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第 10 回日本骨粗鬆症学会 学術奨励賞受賞演題

Hip Structure Analysis によるラロキシフェンの治療評価

髙田潤一[1,2]・三木隆己[3]・今西康雄[4]・中塚喜義[5]・和田博司[6]
中 弘志[3]・射場浩介[1]・吉崎 隆[2]・山下敏彦[1]

はじめに

hip structure analysis（HSA）とは，DXA のデータをもとに大腿骨の近位部を三次元に再構築して，骨強度を評価する方法である[1〜4]。われわれは，この方法を用いて日本人女性の大腿骨近位部の骨強度の経年的減少様式を報告した[5]。それによると HSA による骨強度の減少様式は，年齢別の大腿骨頸部・転子部骨折の発生様式を反映していた。

HSA を用いた骨粗鬆症の薬物治療評価は，ラロキシフェン，アレンドロネート，リセドロネート，ホルモン補充療法，テリパラチド（PTH(1-34)）などが海外から報告されている[4,6〜9]。

本研究は，わが国においてラロキシフェンの治療効果を，HSA を用いて評価した最初の報告である。

◆骨強度（section modulus）

$$= \frac{\text{慣性モーメント}}{\text{外径}} = \frac{\pi/4\ (r_o^4 - r_i^4)}{r_o}$$

増加＝bending strength ↑

◆皮質骨安定性（buckling ratio）

$$= \frac{\text{外径}}{\text{皮質骨幅}} = \frac{r_o}{T_h}$$

減少＝安定性 ↑

r_o：外径，r_i：内径，T_h：皮質骨幅

図 1　骨強度と皮質骨安定性の評価方法

1 HSA

HSA の原理は，他に詳細な報告がなされているため，本稿では簡潔に述べる[1〜4]。通常と同じ方法で股関節の骨密度を DXA で測定し，得られた DXA のデータを pixel ごとに bone mass を算出する。その値をもとに三次元の骨構造を再構築して評価する。

測定する部位は，頸部（最狭部），転子部（頸部軸と骨軸の二等分角線），骨幹部（小転子から頸部幅の 1.5 倍遠位）の 3 ヵ所である。

評価する項目は，二次元骨密度，皮質骨幅，皮質骨面積，section modulus（骨強度），buckling ratio（皮質骨安定性）である。section modulus とは，慣性モーメントを外径で除したものである。この値が高いということは，曲げ強度が強いことを意味する。また，buckling ratio とは，外径を皮質骨幅で除した値である。この値が低いということは，皮質骨の安定性が高いことを意味する（図 1）。

表 1　対象症例の背景因子

	平均値	標準偏差
年齢（歳）	62.4	7.32
身長（cm）	148.6	6.04
体重（kg）	48.7	7.12
body mass index（kg/m^2）	22.0	3.04
頸体角（度）	129.1	4.56
頸部長（cm）	4.72	0.54

Key words：Hip structure analysis，Raloxifene，Osteoporosis

[1] 札幌医科大学医学部整形外科 [2] 北郷整形外科 [3] 大阪市立大学大学院医学研究科老年内科学 [4] 大阪市立大学大学院医学研究科代謝内分泌病態内科学 [5] 野崎クリニック [6] 和田産婦人科

