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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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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

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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.

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

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 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.

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Conflict of interest All authors have no conflicts of interest.

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XII 特　　論

骨粗鬆症治療の医療経済

Osteoporotic treatment from the socio-economic perspectives

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Key words：骨折の絶対リスク，QALY，費用効果分析，費用効用分析，FRAX

はじめに

最近骨折の絶対リスク評価が重視されるようになり，背景要因から10年間の骨折発生リスクを予測するFRAXはその代表的なツールである．また骨粗鬆症に対する治療介入閾値の決定要因についても，従来骨密度が重視されてきたが，最近骨折の絶対リスクに基づいて決定されるようになってきた．以下に述べるようにこれらの流れは医療経済評価に深くかかわるものである．

1　医療経済評価の方法論

医療経済評価は，かかった費用に対する追加的アウトカムとの比較を行うもので，そのアウトカム表示方法によって分析手法が分類される．費用便益分析(cost benefit analysis: CBA)はアウトカムも金銭で表すものだが，健康変化や生命の価値を金銭価値に置き換える方法に様々な議論があり，使用頻度は低い．費用効果分析(cost effectiveness analysis: CEA)は余命延長や骨折防止など罹病率低下などを指標とし，具体的アウトカムによって評価されるので理解しやすいが，問題点もある．骨折抑制を唯一の評価指標としたのでは，例えば女性ホルモン補充療法のように，骨以外にも，効果・望ましくない影響をもつような薬物療法の総合評価はできない．また骨折防止のような疾患特異的指標を用いたのでは，骨粗鬆症に対する薬物療法と，他の慢性疾患に対する薬物療法を比較することはできない．医療経済評価は薬物療法の効果と安全性を統合的に評価し，異なる複数の疾患に対する横断的な評価が求められる政策決定と深くかかわるが，CEAではそのような応用が困難である．

完全な健康状態を1，死を0として，その疾病・障害状態に相当する値を効用値(utility)とし，生存年×効用値で示される値を質調整生存年(quality-adjusted life year: QALY)といい，QALYを1年延長するのに必要な費用を比較する分析手法が費用効用分析(cost utility analysis: CUA)である．CUAは特定の疾患によらない指標なので，異なった疾患に対する，全く異なった医療行為を，共通の土俵上で比較できるという利点があり，近年CUAの使用例が多い．なおQALYに似た概念として，疾患が社会に及ぼす影響を比較する指標として，WHOが提唱するdisability adjusted life years(DALY)がある．

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0047-1852/13/¥60/頁/JCOPY

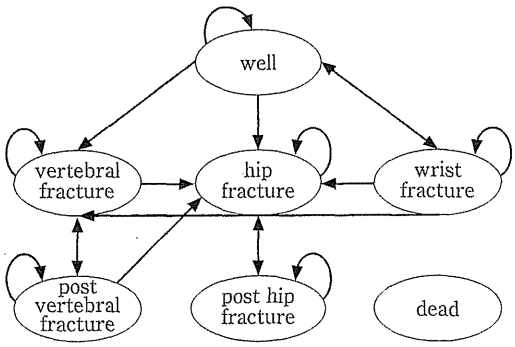

図1 IOF(International Osteoporosis Foundation)によって定められたreference model(文献[1]より引用)

2 モデル分析

医療経済評価においては，多くの場合，モデル分析が行われ，マルコフモデル(Markov model)や判断分析モデルが代表的であるが，ここでは誌面の関係で前者について説明する．**図1**に示すのは，IOF(International Osteoporosis Foundation)がreference modelとして発表したものである[1]．対象者は最初wellの状態からスタートし，一定の確率で，各骨折・死亡などに推移し，次のサイクル(この例では1年)がまたそこから始まり，これを繰り返してシミュレーションが行われる．治療によりwellから骨折への移行確率が減少する．介入に要する費用と各状態において要する費用のデータがあればCEAとなる．また，各状態の効用値と費用のデータがあれば，治療によって増加した費用をQALYで割ることによりCUAとなる．更に患者のシミュレーション開始時の状態(性別・年齢・BMD・既存骨折の有無など)を変化させ，それぞれに対応する骨折率・死亡率などを入力することにより，様々な患者背景に対する分析ができる．これによって，ある薬物による治療介入は，70歳・既存骨折ありの例では，費用対効果に優れるというような分析ができる．このようなモデルによるシミュレーションは，医療経済評価には欠かせない．真のアウトカム(骨粗鬆症であれば骨折抑制)を指標とした大規模臨床試験であっても，せいぜい数年間の研究でしかないが，医療経済評価では更に長期の評価が必要であり，シミュレーションに拠らざるを得ない．また骨粗鬆症においては特に，脊椎圧迫骨折を起こした患者は，次の脊椎圧迫骨折のリスクが数倍に高まっているだけではなく，大腿骨近位部骨折をはじめとする，他部位の骨折リスクも高まっており，動的に状態が推移していくので，モデルによる多様なリスクの総合的な評価が必要となる．

