J Bone Miner Metab (2014) 32:533–538
DOI 10.1007/s00774-013-0525-y

ORIGINAL ARTICLE

Detective value of historical height loss and current height/knee height ratio for prevalent vertebral fracture in Japanese postmenopausal women

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Received: 1 April 2013 / Accepted: 24 September 2013 / Published online: 13 October 2013
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Abstract Vertebral fracture (VFx) is associated with various co-morbidities and increased mortality. In this paper, we have studied the detective value of height loss for VFx using two indices; historical height loss (HHL) which is the difference between the maximal height, and the current height (CH), and CH/knee height (KH) ratio. One-hundred and fifty-one postmenopausal women visiting the outpatient clinic of orthopaedics were studied for their CH, self-reported maximal height, KH, and radiographically diagnosed VFx number(s). VFx was present in 41.1 % of the subjects. Multiple regression analyses revealed that the number of prevalent fractures was a significant predictor of HHL and CH/KH ratio. Receiver operator characteristic curve analysis has shown that for HHL, the area under the curve (AUC) with their 95 %CI in the parentheses was 0.84 (0.77, 0.90), 0.88 (0.83, 0.94), and 0.91 (0.86, 0.96) for $\geq$1, $\geq$2, and $\geq$3 fractures, respectively. For the presence of $\geq$1 VFx, the cut-off value was 4.0 cm (specificity 79 %; sensitivity 79 %). Regarding the CH/KH ratio, AUC was 0.73 (0.65, 0.82), 0.85 (0.78, 0.93), and 0.91 (0.86, 0.96) for $\geq$1, $\geq$2, and $\geq$3 fractures, respectively. For the presence of $\geq$1 VFx, the cut-off value was 3.3 (specificity 47 %; sensitivity 91 %). Both cut-off values for HHL and CH/KH ratio had high negative predictivity across the wide range of theoretical VFx prevalence. Thus, HHL and CH/KH were both good detectors of VFx. Our data would be the basis to determine the cut-off value for the screening or case finding of subjects with VFx.

Keywords Historical height loss · Knee height · Vertebral fracture · Japanese postmenopausal women

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Introduction

Of the various osteoporotic fractures, vertebral fracture (VFx) is the most prevalent. VFx is associated with various unfavorable consequences. For example, gastroesophageal reflux disease [1], chronic low back pain [2], and impaired respiratory or digestive function are common in those with VFx [3, 4]. Representing such co-morbidities, patients with VFx have impaired quality of life (QOL). Even the morphological fracture, which is incidentally diagnosed by X-ray examination without overt clinical signs or symptoms, is associated with impaired QOL [5–8].

Furthermore, recent studies have shown that VFx is associated with increased mortality [9–12]. In addition, prevalent osteoporotic fracture increases the risk of another fracture by several fold [13–16].

Recently the importance of secondary prevention of osteoporotic fractures is increasingly recognized. In the UK, efforts have been made to deliver appropriate information to such patients in collaboration with the medical staffs. Such a system, called a fracture liaison service, has been proven to be effective in the secondary prevention of osteoporotic fractures [17, 18]. In Japan, similar efforts, called an osteoporosis liaison service, have recently been

initiated. Then, of great importance is the case finding of subjects who have sustained an osteoporotic fracture.

VFx is the most problematic, since approximately two-thirds of the VFx patients are without overt clinical symptoms, and a substantial proportion of them are even unaware of their VFx [19, 20]. No doubt BMD measurement by DXA or X-ray examination is useful for the determination of VFx, which, however, would be inappropriate for screening purposes. The screening of subjects with VFx should be done favorably by simple and less costly methods. Since VFx is probably the most important cause of height loss, height measurement can be a good candidate as a tool for the screening of subjects with VFx. The cut-off value of height loss for the prediction of VFx has been reported [20–24], which, however, is almost exclusively limited to the data in Caucasians. Considering the large difference of stature between various nations, such cut-off value must be individually defined for each nation. For this purpose, we have employed the historical height loss (HHL), which was defined as the difference between the maximum height based on the subjects' recall and the current height (CH), and determined the cut-off value of HHL for the case finding of VFx in the Japanese population.

