Our results might not be as generalizable. In addition, the subjects in the Hiroshima cohort consist of atomic-bomb survivors and their controls, who may differ from the general population in Japan. However, our previous studies demonstrated no effects of atomic-bomb radiation on bone mineral density, or spine and hip fracture incidence [14,15], so our findings may be relevant to the Japanese population.

In this study, prevalent vertebral fracture status was assessed semi-quantitatively via lateral spine radiography, a widely used gold standard for identifying vertebral fractures. The prevalence of vertebral fracture is commonly assessed in clinical practice in Japan. Because there are several practical considerations including cost, radiation exposure and patient inconvenience that might preclude obtaining spine radiographs in all patients with low bone mass or osteoporosis, vertebral fracture assessment is not part of osteoporosis treatment guidelines outside of Japan. While our analysis did not use data generated by this approach, lateral spine imaging performed by DXA – vertebral fracture analysis or VFA – at the time of BMD testing in women found to have low bone mass or osteoporosis may provide a practical solution to routine imaging of the spine in clinical practice. VFA involves substantially less radiation exposure and cost, and is less subject to issues of parallax distortion, although it historically has generated images of lower resolution compared with lateral spine radiography. Ongoing refinements in this technology include improvements in resolution. VFA and routine lateral spine radiographs have shown good agreement for identifying vertebral fractures by semi-quantitative assessment.

Our study therefore demonstrates that the use of prevalent vertebral fracture status along with age, BMD, and prior clinical fracture has the capacity to predict future fracture risk at least as well as or better than the risk factors included in the WHO tool [1] but with greater simplicity. Our findings provide the degree to which spine fracture burden offers future fracture risk prediction, show the importance of having such information as part of the routine evaluation for osteoporosis, and provide a practical approach for utilizing this information in Japan.

Disclosures

The authors state that they have no conflicts of interest.

Conflict of interest

Fujiwara S: None.
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ORIGINAL ARTICLE

Ethnic difference of clinical vertebral fracture risk

C. H. Bow · E. Cheung · C. L. Cheung · S. M. Xiao · C. Loong · C. Soong · K. C. Tan · M. M. Luckey · J. A. Cauley · S. Fujiwara · A. W. C. Kung

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Abstract
Summary Vertebral fractures are the most common osteoporotic fractures. Data on the vertebral fracture risk in Asia remain sparse. This study observed that Hong Kong Chinese and Japanese populations have a less dramatic increase in hip fracture rates associated with age than Caucasians, but the vertebral fracture rates were higher, resulting in a high vertebral-to-hip fracture ratio. As a result, estimation of the absolute fracture risk for Asians may need to be readjusted for the higher clinical vertebral fracture rate.

Introduction Vertebral fractures are the most common osteoporotic fractures. Data on the vertebral fracture risk in Asia remain sparse. The aim of this study was to report the incidence of clinical vertebral fractures among the Chinese and to compare the vertebral-to-hip fracture risk to other ethnic groups.

Methods Four thousand, three hundred eighty-six community-dwelling Southern Chinese subjects (2,302 women and 1,810 men) aged 50 or above were recruited in the Hong Kong Osteoporosis Study since 1995. Baseline demographic characteristics and medical history were obtained. Subjects were followed annually for fracture outcomes with a structured questionnaire and verified by the computerized patient information system of the Hospital Authority of the Hong Kong Government. Only non-traumatic incident hip fractures and clinical vertebral fractures that received medical attention were included in the analysis. The incidence rates of clinical vertebral fractures and hip fractures were determined and compared to the published data of Swedish Caucasian and Japanese populations.

Results The mean age at baseline was 62±8.2 years for women and 68±10.3 years for men. The average duration of follow-up was 4.0±2.8 (range, 1 to 14) years for a total of 14,733 person-years for the whole cohort. The incidence rate for vertebral fracture was 194/100,000 person-years in men and 508/100,000 person-years in women, respectively. For subjects above the age of 65, the clinical vertebral fracture and hip fracture rates were 299/100,000 and 332/100,000 person-years, respectively, in men, and 594/100,000 and 379/100,000 person-years, respectively, in women. Hong Kong Chinese and Japanese populations

Cora H. Bow and Elaine Cheung contributed equally.