3 IOFのreference model

異なったモデルを用いたのでは，各報告間の比較検討が行えないため，reference modelが定められたものである．これを用いて，ヨーロッパ9カ国における，アレンドロネートに対するCUAが発表されている[2,3]．CUAにおいて，1QALY延長するのに，社会的に許容される閾値についての，絶対的コンセンサスとなる数字はないが，イギリスのNICE(National Institute for Health and Clinical Excellence)は，£30,000/QALYという値を示しており，WHOは国民1人あたりGDP×3という基準を示している．

4 骨折関連医療費に関する我が国における報告

大腿骨近位部骨折の入院治療費用は，萩野は平均147万円，林は平均140万円と報告し，また大腿骨近位部骨折全体として，萩野は1,300億円，林は1,288億円と算出している[4,5]．大腿骨近位部骨折に関しては，その後の介護費用も考慮すると，社会に対するインパクトは更に大きく，太田らは大腿骨近位部骨折にかかわる年間の医療・介護費用を5,318億–6,359億円と推測している[6]．脊椎圧迫骨折の治療実態の把握は困難だが，萩野は入院治療例に関して平均776,000円と報告し[4]，最近原田らは大腿骨近位部骨折と椎体骨折を合わせた総医療費は2,382億–3,218億円，医療・介護費用は7,974億–9,895億円と推計している[7]．

5 骨折抑制を指標とした医療経済評価

この分野については，欧米の報告が多く，イギリスのNICEからは，多数の出版物が発表されている[8,9]．骨粗鬆症の薬物療法に関する医療経済研究は，当初女性ホルモン補充療法に関するものが多く，乳癌・虚血性心疾患など，骨以外の作用も考慮されていたが，2000年以降は，ビスホスホネートなどの骨粗鬆症特異的治療薬の評価が中心となっている．

アレンドロネートに関する論文が最も多く，ヨーロッパのガイドラインを引用すると，アレンドロネート治療は，既存骨折ありの場合骨密度に無関係に費用対効果に優れ，既存骨折なしの場合，65歳未満ではT値＝−2.5SD未満，3つ以上の危険因子をもつ場合は，50歳でT値＝−2.0SD未満，60歳でT値＝−1.5SD未満にて，費用対効果が良かった[2]．すなわち骨密度が低く，危険因子数が多く，年齢が高く，既存骨折ありの例において，費用対効果に優れ，同様の結果はリセドロネートについても示されている．PTHは，骨折抑制効果には優れるが，高価なので，骨折リスクの高い群でのみ，費用対効果が良かった[9]．

我が国ではモデル分析はほとんど行われていなかったが，ごく最近osteopeniaに対するアレンドロネート治療の費用対効果に関して，背景因子との関連を非常に詳細に検討した論文が発表された[10]．

6 骨折抑制以外の指標を用いた評価

骨以外の作用も含めた評価にはCUAが必須である．ラロキシフェンの費用対効果は，乳癌のリスク軽減効果の評価に大きく依存し，これを認めると非椎体骨折抑制のエビデンスは弱いが，費用対効果が非常に良くなる[9]．またCUAの方法論を用いることにより，骨粗鬆症以外の慢性疾患をも同じ土俵で論じることができ，高血圧・脂質異常症と比較した報告もある[11]．

7 骨折の絶対リスクと治療介入閾値

骨粗鬆症に対する治療介入閾値は，最近骨折の絶対リスクに基づいて閾値を決定する方向に大きく変化している．このような流れは特にイギリスにおいて顕著であり，医療費は有限の資源であり，費用対効果に基づいてその配分を決めるという考え方が背景にある．

イギリスを中心に海外では，絶対リスクに基づいて閾値を決めることは，多くの疾患に関して行われてきた．例えば脂質異常症に対するスタチンに関して，NICEの出版物において，虚血性心疾患の2次予防に投与するのは許容できるが，1次予防については費用対効果が悪く，低リスクの例にむやみに投与することは資源の浪費である，虚血性心疾患の発生率年間3％が閾値であるとまで書かれている[12]．