In the elderly, however, sometimes maximal height or height at youth is unavailable or unreliable. We considered that the ratio of current height (CH) divided by knee height (KH) could be a good alternative to detect VFx, since KH is measurable in most elderly subjects and little affected by aging [25, 26]. Then CH/KH ratio would reflect well the height loss and could be a detector of VFx. Based on these considerations, we have also studied the detective value of CH/KH ratio for VFx, and examined the cut-off value of this index.

Materials and methods

Subjects

The study subjects were 151 patients visiting the outpatient clinic of the Orthopedic Department, Hyogo Medical College. This study was approved by the ethics committee of Sasayama Medical Center, and conforms with the Declaration of Helsinki. Written informed consent was obtained from the subjects after explaining the purpose of this study. Exclusion criteria were as follows: subjects with pre-existing metabolic bone disease, and those with severe skeletal deformities that hinder the anthropometric measurement or the X-ray diagnosis of the skeleton. Consecutive patients meeting such criteria were encouraged to participate in the study. The background profiles of subjects are shown in Table 1.

Table 1 Characteristics of study subjects

	All subjects	Without fracture	With fracture	*p* value
Number of patients	151	89	62	–
Age in years	69.6 ± 9.6	66.9 ± 9.2	73.7 ± 8.7	<0.001
Current height (cm)	149.1 ± 7.2	151.5 ± 6.3	145.6 ± 7.1	<0.001
Height in youth (cm)	153.9 ± 5.4	154.2 ± 5.7	153.6 ± 4.9	0.495
Height loss (cm)	3.2 (1.5, 7.0)	2.0 (0.8, 3.6)	7.0 (4.0, 11.9)	<0.001
Body weight (kg)	49.0 ± 7.4	49.4 ± 7.8	48.5 ± 6.9	0.434
Knee height (cm)	45.1 ± 2.2	45.2 ± 2.2	45.0 ± 2.2	0.548
Current height/knee height	3.3 ± 0.1	3.4 ± 0.1	3.2 ± 0.1	<0.001
Number of fractures	0 (0, 1)	0	2 (1, 3)	<0.001

Data are expressed as mean ± SD. Data for height loss and number of fractures are expressed as median (Q1, Q3) and were analyzed by Mann–Whitney test. Other data were analyzed by Student's *t* test

Measurement of current height and knee height (KH)

CH was measured with a wall-mounted stadiometer. Immediate precision error (expressed as the within-subject standard deviation), 6-month precision, and 12-month precision have been reported to be 0.17, 0.38, and 0.42 cm, respectively [27]. The stadiometer was calibrated prior to each use with a 60-cm rod of a metal alloy resistant to temperature-induced change in length.

KH was measured at a sitting position, with the subject's leg raised, the knee and ankle both at a 90° angle [28].

Maximal height was obtained by the patient's recall. Historical height loss (HHL) was defined as the difference between the maximal height and the CH.

Diagnosis of vertebral fracture (VFx)

The diagnosis of vertebral fracture was made by one of the authors (KY). Lateral and anteroposterior radiographs of the thoracic and lumbar spine were taken, and semi-quantitatively assessed by KY as follows: grade 0, normal; grade 1, a decrease in the height of any vertebra of 20–25 %; grade 2, a decrease of more than 25 % to less than 40 %; grade 3, a decrease of 40 % or more [29, 30].

Statistical analyses

Data were analyzed with SPSS 19.0J. Comparison of the two independent variables was made by Student's *t* test or

Mann–Whitney test. Multiple regression analyses were performed to identify the independent variables that affect the HHL and CH/KH ratio. The value of the variables for detecting VFx was analyzed using the receiver operator characteristic (ROC) curve. The detective value was evaluated by the area under the curve (AUC) with the larger value indicating the better diagnostic value. The appropriate cut-off value was determined using Youden's index [31]. Then, with the cut-off value thus determined, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and positive likelihood ratio (with 95 %confidence intervals; 95 %CI) were calculated.