C. H. Bow · E. Cheung · C. L. Cheung · S. M. Xiao · C. Soong · K. C. Tan · A. W. C. Kung
Department of Medicine, The University of Hong Kong, Hong Kong, China

C. Loong
Department of Medicine, Queen Mary Hospital, Hong Kong, China

M. M. Luckey
St. Barnabas Osteoporosis & Metabolic Bone Disease Center, New York, NY, USA

J. A. Cauley
Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA, USA

S. Fujiwara
Department of Clinical Studies, Radiation Effects Research Foundation, Hiroshima, Japan

C. H. Bow (✉)
Department of Medicine, The University of Hong Kong, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong, China
e-mail: cbow@hku.hk

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have a less dramatic increase in hip fracture rates associated with age than Caucasians. At the age of 65 or above, the hip fracture rates for Asian (Hong Kong Chinese and Japanese) men and women were less than half of that in Caucasians, but the vertebral fracture rate was higher in Asians, resulting in a high vertebral-to-hip fracture ratio.
Conclusions The incidences of vertebral and hip fractures, as well as the vertebral-to-hip fracture ratios vary in Asians and Caucasians. Estimation of the absolute fracture risk for Asians may need to be readjusted for the higher clinical vertebral fracture rate.

Keywords Asian · Chinese · Fracture incidence · Osteoporosis · Vertebral fracture

Introduction

Osteoporosis is a disease associated with decreased bone mass and bone strength and leads to increased fracture risk. Osteoporosis has become a major public health concern in the past decade due to the high prevalence and health care costs associated with it. Vertebral fractures, despite being the most common osteoporotic fracture, accounting for nearly 50% of all osteoporotic fractures, have received little attention compared to hip fractures. Data on the epidemiology of vertebral fractures in Asia remain sparse [1]. It has been shown that both symptomatic and asymptomatic vertebral fractures are predictors of future osteoporotic fractures [2] and are associated with physical deformity, as well as reduced mobility and quality of life [3, 4], and increased mortality [5, 6].

Unfortunately, obtaining accurate information on vertebral fracture is made difficult by the variable presentation of symptoms and the lack of a gold standard for the definition of vertebral fracture. Although vertebral fractures typically present with back pain, height loss and kyphosis, up to 75% of vertebral fractures were not diagnosed clinically due to the absence of specific symptoms in some cases and the difficulty in determining the cause of these physical symptoms [7]. Numerous methods were developed to help objectively identify morphometric vertebral fractures. The more important ones include the quantitative methods of measuring vertebral body height on radiographs [8, 9], as well as the semi-quantitative method proposed by Genant et al. [10]. These assessments use different cut-offs to define the presence of a vertebral fracture, and the reference for comparison of vertebral height could either be the individual's adjacent vertebral body or the mean of a reference population. These variations affected the sensitivity and specificity of the assessments resulting in high false-negative and false-positive rates and also created a considerable discordance of results in assessing the prevalence and incidence of vertebral fractures [11–13]. Also, vertebral fractures can also be confused with normal variants in vertebral shape or other end-plate deformities caused by other diseases Therefore, the exclusion of other vertebral deformities in order to make a correct diagnosis of vertebral fracture can only be accomplished by visual inspection and expert interpretation of the radiograph [14].

The lack of a gold standard for a definition of vertebral fracture makes it difficult to assess the true incidence of vertebral fractures. Previous cross-sectional and retrospective studies have suggested a similar prevalence of vertebral fracture in Asians and Caucasians [15–19] despite their lower hip fracture rates [20]. The World Health Organization (WHO) developed fracture risk assessment algorithms (FRAX®) to provide 10-year probabilities of hip fracture and major osteoporotic fracture (clinical spine, hip, humerus and forearm) based on a clinical risk factor profile and country-specific fracture and death incidence. The most complete models available are from the UK, Sweden, Japan and the US since the epidemiology of the relevant fractures is established [21]. However, the FRAX® models for some other countries (France, Spain, Italy, Turkey, Mainland China Hong Kong, etc.) are based on hip fracture risk alone due to the lack of ethnic-specific data and use assumptions, i.e. the site of fracture ratios observed from the Swedish population, to derive the relevant risk functions for other major fractures including vertebral fractures [22]. The objectives of this study were (1) to report the incidence rates of clinical vertebral and hip fractures in a prospective cohort of Chinese men and women, (2) to compare the clinical vertebral and hip fracture rates with those of other ethnic groups, and (3) to evaluate whether a fracture prediction model that assumes a universal spine-to-hip fracture ratio may be biased.