FRAXの提唱も，このような背景のもとに理解すべきであり，その例としてリセドロネートに対する医療経済評価の論文を紹介する[13]．**図2**に示すのは，骨密度・年齢・既存骨折その他，種々の背景因子を変化させて10年間の骨折発生リスクを算出し，それと1QALY延長に要する費用との関係をみたものである．許容限度を£20,000/QALY，£30,000/QALYとした場合，18.6％，13.0％の骨折リスクが閾値とされた．今後はこのような分析が増加するものと思われる．

8 再骨折の予防と骨粗鬆症リエゾンサービス

最近骨粗鬆症リエゾンサービスが提唱され，最初の骨折を経験することにより，次の骨折や大腿骨近位部骨折のようなより重篤な骨折のリスクが非常に高くなるので，専門的知識をもったコメディカルも積極的に関与して，再骨折を予防することが求められている．これも特にイギリスでは，医療費抑制が根本にあり，fracture liaison service（FLS）は費用対効果に優れ，医療費抑制に貢献したことが，FLS発祥の地であるスコットランドから報告されている[14]．

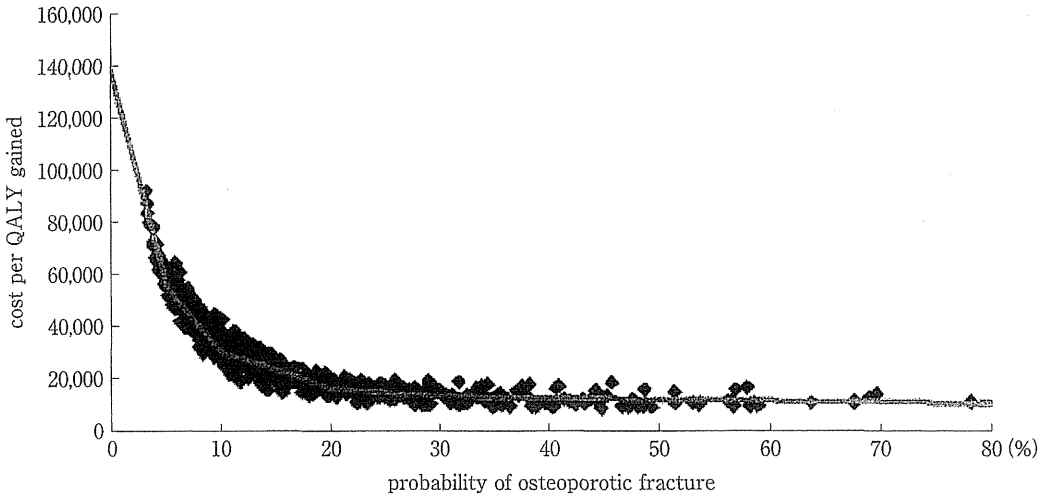

図2 リセドロネート治療に関する，10年間の骨折発生リスクと QALYを1年延長するのに必要な費用の関係(文献[13]より引用)

9 社会全体としての骨折予防

高リスクの対象者限定で治療介入を行えば，費用対効果は優れているが，社会全体を考えると問題がある．高リスク群限定で治療を行うと，費用対効果は良いが，これで予防できるのは28％の骨折のみであり，残りの72％はより低リスク群から発生するので，社会全体として予防できる骨折の絶対数は限られるという，シミュレーション結果も発表されている[15]．そのような対象者には，栄養・運動など生活習慣改善による介入になるのであろうが，今後の研究が必要である．

おわりに

この分野における我が国からの報告は非常に少ない．いうまでもなく，医療経済評価は，国別に状況が全く異なるので，骨折の絶対リスク重視の時代に対応した，我が国発の研究が求められる．