Results

Comparison of the characteristics between subjects with fracture and without fracture

The number of subjects without and with VFx was 89 (58.9 %) and 62 (41.1 %), respectively. Those with VFx were older and had lower CH (Table 1). Subjects with VFx had lost more height (7.0 cm; Q1, Q3 4.0, 11.9) than those without VFx (2.0 cm; Q1, Q3 0.8, 3.6). There was a significant difference between subjects with VFx and without it in CH/KH ratio (3.2 ± 0.1 vs 3.4 ± 0.1), which remained significant after adjustment for age (data not shown).

Evaluation of the relationship between historical height loss and prevalent vertebral fracture

By regression analysis, the relationship between HHL and the number of prevalent fractures was defined as: HHL (cm) = 0.17 × age + 1.30 × number of fractures − 8.31 ($r^2 = 0.54$, $p < 0.001$). The height loss per each fracture was 1.30 cm with a 95 %CI from 1.04 to 1.55 cm. (data not shown).

The detective ability and cut-off value of HHL for VFx were evaluated by ROC analysis. For the presence of one or more VFx, AUC was 0.84 (95 %CI, 0.77, 0.90), and the cut-off value was determined to be 4.0 cm with the specificity and sensitivity being 79 % and 79 %, respectively. At the VFx prevalence of 41.1 % in the current study population, PPV and NPV was 71 % (95 %CI, 64, 78) and 85 % (95 %CI, 78, 90), respectively. With HHL ≥ 4.0 cm, the likelihood ratio was 3.61 (95 %CI; 2.54, 4.99).

As shown Table 2, detective values were determined across a wide range of theoretical fracture prevalence that might be encountered in clinical practice by applying the sensitivity and specificity corresponding to HHL ≥ 4.0 cm. The PPV was low across most of the range. In contrast, the NPV remained high at the prevalence rates likely to be encountered in most clinical practice, and dropped below 80 % only at the prevalence exceeding 50 %.

As shown in Table 3, the cut-off values of HHL were 4.0, 4.4, and 6.0 cm for one or more, two or more, and three or more fractures, respectively.

Evaluation of the relationship between CH/KH ratio and prevalent vertebral fracture

Similarly, the relationship between CH/KH ratio and the number of prevalent fractures was defined as: CH/KH ratio = −0.01 × age − 0.03 × number of fractures + 3.74 ($r^2 = 0.38$, $p < 0.001$). The CH/KH ratio per fracture was −0.03 with a 95 %CI from −0.04 to −0.02 (data not shown).

The detective value of CH/KH ratio was also studied by ROC analysis. AUC was 0.73 (95 %CI, 0.65, 0.82) for one or more fractures. For the presence of one or more VFx, the cut-off value was determined to be 3.3 with the specificity and sensitivity being 47 and 91 %, respectively. At the VFx prevalence in the current subjects, PPV and NPV were 54 % (95 %CI, 48, 57) and 88 % (95 %CI, 75, 95), respectively. With CH/KH ratio ≤3.3, the likelihood ratio was 1.70 with a 95 %CI from 1.35 to 1.95.

Table 2 Detective values (post-test probability) at various fracture prevalence

HHL	Theoretical prevalence (%)[a]				
	1	5	10	25	50
Positive predictive value (%)	4	17	29	56	79
Negative predictive value (%)	100	99	97	92	79

[a] Values were derived assuming sensitivity = 79 % and specificity = 79 % in HHL ≥ 4.0 cm

Table 3 Cut-off value of HHL for the presence of various number(s) of vertebral fracture(s)