Methods

Hong Kong

This is the first prospective study of clinical vertebral fracture in an Asian population and is a part of the prospective Hong Kong Osteoporosis Study in which community-dwelling Southern Chinese men and women aged 50 or above were recruited from health fairs held in various districts in Hong Kong since 1995 [19, 23]. Baseline demographic data including anthropometric measurements, low-trauma fracture history after the age of 45 years, age at menopause and the use of hormone replacement therapy, medical history and symptoms associated with clinical vertebral fractures were obtained using a structured questionnaire at baseline. Subjects with conditions associated with vertebral deformity, including

osteomalacia, Paget's disease, Scheuermann's disease, hyperparathyroidism, renal bone disease and malignancy with bone metastasis, were excluded. Information on symptoms associated with vertebral fractures was also collected, including difficulty in bending forward, kyphosis (occiput-to-wall >0 cm and/or gap between the costal margin and iliac crest <3 fingerbreadths), low back pain and height loss more than 2 cm since the age of 25 years. These data were collected from interviews conducted by a trained research assistant.

All subjects were followed annually via telephone interviews using a structured questionnaire for assessment of the clinical outcome of incident fractures, falls, hospitalization, use of anti-osteoporotic medications, living status and functional status. Subjects who commenced anti-osteoporosis medication prior to the occurrence of a primary fracture were excluded. Medical history and incident fractures were verified with the computerized patient information system of the Hospital Authority of the Hong Kong Government. For this study, only non-traumatic incident hip fractures and clinical vertebral fractures were included in the analysis. Hip fractures were defined as having a diagnosis coded as International Classification of Disease, Tenth Revision (ICD-10) S72.0-S72.2 (fracture of the femoral neck, intertrochanteric, trochanteric, or subtrochanteric), and clinical vertebral fractures were identified in subjects who received medical attention from a physician with a diagnosis coded as ICD-10S22.0-S22.1 (fracture of the thoracic vertebra/multiple thoracic vertebrae), S32.0 or S32.7 (fracture of the lumbar vertebra/multiple lumbar vertebrae). Pathological fractures or fractures caused by traffic accidents or falls from standing heights were excluded. The study was approved by the Institutional Review Board of the University of Hong Kong and the Hong Kong West Clusters Hospital of the Hospital Authority.

Japan

The hip and clinical vertebral fracture incidence rates for the Japanese were obtained from previously published data used to develop the Japanese version of FRAX® [24]. The hip fracture incidence rate was based on data from a census study in Tottori Prefecture, Japan, in 1994 [25]. The incidence of vertebral fracture was based on data obtained from the Adult Health Study in Hiroshima, Japan [26]. Participants were followed through biennial medical examination including radiology assessments since the establishment of the study in 1958. A total of 2,613 subjects (763 men and 1,593 women) who attended at least two follow-up examinations in 1994 to 2000 were included in the analysis. An incident morphometric vertebral fracture was diagnosed by lateral and posterior–anterior chest and spinal X-rays using the semi-quantitative assessment [12], in which a decrease of at least 20% in height of any vertebral body from initial reading to the end of the study was defined as a morphometric vertebral fracture. Since the incidence of clinical vertebral fracture was not known in Japan, the ratio of clinical fracture to morphometric fracture incidence was assumed to be the same in Japan as it was for Sweden when the Japanese version of FRAX® was developed, i.e. 30% of morphometric vertebral fractures were assumed as clinical fractures [24, 27].

Sweden

The incidence rates of hip and clinical vertebral fractures for Swedish Caucasians were also obtained from a previously published study by Kanis et al., in which all incident fractures, including hip fractures (1991) and clinical vertebral fractures (1993 and 1994) were identified from files at the Department of Diagnostic Radiology in Malmo, Sweden, for the relevant year. Only vertebral fractures that came to clinical attention were captured, and subjects who previously sustained a fracture of the same type were excluded from analysis. The annual incidences of hip and clinical vertebral fractures were calculated for men and women by age [28].

Statistical analyses

Baseline characteristics of the Chinese subjects are expressed in means±SD for continuous variables and in percentage for categorical variables. Time to incident hip or vertebral fractures was calculated according to the date of X-ray reports or physician's consultations when the diagnosis was made. The average follow-up period for all subjects was 4.0±2.8 (range, 1 to 14) years, with a total follow-up of 14,733 patient-years. Subjects who had received anti-osteoporosis medication after sustaining a fracture during the follow-up period or those who deceased at the time of analysis were analysed up to their time of treatment initiation or last contact time point. Incidence rates were reported as rate per 100,000 person-years. The incidence rates of vertebral and hip fractures were compared to the published data from Japan and Sweden. Vertebral-to-hip fracture ratios were used to demonstrate the proportion of vertebral fractures in relation to hip fractures in different populations.