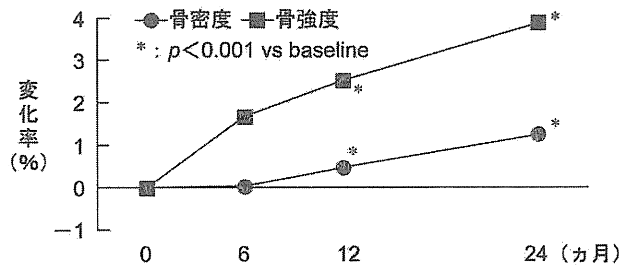

図2　頸部における骨密度と骨強度（section modulus）の変化

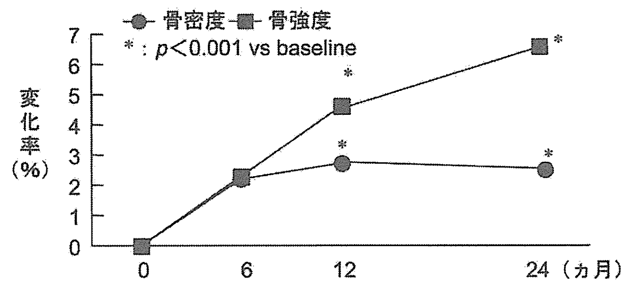

図3　転子部における骨密度と骨強度（section modulus）の変化

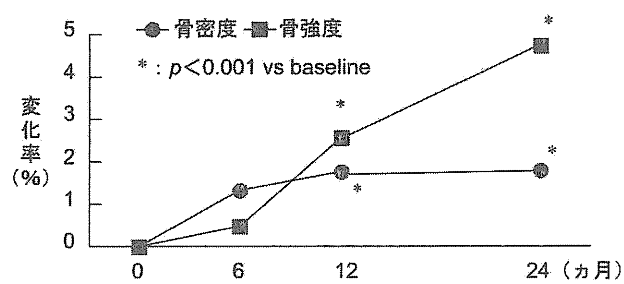

図4　骨幹部における骨密度と骨強度（section modulus）の変化

2　対象と方法

ラロキシフェンを 6 ヵ月以上服用した閉経後骨粗鬆症患者 198 例を対象とした。対象症例の年齢，身長，体重，body mass index（BMI），頸体角，頸部長の平均値と標準偏差を表 1 に示す。DXA は 6〜12 ヵ月ごとに測定し，HSA 解析を行った。

3　結　　果

1）骨密度と骨強度（section modulus）の経時的変化（図 2〜4）

各部位における骨密度と骨強度の治療開始時からの変化率を検討した。頸部は骨密度が 12 ヵ月後より有意に増加し，24 ヵ月後には 1.27%の有意な増加がみられた。一方，骨強度は 24 ヵ月後には 3.90%と骨密度よりも高い増加率を示した（図 2）。転子部は 24 ヵ月後において骨密度が 2.55%増加し，骨強度は 6.60%の増加を示した（図 3）。また，骨幹部では骨密度と骨強度はそれぞれ 1.80%，4.74%の増加が認められた（図 4）。すべての部位において，骨強度の増加率は骨密度の増加率よりも高値を示した。

2）各評価項目の 12 ヵ月後の変化率（図 5）

各評価項目の 12 ヵ月後の変化率を示す（図 5）。皮質骨面積は 3 部位ともに有意な増加が認められた。皮質骨幅と皮質骨安定性は頸部では改善が

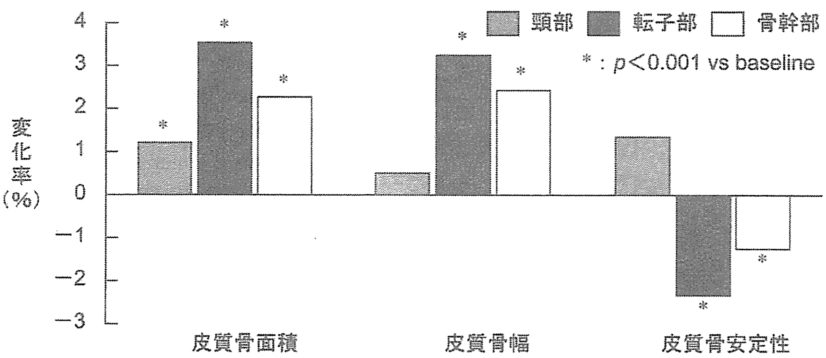

図 5　各評価項目の 12 ヵ月後の変化率

表 2　骨強度と各項目の相関係数

	頸部	転子部	骨幹部
骨密度	0.794*	0.535*	0.628*
皮質骨面積	0.797*	0.879*	0.856*
皮質骨幅	0.785*	0.757*	0.561*
皮質骨安定性	−0.648*	−0.557*	−0.361*

*：$p<0.001$

みられなかったが，転子部と骨幹部では有意な改善が認められた。

3）骨強度と各評価項目の相関関係（表 2）

ラロキシフェン投与 12 ヵ月後における骨強度と各評価項目との相関を検討した。骨強度は，すべての部位で皮質骨面積と最も高い相関係数を示した。さらに，骨密度と皮質骨幅においても高い相関係数を認めた。一方，皮質骨安定性とは負の相関を認めた（表 2）。

4 考　　察

HSA は DXA の値をもとに三次元の骨構造を評価する方法である。この方法を用いた骨粗鬆症の薬物治療評価としては，ラロキシフェン，アレンドロネート，リセドロネート，ホルモン補充療法，テリパラチド（PTH(1-34)）などが海外から報告されている[4,6~9]。

今回，われわれは日本人骨粗鬆症患者におけるラロキシフェンの治療効果を HSA により評価した。その結果，頸部，転子部，骨幹部における骨密度，骨強度，皮質骨面積と転子部，骨幹部における皮質骨幅と皮質骨安定性は治療開始時と比較して有意な改善を認めた。また，骨強度の増加率は骨密度の増加率よりも有意に高値を示した。