Fracture numbers	Cut-off value (cm)	AUC	LR+	PPV (%)	NPV (%)
Fx +1 ($n = 62$)	4.0	0.84 (0.77–0.90)	3.61 (2.54–4.99)	0.71 (0.64–0.78)	0.85 (0.78–0.90)
Fx +2 ($n = 37$)	4.4	0.88 (0.83–0.94)	3.51 (2.63–4.09)	0.53 (0.46–0.57)	0.96 (0.91–0.98)
Fx +3 ($n = 24$)	6.0	0.91 (0.86–0.96)	4.48 (3.25–5.05)	0.46 (0.38–0.49)	0.98 (0.94–1.00)

Cut-off value of HHL, area under the curve (AUC), likelihood ratio (+LR), positive predictive value (PPV) and negative predictive value (NPV) profiles for the detection of various number(s) of vertebral fracture(s). The numbers in the parentheses show the 95 %CI

Table 4 Detective values (post-test probability) at various fracture prevalence

CH/KH	Theoretical prevalence (%)[a]				
	1	5	10	25	50
Positive predictive value (%)	2	8	16	36	63
Negative predictive value (%)	100	99	98	94	84

[a] Values were derived assuming sensitivity = 91 % and specificity = 47 % in CH/KH ratio ≤3.3

In CH/KH ratio, The PPV was low across most of the range. The NPV remained high at the prevalence rates likely to be encountered in the daily clinical practice (Table 4).

Cut-off value for the detection of various numbers of VFx is shown in Table 5. For detecting two or more, or three or more fractures, a cut-off value of CH/KH ratio was ≤3.2.

Discussion

Recently, "Guideline for the Prevention and Treatment of Osteoporosis 2011" was published in Japan [32], which will be abbreviated as "Guideline 2011" hereafter. It states that the measurement of height and weight is useful for the screening of osteoporosis, and BMD measurement or X-ray examination is recommended to those with height loss greater than 2 cm (grade B). In our present study, ROC analysis has yielded the excellent AUC value of 0.84 (95 %CI; 0.77, 0.90) with a cut-off of 4.0 cm. Such difference is likely to arise from the methodological reasons as discussed below.

Height loss can be evaluated by two methods. One is the historical height loss (HHL) which was employed in our study. It is an index for the prevalent VFx [2, 21, 22, 33, 34]. The other method is the prospective one based on the serial height measurements, which will reflect the incidence of new VFx [24, 35, 36]. The latter would not be suitable to identify those with prevalent VFx in the screening of large number of subjects. Although the description on the usefulness of height loss in "Guideline 2011" apparently refers to the prediction of prevalent VFx, the distinction of these two methods is not mentioned, and papers based on both methods are cited [24, 35].

Furthermore, two methods are available for estimating HHL. One is the measurement height (MH), in which the subjects' current maximal height is directly measured. MH, however, has some technical errors including one inherent in the measuring device, positioning variability and true biological changes over time. The other is the subject's tallest recalled height (TRH). Comparing these two methods, it is obvious that TRH is more suitable for the screening purpose.

Briot et al. [33] have reported that previous VFx was the best predictor of a HHL of 3 cm or more and also that of 6 cm or more using multivariable analysis. They have also shown by multivariable analysis that the cut-off value of 4 cm predicted well the presence of VFx. This value, however, does not seem to be fully validated for its clinical usefulness since such parameters as PPV and NPV are not given.

In another paper, Siminoski et al. [21], reported that likelihood ratio (LR) for VFx was 2.8 (95 %CI; 1.3, 6.0) in subjects with HHL between 6.1 cm and 8.0 cm, whereas it was not significantly different from unity in those with less HHL. They have concluded that HHL less than 6 cm rules out prevalent VFx and subjects with HHL more than 6 cm should have spine radiographs. With this threshold, the sensitivity and specificity were 30 and 94 %, respectively. In our study, the cut-off value was determined to be 4.0 cm with the specificity and sensitivity being 79 % and 79 %, respectively. With regard to the difference from our threshold, several reasons might be considered. First, their subjects were Caucasians. Second, we have used "Youden's Index" for the calculation of HHL threshold, while Siminoski et al. [21] have screened various cut-off values starting from 0 to 8 cm with 2.0 cm intervals. For the purpose of screening or case-finding, however, there remains the possibility that by employing their high threshold, a significant number of subjects with VFx may be overlooked considering the low sensitivity. Our cut-off value with good sensitivity and specificity might have usefulness for screening purposes of prevalent VFx.