Results

A total of 4,116 Southern Chinese subjects (2,302 women and 1,810 men) aged 50 or above were included in the analysis. The mean age at baseline was 62±8.2 years for

women and 68±10.3 years for men. Of the women, 37.2% and 63.4% of men were above the age of 65 years. Baseline demographic information and characteristics are shown in Table 1. Of the men, 55.5% and 72.1% of women reported having difficulty bending forward, kyphosis, low back pain and/or height loss >2 cm since the age of 25. However, only 2.7% of men and 5.5% of women reported a history of past clinical vertebral fracture.

Two hundred and sixty-seven subjects had died at the time of analysis (77 women and 190 men), and 353 patients (333 women and 19 men) received anti-osteoporosis medication after sustaining a fracture during the follow-up period. The data for these subjects were analysed up to their last contact time point or time of treatment initiation, respectively. During the follow-up period, 57 clinical vertebral fractures and 34 incident hip fractures were reported (11 vertebral fractures and 10 new hip fractures in men; 46 vertebral fractures and 24 new hip fractures in women). The incidence for vertebral fractures was 194 per 100,000 person-years in men and 508 per 100,000 in women (overall female/male ratio=2.6:1), and the incidence for hip fractures was 176 per 100,000 person-years in men and 265 per 100,000 person-years in women (female/male ratio=1.5:1). Table 2 shows the incidence rates of clinical vertebral and hip fractures according to sex and age groups. Both clinical vertebral and hip fracture incidences increased exponentially with increasing age in both sexes. Men aged 50–55 years had a fracture incidence of 50 per 100,000 person-years for the vertebra and 10 per 100,000 for the hip versus men aged 85 years and above who have a vertebral fracture incidence of 954 per 100,000 person-years and a hip fracture incidence of 477 per 100,000 person-years. Similarly, incidences of vertebral and hip fracture increase from 219 and 16 per 100,000 person-years in women 50 years of age to 2,689 and 1,377 per 100,000 person-years, respectively, at age 85. Overall, men older than 65 years have a vertebral fracture incidence of 299 per 100,000 person-years and hip fracture incidence of 332 per 100,000 person-years, and the overall incidence of vertebral and hip fractures for women older than 65 years were 594 per 100,000 person-years and 379 per 100,000 person-years, respectively.

The fracture incidence of Chinese subjects was compared to those of the Swedish and Japanese populations. The incidence rates of hip fractures in Caucasian men and women rose exponentially with age, whereas the rise was near linear for vertebral fractures. In contrast, for Asian women in Hong Kong and Japan, the incidence rate for vertebral fractures rose exponentially with age, whereas the rise was near linear for hip fractures. In Asian men, both the incidence rates of vertebral and hip fractures rose near linearly with age. The hip fracture incidences in Hong Kong men and women were similar to those of Japan but much lower than those of the Caucasian population in Sweden. For example, the hip fracture rates for Hong Kong men and women aged 65 to 69 years old were only 49% and 33%, respectively, of those of the Caucasian men and women in the same age group. However, the incidence of vertebral fractures in Asian men was similar to that of Caucasian men; and Asian women have a much higher

Table 1 Clinical characteristic of the study population (Mean±SD)

	Men (n=1,810)	Women (n=2,302)
Years of follow-up (mean±SD (range))	3.5±2.9 (1–14)	4.7±2.6 (1–14)
Age (year)	68±10.3 (50–99)	62±8.2 (50–91)
Height (cm)	164.6±6.5	152.7±6.0
Weight (kg)	62.9±10.3	55.3±9.1
Body mass index (kg/m^2)	28.1±8.4	23.7±3.7
Number of postmenopausal women	–	2,229 (96%)
Age at menopause (year)	–	49.5±4.0
Current or history of hormone replacement therapy	–	217 (9.4%)
Difficulty bending forward	185 (10.2%)	365 (15.8%)
Kyphosis	78 (4.3%)	126 (5.5%)
Low back pain	510 (28.2%)	1,336 (58.0%)
Height loss >2 cm since 25 years old	442 (24.4%)	854 (37.1%)
Have at least one of the above symptoms	1,004 (55.5%)	1,660 (72.1%)
History of clinical vertebral fracture	48 (2.7%)	126 (5.5%)
History of hip fracture	24 (1.7%)	31 (1.3%)
Incident clinical vertebral fracture at follow-up	11 (0.6%)	46 (2.0%)
Incident hip fracture at follow-up	10 (0.6%)	24 (1.0%)