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Ⅳ. 資 料

厚生労働科学研究・研究成果等普及啓発事業による成果発表会

骨粗鬆症の予防と簡便なチェック法

12/15 日曜日

午後1時15分～
（開場 午後1時）

東浦町勤労福祉会館

入場無料
（先着80名）

簡便な骨粗鬆症検診法
森脇佐和子（国立長寿医療研究センター研究員）

身長低下と骨粗鬆症
～身長が低くなったのは年齢のせい？～
田中 清（京都女子大学教授）

チャレンジ♪ 楽しくエクササイズ
塩澤恵美（厚労省認定 健康運動実践指導者）

身近にある骨粗鬆症
～骨粗鬆症の正しい知識と自己チェック～
田中伸哉（埼玉医科大学講師）

骨粗鬆症予防のための食事
上西一弘（女子栄養大学教授）

総合司会　新飯田俊平（研究代表者・長寿研）

主催：国立長寿医療研究センター（バイオバンク）愛知県大府市森岡町源吾35 ☎ 0562-46-2311（代表）　共催：公益財団法人長寿科学振興財団

厚生労働研究・研究成果等普及啓発事業による成果発表会

骨粗鬆症の予防と簡便なチェック法

みなさんは日頃、『骨』について考えることがありますか？
ヒトは年を取るにつれ、どんどん骨が減っていきます。
骨折や寝たきりになるなど、元気な生活が送れない原因が潜んでいる可能性があるのです。
健康な骨を維持するために、ちょっと一緒に骨について考えてみませんか。

簡便な骨粗鬆症検診法

森脇佐和子（国立長寿医療研究センター研究員）

骨検診を受けたことがありますか？私たちは尿から簡便に骨の状態を調べられる方法について研究しています。今回その研究成果を報告します。

身長低下と骨粗鬆症

～身長が低くなったのは年齢のせい？～

田中 清（京都女子大学教授）

年を取ると身長が低下し、背中・腰が曲がるのは当たり前ではなく、骨粗鬆症による脊椎圧迫骨折が重要な原因です。軽視されがちですが、内臓機能低下・QOL（生活の質）低下を起こします。

チャレンジ♪ 楽しくエクササイズ

塩澤恵美（厚労省認定 健康運動実践指導者）

楽しく無理なく続けられる運動で心身ともにリフレッシュ！しなやかなカラダは若さの秘訣です。一緒に体を動かしてみましょう。

身近にある骨粗鬆症

～骨粗鬆症の正しい知識と自己チェック～

田中伸哉（埼玉医科大学講師）

日本には約1300万人の骨粗鬆症患者がいると言われ、その約70%が未治療となっています。我々は骨粗鬆症の可能性のある方をより安価により確実に見つけ出す方法について検討してきましたので報告します。