ラロキシフェンの大規模臨床試験（MORE 試験）では，ラロキシフェン群はコントロール群と比較して，腰椎骨密度は 2.6%の増加を認め，椎体骨折発生の相対リスクは 0.7（0.5～0.8）と有意な骨折抑制効果が認められた[10]。一方，大腿骨頸部では骨密度が 2.1%増加したものの，大腿骨近位部骨折の相対リスクは 1.1（0.6～1.9）と有意な骨折抑制効果は認められなかった。しかしながら，MORE 試験の HSA 解析では，大腿骨頸部，転子部，骨幹部において骨強度の有意な増加が認められている[7]。このように，ラロキシフェンは大腿骨近位部の骨密度と骨強度をともに増加させるが，骨折リスクの低下は証明されていない。この理由として，プラセボ群の骨折発生率が椎体では 10.1%であったのに対し，大腿骨近位部では 0.7%と低く，十分に有意差を検定することができなかったことも考えられる。

ラロキシフェンは，骨折抑制効果における骨密度増加の寄与が少ないとされている。今後の課題として，HSA で示された骨強度の増加が大腿骨近位部骨折の抑制を示しているかを検討する必要がある。

ま と め

1）HSA を用いてラロキシフェンの治療評価を行った。

2）骨密度と骨強度は12ヵ月後から増加していた。骨強度の増加率は骨密度の増加率よりも高かった。

3）骨強度は，骨密度，皮質骨幅，皮質骨面積と有意な正の相関を示し，皮質骨安定性とは有意な負の相関を示した。

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ORIGINAL ARTICLE

Recent trends in the incidence and lifetime risk of hip fracture in Tottori, Japan

H. Hagino · K. Furukawa · S. Fujiwara · T. Okano · H. Katagiri · K. Yamamoto · R. Teshima

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Abstract
Summary Hip fracture incidence from 2004 to 2006 in the Tottori prefecture of Japan was investigated and compared with previously reported rates. The age- and gender-specific incidence of hip fracture in the Tottori prefecture has not plateaued, as has been reported for populations in Northern Europe or North America.
Introduction Recent data from Northern Europe and North America indicate that the incidence of hip fracture has plateaued, whereas most reports from Asia indicate that the incidence is increasing. The aims of this study were to investigate the recent incidence of hip fracture in the Tottori prefecture, Japan, and to compare it with previous reports.
Methods All hip fractures in patients aged 35 years and older occurring between 2004 and 2006 were surveyed in all of the hospitals from the Tottori prefecture. The age- and gender-specific incidence rates were then calculated. Using these and previously reported data, the estimated number of hip fracture patients was determined using the age- and gender-specific incidence rates in each year from 1986 to 2006.
Results The survey identified 851, 906, and 1,059 patients aged 35 years and older, in 2004, 2005, and 2006 respectively. The residual lifetime risk of hip fracture for individuals at 50 years of age was estimated to be 5.6% for men and 20.0% for women. The estimated number of patients from 1986 to 2006 showed a significant increase over time for both genders.
Conclusions The age- and gender-specific incidence of hip fracture in the Tottori prefecture, Japan has not plateaued for either gender.

Keywords Epidemiology · Hip fracture · Incidence · Lifetime risk · Osteoporosis

H. Hagino · H. Katagiri
Rehabilitation Division, Tottori University Hospital,
Yonago, Japan

K. Furukawa
Department of Statistics,
Radiation Effects Research Foundation,
Hiroshima, Japan

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

T. Okano · R. Teshima
Department of Orthopedic Surgery, School of Medicine,
Faculty of Medicine, Tottori University,
Tottori, Japan

K. Yamamoto
Department of Orthopedic Surgery, Hakuai Hospital,
Tottori, Japan

H. Hagino (✉)
School of Health Science, Faculty of Medicine, Tottori University,
Yonago, Tottori 683-8503, Japan
e-mail: hagino@med.tottori-u.ac.jp

Introduction

Hip fracture is the most significant osteoporotic fracture in terms of health outcomes, quality of life, and cost. As a result of the aging population, the burden of these fractures on our health care systems is increasing and the absolute number of hip fractures is expected to increase significantly during the next few decades. It has been estimated that the total number of hip fractures worldwide will increase from 1.3 million in 1990 to 2.6 million by the year 2025 and to 4.5 million by the year 2050 [1]. To predict the number of patients requiring treatment for hip fractures during the coming decades, however, it is necessary to determine whether the number of fractures is rising more rapidly than can be accounted for by demographic changes alone.

A growing number of epidemiological surveys show an exponential increase in the incidence of hip fracture with age among different ethnic groups. In addition, data obtained beginning in the 1990s from Northern Europe [2, 3], North America [4], and Australia [5] indicate that previously observed age-specific increases in the incidence of hip fracture have plateaued. We previously performed a hip fracture survey in the Tottori prefecture and found that the incidence of hip fracture increased from 1986 to 2001; this agreed with most other studies from Asia, which indicated an increase in the incidence of hip fracture over time [6].