Table 2 Incidence (per 100,000 person-years) of hip and clinical vertebral fracture according to sex and age groups

Fracture site and age group	Men	Women	F/M
Hip			
50–54	10	16	1.6
55–59	21	31	1.5
60–64	46	57	1.2
65–69	99	103	1.0
70–74	215	273	1.3
75–79	348	527	1.5
80–84	602	1,059	1.8
85+	477	1,377	2.9
Vertebral			
50–54	50	219	4.4
55–59	111	313	2.8
60–64	165	516	3.1
65–69	95	564	5.9
70–74	226	874	3.9
75–79	450	1,205	2.7
80–84	594	2,119	3.6
85+	954	2,689	2.8

vertebral fracture incidence than Caucasian women (Fig. 1a and b). Among older women aged 80 or above, the incidence of vertebral fracture in Asians almost doubled to that of Swedish Caucasian women.

The spine-to-hip fracture ratios also differed between different Asians and Caucasians. Although vertebral fractures occur with a higher incidence earlier in life than hip fractures in both Asians and Caucasians, Asians have a much higher spine-to-hip fracture ratio than Caucasians, meaning vertebral fractures have a higher proportion to hip fractures in Asians than in Caucasians, especially among subjects younger than 65 years (Table 3).

Discussion

Vertebral fractures are the most common type of osteoporotic fractures, and they are well known as an independent predictor of future osteoporotic fractures, including both vertebral and non-vertebral fractures [22]. However, reports about the incidence of vertebral fracture are scant because of the discrepancies in the definition of vertebral fracture and the difficulties in recognizing them clinically. A

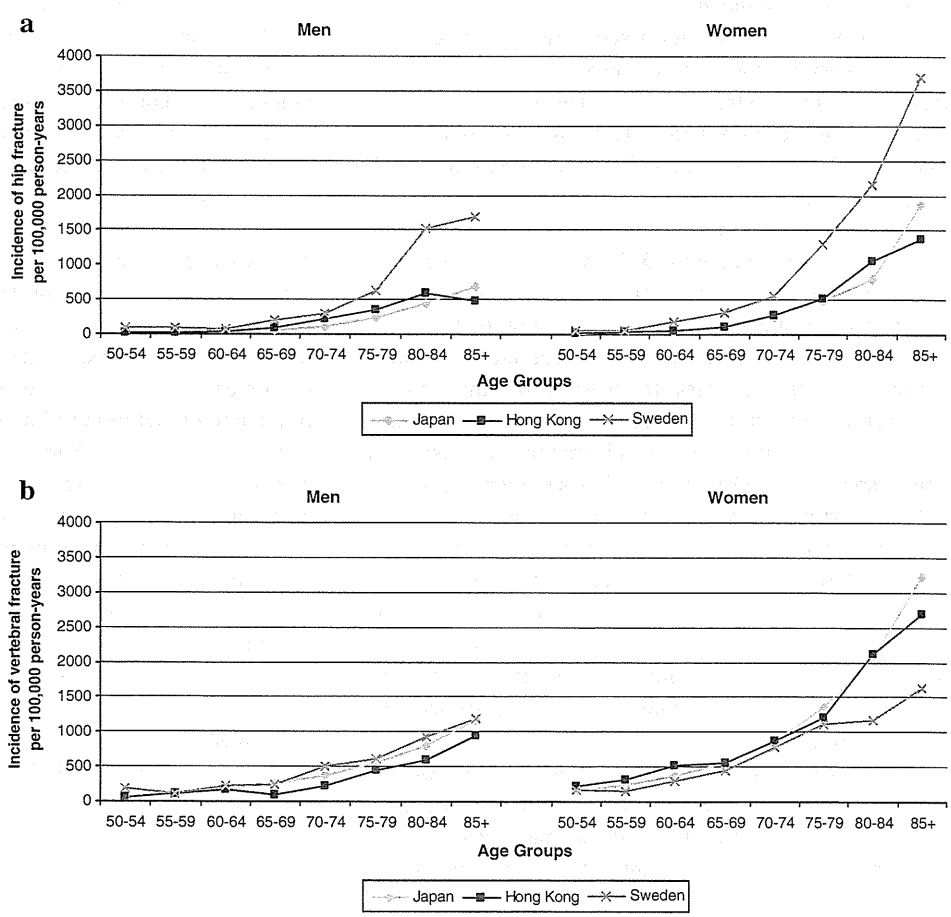

Fig. 1 Age-specific incidence rates (per 100,000 person-years) in Hong Kong compared to Japanese and Swedish Caucasians for hip fracture (**a**) and clinical vertebral fracture (**b**)