骨粗鬆症予防のための食事

上西一弘（女子栄養大学教授）

骨粗鬆症の食事の基本は、バランスよく食べること。それに加えてカルシウムをはじめ重要な栄養素がいくつかあります。今回はそれらを紹介したいと思います。

日時

12月15日（日）

13:15～（開場 13:00）

（15:30 終了予定）

場所

東浦町勤労福祉会館

駐車場に限りがあるため公共交通機関をご利用ください

入場

無料（先着80名）

司会：新飯田俊平（研究代表者・長寿研）

主催：国立長寿医療研究センター

愛知県大府市森岡町源吾35
☎ 0562-46-2311（代表）

共催：公益法人 長寿科学振興財団

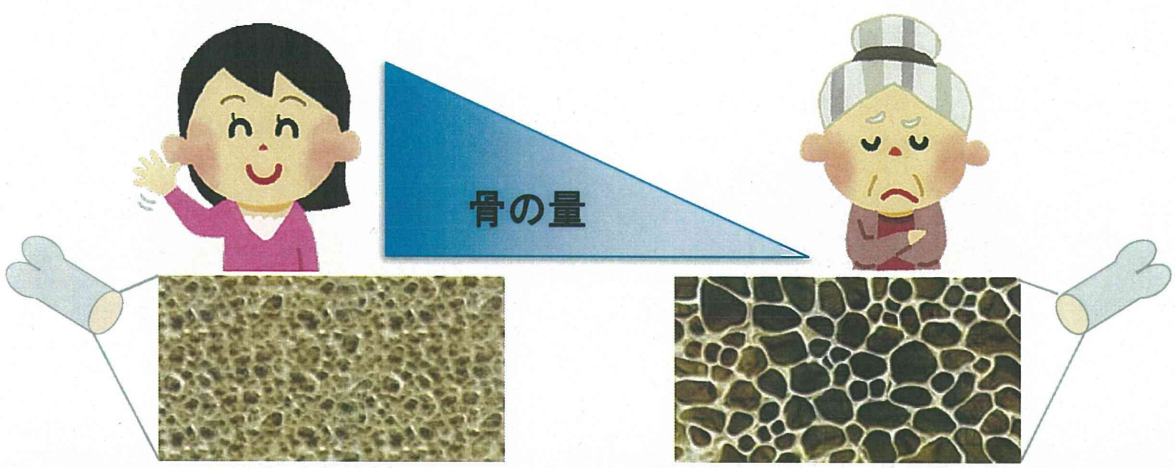
厚生労働研究・研究成果等普及啓発事業による成果発表会

簡便な骨粗鬆症検診法

国立長寿医療研究センター

森脇 佐和子

年を取ると骨は？

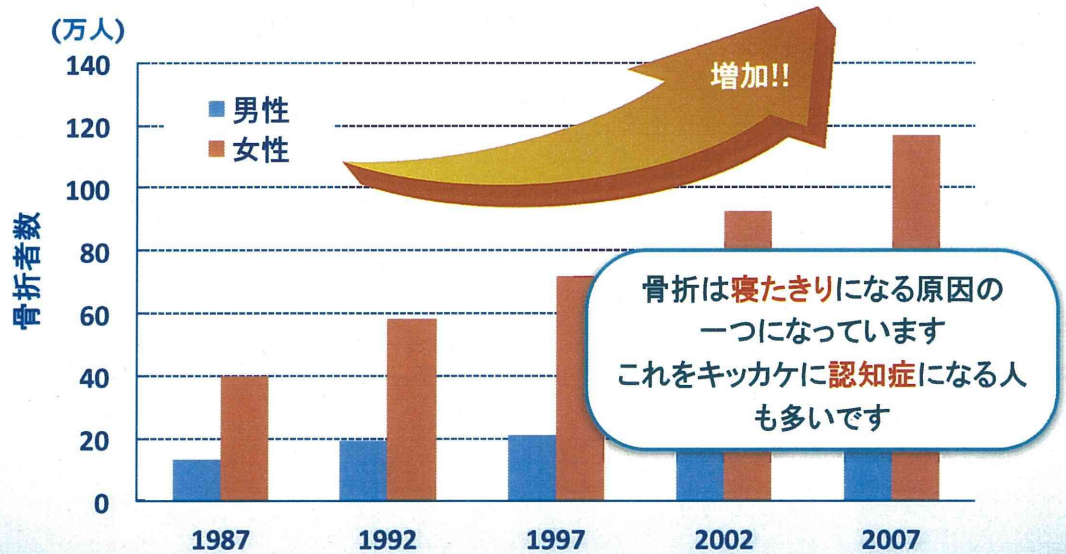


骨が緻密

骨がスカスカ→骨粗鬆症
骨折リスク↑

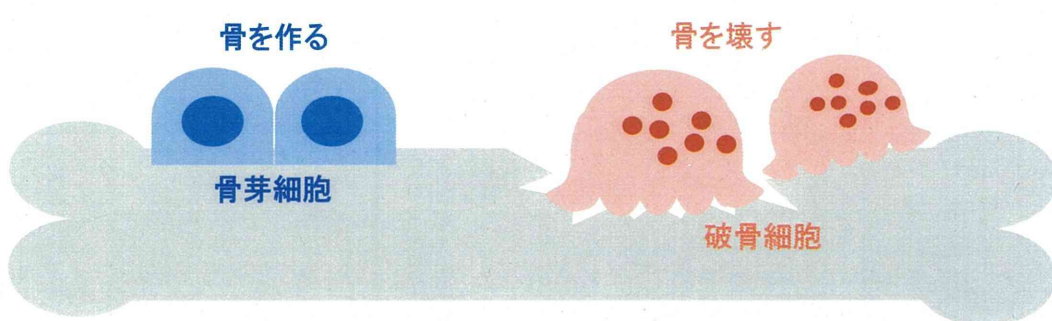
スカスカになった骨を元に戻すのは困難！
いかに減らさないように気をつけるかが大事！