To estimate the real burden of this problem, a long-term prospective population-based study specifically examining the age distribution and changes in the incidence rates of hip fracture is essential. There is, however, a paucity of long-term data on the changes in these rates in men and women within defined communities. The aims of this study were to investigate hip fracture incidence rates in the Tottori prefecture from 2004 to 2006 and to compare them with previously reported rates.

Patients and methods

Data sources

In 2006, the Tottori prefecture, which is located in midwestern Japan, had a population of 603,987, including 176,255 men and 208,582 women aged 35 years and older. The percentages of the population aged 65 years and older, 75 years and older, 85 years and older, and 90 years and older in 2006 were 24.6% (20.4% of men; 28.4% of women), 12.9% (9.4% of men; 16.1% of women), 3.5% (1.8% of men; 5.0% of women), and 1.4% (0.6% of men; 2.0% of women) respectively.

As previously stated [6], all hip fractures in patients 35 years and older that occurred between 2004 and 2006 were surveyed in all of the hospitals in the Tottori prefecture. This included 30 hospitals with orthopedic or general surgery departments; according to the hospital records, survey registration was performed by the doctors or medical staff in each of these hospitals. Registration information included gender, age, area of residence, date of fracture, type of fracture (neck or trochanteric), and treatment. Patients residing in other prefectures were excluded. Duplication of cases was determined using the patients' ages, dates of fracture, types of fracture, and areas of residence. As previously reported [6], we investigated the data collection methods at the three hospitals with the most hip fracture patients in each year, which covered one-third of the total number of patients in this prefecture. This confirmed that the methods used to register the patients with hip fractures were consistent with those used in previous observational periods.

The study was approved by the local ethics research committee at the Faculty of Medicine, Tottori University.

Statistical analysis

The patients were divided into groups according to their age (subdivided into 5-year increments), gender, and fracture type (neck or trochanteric fracture). The age- and gender-specific incidence rates (per 100,000 person years) were calculated based on the population of the Tottori prefecture during each year. Every 5 years in Japan, a national census is performed on 1 October, including in 2005 during the observation period. The age- and gender-specific populations for each survey year were estimated by the Bureau of Statistics of the Tottori prefecture government office according to resident registration records.

To determine recent trends in the hip fracture incidence, a test of trends of proportions in quantitatively ordered samples was used [7]. The age- and gender-specific incidence (per 100,000 person years) from 1986–1988, 1992–1994, and 1998–2001, which we have previously reported [6, 8], were used for this analysis. The expected number of patients, age-adjusted to the population structure from 1986 in the Tottori prefecture (35 years and older), was calculated from the age- and gender-specific incidence rates in each observation year. The overall and slope Chi-squared values were examined. Additionally, we elucidated the influence of the expansion in the elderly population using the age-adjusted incidence in two age groups: 85–89 years old and 90 years and older.

Lifetime risks of hip fracture for 50-year-old men and women in the population were estimated by simple approximation using the incidence data and the age- and gender-specific incidence and life tables for the Japanese population in 2006 released by the Ministry of Health, Labour and Welfare of Japan (http://www.mhlw.go.jp/english/database/index.html).

To compute the lifetime risks, Pr was defined as the probability of having no hip fracture until death for a 50-year-old man or woman. This probability may be discretely approximated using the following formula:

$$\begin{aligned}\Pr &= d50(1-I50) + (1-d50)(1-I50)d51(1-I51)\\ &\quad + (1-d50)(1-I50)(1-d51)\\ &\quad \times (1-I51)d52(1-I52) + \cdots\end{aligned}$$

where $d50$ is the probability of dying between the ages of 50 and 51 years, $I50$ is the probability of having a fracture between the ages of 50 and 51 years, and so on. These values were replaced with the corresponding incidence or mortality rates in this study. The residual lifetime risk of an individual aged 50 years experiencing a hip fracture is then estimated by 1 − Pr.

The significance of the difference in proportions of patients with left or right fractures was examined using Chi-squared testing. The monthly variation in the number of patients was tested using the Friedman test. $P<0.05$ was regarded as significant.

Results

Characteristics of patients aged 35 years and older with hip fracture

Registration was performed in all hospitals during the entire observation period. As a result, this survey covered all patients with hip fractures. The survey identified 851 (161 men and 690 women), 906 (170 men and 736 women), 1,059 (191 men and 868 women) patients aged 35 years and older in 2004, 2005, and 2006 respectively. Categorizing the patients by fracture type, there were 360 neck fractures (63 men and 297 women) and 487 trochanteric fractures (97 men and 390 women) in 2004 (4 fractures were undetermined); 338 neck fractures (61 men and 277 women) and 547 trochanteric fractures (103 men and 444 women) in 2005 (21 fractures were undetermined); and 424 neck fractures (84 men and 340 women) and 617 trochanteric fractures (102 men and 515 women) in 2006 (18 fractures were undetermined).