TRH, however, is not free from artifact errors such as "over-reported height" [21, 33, 37, 38]. In the paper using

Table 5 Cut-off value of CH/KH ratio for the presence of various number(s) of vertebral fracture(s)

Fracture numbers	Cut-off value	AUC	LR+	PPV (%)	NPV (%)
Fx +1 (n = 42)	3.3	0.73 (0.65–0.82)	1.70 (1.35–1.95)	0.54 (0.48–0.57)	0.88 (0.75–0.95)
Fx +2 (n = 26)	3.2	0.85 (0.78–0.93)	7.77 (4.35–12.56)	0.72 (0.60–0.81)	0.93 (0.88–0.97)
Fx +3 (n = 17)	3.2	0.91 (0.86–0.96)	4.72 (2.88–6.14)	0.48 (0.36–0.55)	0.96 (0.91–0.99)

Cut-off value of CH/KH ratio, area under the curve (AUC), likelihood ratio (LR+), positive predictive value (PPV) and negative predictive value (NPV) profiles for the detection of various number(s) of vertebral fracture(s). The numbers in the parentheses show the 95 %CI

TRH, the amount of height that had been lost from the tallest stature was underestimated both in those without prevalent VFx and those with VFx by 0.7 ± 2.5 and 1.6 ± 3.3 cm, respectively [21]. Thus, caution is required in the interpretation of TRH.

These considerations have led us to investigate the possible usefulness of knee height as the parameter to reflect the height at youth. Bunout et al. [39] reported that knee height can be used as an accurate measurement of height loss in the elderly, and also a significant predictor of femur and spine bone mineral densities in addition to hip circumference. In previous reports, including theirs, however, the possible usefulness of the CH/KH ratio to predict the prevalent VFx has not been described. In the current data, AUC was 0.73 (95 %CI; 0.65, 0.82), and the cut-off value was decided to be 3.3 with a specificity of 47 % and sensitivity of 91 %. Thus, from the current data, this ratio had detective value for the prevalent VFx, although less than that of HHL.

Comparing the two parameters, the cut-off value of HHL in our study was dependent on the VFx numbers, whereas that of the CH/KH ratio was not. One of the reasons might be the far smaller standard deviations of the CH/KH ratio, resulting in the lower sensitivity. Thus, HHL might be a more sensitive index for detecting VFx than the CH/KH ratio. Sensitivity and specificity are independent of the disease prevalence in the study population, and denote the characteristics of the diagnostic test. In contrast, PPV and NPV are influenced by the prevalence. Then, we have evaluated these values across the various theoretically simulated prevalence ranges. HHL and CH/KH ratio were both characterized by the low PPV and high NPV. Thus, high NPV suggests that HL less than 4.0 cm or CH/KH ratio greater than 3.3 is indicative of the absence of VFx with moderate to high accuracy. Considering the low PPV, however, HHL $\geq$ 4.0 cm and CH/KH ratio $\leq$ 3.3 suggests, but does not confirm the prevalence of VFx. From these characteristics, HHL and CH/KH ratio are likely to be of value for the screening purpose.

The limitation of our data would be twofold. First, the number of subjects studied is moderate. Second, the study subjects are limited to those attending the osteoporosis clinic of the orthopedics department. Thus, the current subjects may not represent the general population. Nevertheless, both of the two indices; HHL and CH/KH ratio had good values of AUC, sensitivity, and specificity, suggesting the clinical relevance of our data.

In summary, we have presented the cut-off values for HHL and CH/KH ratio to detect VFx in the Japanese population for the first time. Although additional studies including more subjects are required, the current data would be the basis to decide the cut-off values in the future guideline.

Acknowledgments This work was supported by the Health Labour Sciences Research Grant (Principal Investigator; Shumpei Niida).

Conflict of interest All authors have no conflicts of interest.

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