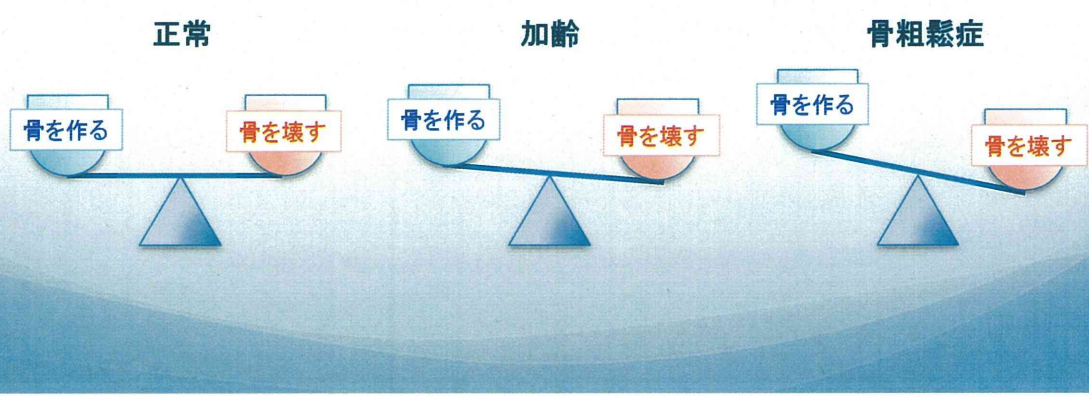
大腿骨頸部骨折者数



Orimo, H. *et al.*, 2007

骨は作って壊されて





骨の検査方法

- 骨を直接調べる方法

全身＞手足など一部

大型装置のため調べられる病院が限られる

- 骨を間接的に調べる方法

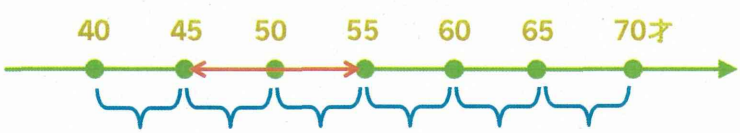
血液や尿に含まれる
壊れた骨の成分を調べます

骨の検診

- 骨粗鬆症検診

40, 45, 50, 55, 60, 65,70才の5年ごと（節目検診）

骨は急激な変化がないので5年ごとで大丈夫
ということだけど…

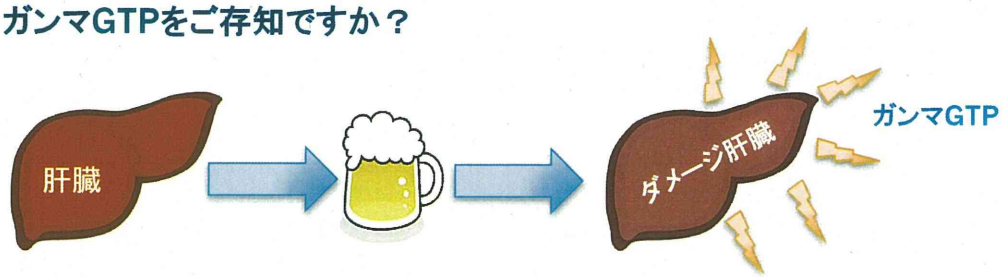


この間、本当に変化は起こりにくいの？

女性は閉経を迎えます！
女性ホルモンが減ると骨は影響を受けます！
ここから急激に骨が減っていくのだけど…

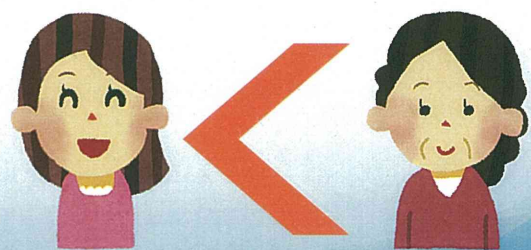
尿に出てくるガンマGTP

- ガンマGTPをご存知ですか？



- 尿ガンマGTPをご存知ですか？