Right hips were fractured in 1,421 patients and left hips were fractured in 1,395 patients, with no significant difference between the numbers of right and left fractures. The maximum number of fractures occurred in January (267), whereas the smallest number occurred in August (189). There was no statistically significant difference among months during the 3-year period from 2004 to 2006. Including the data from the previous observational periods (1986–1988, 1992–1994, 1998–2001, and 2004–2006), a significant seasonal change in the incidence was noted, with a higher incidence observed in the winter and a lower incidence identified in the summer months ($p<0.006$, by Friedman test).

Incidence of hip fracture between 2004 and 2006

In the population aged 35 years and older, the crude incidence of hip fractures was 244.8 per 100,000 person years from 2004 to 2006, and the gender-specific incidence was 99.1 per 100,000 person years for men and 368.0 per 100,000 person years for women. Although the incidence rate of hip fractures increased with age (Table 1), the absolute number of hip fractures peaked in the 80- to 84-year-old population of men and in the 85- to 89-year-old population of women.

After categorizing the fracture types, the incidence of neck fractures averaged during the 3-year period (from 2004 to 2006) in men and women was 58.6 and 143.7 (70- to 74-year-old group), 101.1 and 309.0 (75- to 79-year-old group), 160.9 and 477.9 (80- to 84-year-old group), 301.6 and 634.7 (85- to 89-year-old group), and 391.5 and 820.1 (≥90-year-old group) respectively. The incidence of trochanteric fractures was 62.9 and 105.5 (70- to 74-year-old group), 128.8 and 244.7 (75- to 79-year-old group), 289.7 and 730.2 (80- to 84-year-old group), 575.4 and 1,470.5 (85- to 89-year-old group), and 619.6 and 2,070.0 (≥90-year-old group) respectively.

Table 1 Age- and gender-specific incidence of hip fracture in Tottori Prefecture, Japan

Age group	Men						Women						Average	
(years)	2004	*n*	2005	*n*	2006	*n*	2004	*n*	2005	*n*	2006	*n*	Men	Women
35–39	0.0	0	6.0	1	11.5	2	5.9	1	5.9	1	5.7	1	5.8	5.8
40–44	5.8	1	5.8	1	12.2	2	0.0	0	0.0	0	5.8	1	7.9	1.9
44–49	24.9	5	26.0	5	26.8	5	5.0	1	0.0	0	26.5	5	25.9	10.5
50–54	8.5	2	17.6	4	13.7	3	39.2	9	22.6	5	4.7	1	13.3	22.1
55–59	13.4	3	24.8	6	34.6	9	31.6	7	33.5	8	50.7	13	24.3	38.6
60–64	61.3	11	16.6	3	47.1	8	71.6	14	31.0	6	88.3	16	41.7	63.7
65–69	110.7	18	106.4	17	81.7	13	163.7	32	78.8	15	164.4	31	99.6	135.7
70–74	150.8	24	88.6	14	131.5	21	270.3	53	192.9	39	299.2	60	123.6	254.1
75–79	185.5	24	249.0	33	270.6	36	508.0	96	568.7	109	620.8	120	235.0	565.8
80–84	441.8	31	554.9	43	391.7	33	1,163.7	163	1,301.9	196	1,258.3	196	462.8	1,241.3
85–89	665.3	22	915.0	31	1,107.3	39	2,035.8	166	1,953.7	174	2,437.5	230	895.9	2,142.3
90+	1,246.9	20	730.8	12	1,116.7	20	2,605.6	146	3,089.1	183	3,024.6	191	1,031.5	2,906.5

Incidence data are per 100,000 person years

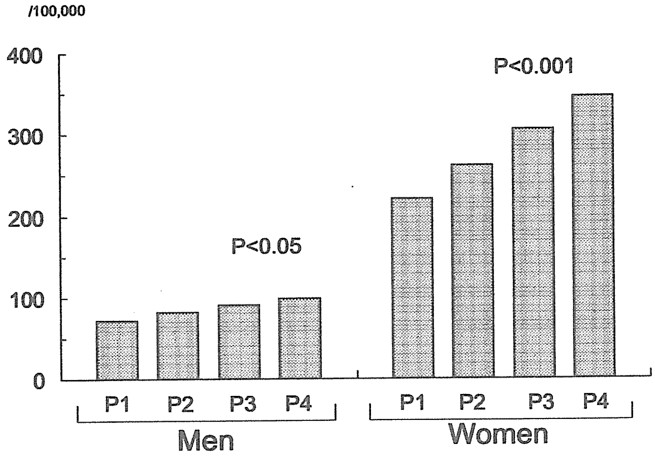

Fig. 1 Trends in the incidence of hip fracture per annum (patients aged 35 years and older). Data are the expected number of patients adjusted for the age- and gender-specific incidence in each year standardized using the 1986 population structure in the Tottori prefecture. In the population aged 35 and older, 154,774 individuals were men and 183,157 were women in 1986. P1: 1986–1988; P2: 1992–1994; P3: 1998–2001; P4: 2004–2006. The incidence in the periods 1986–1988, 1992–1994, and 1998–2001, which we have previously reported [6, 8], was used. χ^2 (overall) was 24.7 ($p<0.05$) for men and 110.0 ($p<0.001$) for women. χ^2 (slope) was 16.4 ($p<0.01$) for men and 97.7 ($p<0.001$) for women

The residual lifetime risk of hip fracture for individuals aged 50 years was estimated to be 5.6% for men and 20.0% for women.