Table 3 Age- and sex-specific clinical vertebral-to-hip fracture ratio in Hong Kong compared to Japanese and Swedish Caucasians

	Men			Women		
Age group	Japan [24]	Hong Kong	Sweden [28]	Japan [24]	Hong Kong	Sweden [28]
50–54	3.9	5.0	2.2	N/A[a]	13.7	2.6
55–59	7.1	5.3	1.4	4.7	10.1	2.9
60–64	2.8	3.6	3.2	8.9	9.1	1.6
65–69	4.1	1.0	1.2	6.3	5.5	1.4
70–74	3.5	1.1	1.7	3.4	3.2	1.4
75–79	2.3	1.3	1.0	2.8	2.3	0.8
80–84	1.8	1.0	0.6	2.6	2.0	0.5
85+	1.7	2.0	0.7	1.7	1.1	0.4

[a] Clinical vertebral-to-hip fracture ratio for Japanese women aged 50–54 was not available since the hip fracture incidence for this group was zero

previous study has shown that the postmenopausal women in Hong Kong, Beijing and Taiwan have a similar prevalence of morphometric vertebral fracture as Caucasian women in the USA and Europe (about 25% in all regions), in contrast to the marked worldwide variations in the prevalence of hip fractures [21]. The present study further confirmed that, although the risk of hip fractures in Asians was low, Asian men do have a vertebral fracture risk similar to Caucasian men, and Asian women have an even higher clinical vertebral fracture risk than Caucasian women.

The observed ethnic differences in fracture incidences may be due to the fact that hip fracture risk was affected by fall risk, whereas the risk of vertebral fracture mostly depends on bone strength [13]. Despite the low hip fracture rate in our population, Hong Kong women had a higher prevalence of osteoporosis (bone mineral density T-score≤ -2.5 at any one site in reference to ethnic-specific peak young mean according to the ISCD recommendation) than US Caucasian women (35.8% vs. 20%, respectively) [29, 30] and a similar prevalence of about 6% in Hong Kong and US Caucasian men [31]. In view of the ethnic differences, it is important to obtain accurate information on population fracture risk to characterize the absolute fracture risk of individual subjects. At present, information on the risk of clinical vertebral fracture in Asians is lacking, and the WHO fracture risk assessment algorithms (FRAX®) estimated population-specific absolute major osteoporotic fracture risks based on the assumption that the ratio of hip-to-vertebral fracture is the same as that observed in Swedish populations to provide. However, our study demonstrated the variations of the spine-to-hip fracture ratios between ethnic groups; thus, a fracture prediction model that assumes a universal spine-to-hip fracture ratio may be biased.

Our previous prospective study on Southern Chinese men over 50 years old has shown that the FRAX® algorithm seemed to overestimate the 10-year major osteoporotic fracture risk in subjects with low fracture risk, but underestimated the risk for high-risk groups [29]. Results from the current study raise a concern that a model that presumes a ratio of vertebral fractures to hip fractures in a Swedish population might underestimate the risk of vertebral fractures in Asians, resulting in a general underestimation of the absolute risk of major osteoporotic fracture.

Strengths of this study include the use of a community-based population to investigate the incidence rate of clinical vertebral fractures. All clinical vertebral fractures and hip fractures were confirmed by the medical record. A major limitation of the present study is that the comparisons to incidence rate of clinical vertebral fracture to other ethnic groups were based on published literatures, and the data among Asian countries are scanty. Japan is the only country in Asia that reported the incidence rate on morphometric vertebral fractures based on a radiographic survey in a community-based population. Also, the Japanese data used for comparison came from the early 1990s, and there has been some evidence that hip fracture rates are increasing in Asians [20]. The impact on the change in epidemiology of fracture in Asians has not been evaluated. Another drawback of the present study is that only the incidences of clinical vertebral fractures were reported due to the lack of a common definition of morphometric vertebral fractures in other publications. Furthermore, the sample size and the number of fractures recorded in the men's cohort were small, and this study may have underestimated the fracture rates in the general male population.

In conclusion, this study demonstrated that while the hip fracture incidence in Asians is lower than in Caucasians, the incidence of clinical vertebral fractures was at least as high in Asians as in Caucasians.

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Conflicts of interest None.

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