骨が減ってきている人ほど、尿に排泄されるガンマGTPの量が多いことが分かりました！



肝機能とは関係ありません！

もっと手軽に検査できる方法はないのか？

骨粗鬆症を尿ガンマGTPで調べることができないだろうか？

★ 利点 ★

尿検査なので、体への負担が少ない！

一般検診で調べられるかも？

手軽！

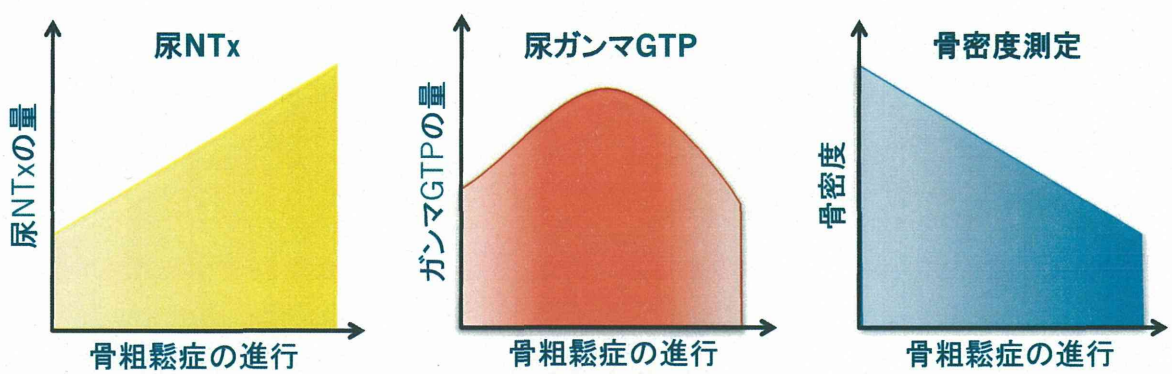
尿ガンマGTPの調査

東浦町・大府市の住民検診で5年間調査を実施。
のべ5,500人の女性に協力頂きました。

一日の中で変動を避けるため

合わせて骨密度測定、既存の骨粗鬆症マーカー検査も実施

尿ガンマGTPの特徴



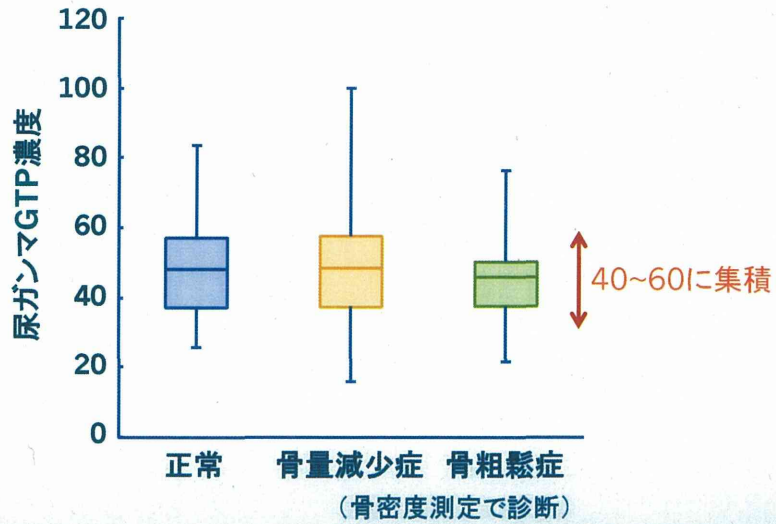
骨量減少症エリア

↓

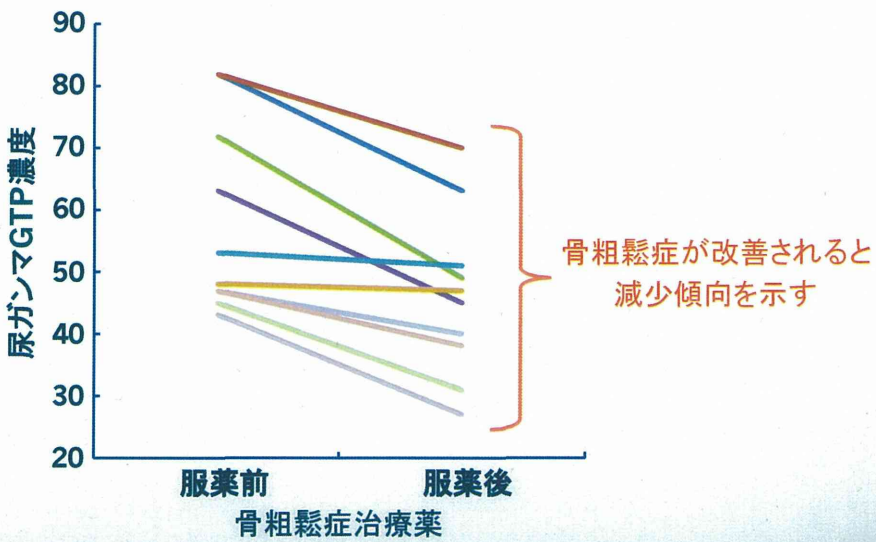
骨が減ってきている人が高値を示した！

骨粗鬆症を予防するために利用できる可能性

尿ガンマGTPの実際



骨粗鬆症治療による尿ガンマGTPの変化



Asaba, Y. *et al.*, 2006