Changes in incidence during the 20-year period

During the 20-year observational period, the total population aged 35 years and older in this area grew 1.14-fold, whereas that aged 85 years and older grew 3.18-fold (from 6,662 to 21,163). From 1986 to 1988, 916 hip fractures were reported in patients 35 years and older, whereas 2,816 hip fractures were identified in this patient population in the period from 2004 to 2006. The number of hip fractures among women increased 3.3-fold, from 692 to 2,294, and that among men increased 2.3-fold, from 224 to 522.

The expected number of patients adjusted for the age- and gender-specific incidence in each year and standardized using the population structure of 1986 showed significant increases from 1986 to 2006 for both genders (Fig. 1). The mean age- and female-specific incidence in the 85- to 89- and ≥90-year-old age groups was 1,179.2 and 1,506.9 per 100,000 person years from 1986 to 1988, 1,632.8 and 1,838.0 per 100,000 person years from 1992 to 1994, 1,810.9 and 2,407.5 per 100,000 person years from 1998 to 2001, and 2,142.3 and 2,906.5 per 100,000 person years from 2004 to 2006 respectively. Those for men in the 85- to 89- and ≥90-year-old age groups were 551.5 and 871.9 per 100,000 person years from 1986 to 1988, 572.6 and 887.3 per 100,000 person years from 1992 to 1994, 632.9 and 1,059.3 per 100,000 person years from 1998 to 2001, and 895.9 and 1,031.5 per 100,000 person years from 2004 to 2006 respectively.

Figure 2 shows the average age- and gender-specific incidence for neck and trochanteric fractures from the periods 1986–1988, 1992–1994, 1998–2001, and 2004–2006. For both genders, the incidence of both types of fracture was significantly higher in 2004–2006 than in all other survey periods. The expected numbers of patients with neck fracture adjusted for the age- and gender-specific incidence in each year and standardized by the population structure of 1986 was 22.0 for men and 87.0 for women in 1986, and 47.2 for men and 175.0 for women in 2006. The expected numbers of trochanteric fractures in men and

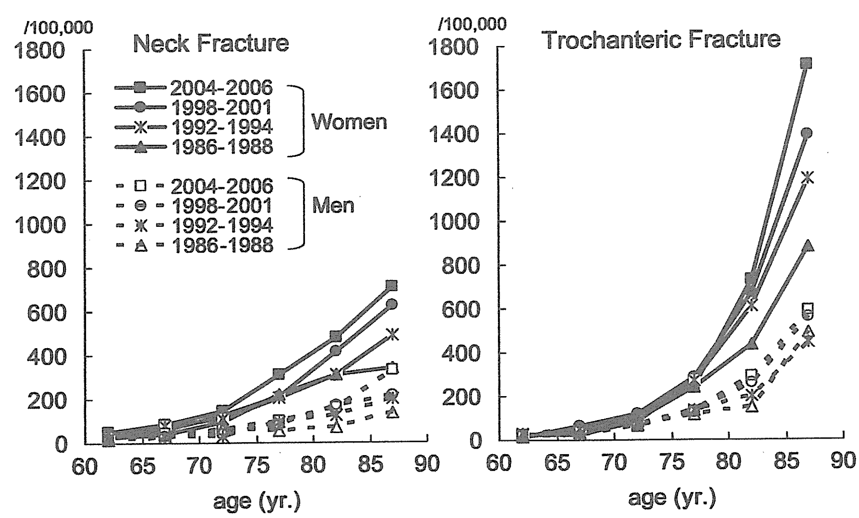

Fig. 2 Age- and gender-specific incidence of neck and trochanteric fractures between 1986 and 2006. Incidence data are per 100,000 person years. Incidence from the periods 1986–1988, 1992–1994, and 1998–2001, which we have previously reported [6, 8], were used for comparison

women were 39.0 and 119.0 in 1986 and 57.0 and 202.2 in 2006 respectively. These increases were statistically significant, with the exception of trochanteric fractures in men.

Discussion

In this study, we have demonstrated that the age-specific incidence of hip fracture in the Tottori prefecture has not stabilized, but rather has slightly increased during the past two decades. This observational study began in 1986 and has been carried out using 3-year intervals, except for the 4-year survey from 1998 to 2001. The catchment area, the methods of identifying hip fracture patients, and the definitions of fracture were identical to those used in previous studies [6, 8]. The proportion of the population aged 65 years and older in the whole of Japan was 20.8% in 2006, whereas it was 24.6% in Tottori. In the Tottori prefecture, there are 6.6 general hospitals per 100,000 persons (6.2/100,000 persons for the whole of Japan) and the average monthly income is ¥504,729 (US$4,799) per family unit (¥525,716 [US $4,997] for the whole of Japan) in 2006. Based on these data, the Tottori prefecture has a higher percentage of seniors, but is representative of Japan based on the medical resources and family economics. Because the Tottori prefecture is on the coast and is surrounded by mountains, all patients with fractures must be treated at a hospital within the prefecture. Japanese citizens are legally obliged to belong to one of several government-subsidized health insurance programs, and thus every patient with hip fracture is treated in a hospital. These circumstances contribute to the validity of this longitudinal survey. The incidence observed during the 20-year period in the Tottori prefecture was in the middle of the range observed within Japan as a whole over the same period [9, 10], suggesting that the data from this study are representative of the Japanese population.

Several studies have suggested a wide geographic variation in hip fracture incidence between countries, with the highest rates reported for northern European countries [2, 3] and the United States [11], and the lowest rates reported in Africa and some Asian populations [6, 12, 13]. The Japanese incidence presented in the current study is slightly higher than that reported recently in Korea [14] or Taiwan [15]. In general, people who live in latitudes farther from the equator seem to have a higher incidence of fracture [16].

The lifetime risk of hip fractures for individuals aged 50 years is estimated to be 22.9% for women and 10.7% for men in Sweden, and 11.4% and 3.1% respectively in the UK [17, 18]. The average life expectancy at birth for Japanese individuals has steadily increased, reaching 78.56 years for men and 85.52 years for women in 2005. The life expectancy for 50-year-old men was 29.26 years and that for women was 35.94 years in 2005. Although the incidence of hip fracture in Japan is lower than that in Sweden, longer lifespans have elevated the residual lifetime fracture risk for individuals 50 years of age.

This type of increase has been observed in longitudinal data from several areas within Japan [19] and in nationwide surveys [10], in which the incidence was increased in both men and women, particularly among individuals at least 80 years old; the present study demonstrated the same tendency. In the Tottori prefecture, the total population decreased by 2.1% from 1986 to 2006, whereas the population aged 85 years and older more than tripled. This expansion in the elderly population may have affected our findings. To address this possibility, we compared the age-adjusted incidence with previous observations in the population aged between 85 and 89 years and in that aged 90 years and older. We found a substantial increase in women in the incidence in these age groups and in men 85 to 89 years old. This age-specific increase in these older populations indicates that the increase in hip fracture incidence is not completely due to a proportional change in the population structure.

Decreases in the incidence of hip and wrist fractures have been observed in Ontario, Canada; the authors suggested that the higher diagnosis rates for osteoporosis and the shift from specialist to primary care observed in the late 1990s resulted in a greater number of women with osteoporosis receiving appropriate diagnosis and treatment, which coincided with the reduction in fracture rates [20]. A nationwide decline in the incidence of hip fracture has been also been reported in Finland; potential reasons proposed by the authors included a cohort effect toward a healthier elderly population, increased body mass index, improved functional ability in the elderly, specific actions to prevent and treat osteoporosis, and effective programs and interventions for fall prevention [21]. Bone mineral density in older Japanese individuals has been increasing recently. The Miyama study conducted in 1990 and in 2000 showed significant improvements in the bone density of the femoral neck in men in their 60s and in women in their 50s, suggesting that bone fragility may be generally less severe than before in Japan [22]. This is probably a result of increased body weight among Japanese individuals; increases in obesity, however, may result in decreases in hip fracture similar to the data described from Northern Europe. Therefore, risks of fracture other than bone fragility should be assessed to help explain the increase in the incidence in Japan. We reported that one significant preventive factor for distal radius fractures among Japanese individuals was the use of a futon (as opposed to a bed) [23]. We speculated that futon use helps to maintain some level of physical activity, resulting in a reduced risk of falls. Moreover, the overall decrease in physical activity of a Westernized lifestyle may explain the increase in fracture incidence among Japanese patients. Another explanation may be that more seniors with poor health due to other conditions are being treated, which results in people living longer at a time when their risk of falling is considerably high.

The incidence of neck fracture is higher than that of trochanteric fracture in Northern European and African populations, whereas neck fracture is less common in Japanese populations [3, 13, 24, 25]. This study showed that an increasing number of patients in the Tottori prefecture are suffering neck fracture relative to trochanteric fracture; the increases in age-standardized incidence during the two decades for neck fracture was 115% in men and 101% in women, and those for trochanteric fracture were 46% and 70% respectively. On the other hand, a recent survey in Sweden showed that the neck-to-trochanteric fracture incidence ratio had leveled off [2]. Although the reason for these trends is uncertain, the neck-to-trochanteric fracture ratio in Japan is approaching values observed in Northern European populations.

Our study has some limitations, particularly with regard to the data collection. The method of data collection was consistent, and, as mentioned before, we checked patient enrollment in three monitoring hospitals [6]. Second hip fractures in the same patient during the observational period were not specifically identified in the present survey, which may have affected the result. Moreover, hip fracture patients living in the Tottori prefecture and treated outside the prefecture may have been missed during the registration. The number of such patients, however, is likely to be very small.

We conclude that the age- and gender-specific incidence of hip fracture in the Tottori prefecture of Japan has not plateaued as it has for populations in Northern Europe and North America. This presents a remarkable challenge to the Japanese health care system. An estimated 12 million patients have osteoporosis in Japan, and only 20–25% are being treated with anti-osteoporotic medication. Appropriate diagnosis and treatment of osteoporosis is essential, and more effective interventions for preventing falls are needed.

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Conflicts of interest None.

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ORIGINAL ARTICLE

Sequential change in quality of life for patients with incident clinical fractures: a prospective study

H. Hagino · T. Nakamura · S. Fujiwara · M. Oeki · T. Okano · R. Teshima

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Abstract

Summary Health-related quality of life in elderly women with sustained incident fractures was assessed prospectively for 1 year, using the EuroQol standard. Loss of QOL was more severe in patients after hip or vertebral fractures than those with wrist fracture. QOL was not completely restored in patients suffering from hip fracture.

Introduction Osteoporosis-related fractures decrease mobility, social interaction, and emotional well-being. All of these characteristics determine health-related quality of life (HR-QOL). In this study, we assessed HR-QOL in elderly women following incident clinical fractures.

Methods Thirty-seven patients with hip fractures (mean age 76.1 years), 35 with vertebral fractures (mean age 72.6 years), and 50 with wrist fractures (mean age 68.6 years) were enrolled. HR-QOL was prospectively measured using EuroQol (EQ-5D) before the fracture, 2 weeks, 3 months, 6 months, and 1 year after the fracture.

Results During the observation period, reduction of EQ-5D values was greatest in the hip fracture group. In the wrist fracture group, EQ-5D values at 6 months after the fracture showed recovery; however, in the hip and vertebral fracture groups, recovery was significantly lower than before the fracture. One year after the fracture, EQ-5D values were not significantly different from prefracture values in the vertebral and wrist fracture groups, but remained significantly lower in the hip fracture group.

Conclusions Loss of QOL was more severe in patients after hip or vertebral fractures than in patients with wrist fracture. HR-QOL was not completely restored in patients suffering from hip fracture.

Keywords Hip fracture · Quality of life · Vertebral fracture · Wrist fracture

H. Hagino
Rehabilitation Division, Tottori University Hospital,
Yonago, Japan

H. Hagino · M. Oeki
Department of Fundamental Nursing, School of Health Science,
Faculty of Medicine, Tottori University,
Yonago, Japan

T. Nakamura
Department of Orthopedic Surgery,
University of Occupational and Environmental Health,
Fukuoka, Japan

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

T. Okano · R. Teshima
Department of Orthopedic Surgery, Faculty of Medicine,
Tottori University,
Yonago, Japan

H. Hagino (✉)
School of Health Science, Tottori University,
Yonago, Tottori 683-8503, Japan
e-mail: hagino@med.tottori-u.ac.jp

Introduction

The severity of osteoporosis ranges widely from mild cases with no symptoms or only a single minor fracture during a lifetime to severe cases with multiple fractures and sequelae. The risk of vertebral and limb fractures, such as those of the hip and wrist, increases with the progression of osteoporosis. Among the elderly, osteoporosis-related fractures are so prevalent that they cause significant morbidity. Data from the 1990s or later from Northern Europe [1] and North America [2–4] indicate that the incidence of hip fractures does not increase with time; however, most reports from Asian countries, including Japan, do show an increase [5, 6]. According to a survey performed between 1986 and 1995, the incidence of wrist and proximal humerus fractures also significantly increases with time [7]. With the rapidly increasing elderly population in Asian countries, osteoporosis-related fractures are becoming responsible for considerable health expenditures.

In addition to causing pain and disturbance of physical function, fractures may decrease mobility, social interaction, and emotional well-being [5]. All of these characteristics determine quality of life (QOL). A growing number of studies show that fragility fractures in elderly patients have a considerable impact on QOL; however, there have been only a few studies of generic health-related quality of life (HR-QOL) measured prospectively in patients with incident fractures [8–10]. There have been no reports specifically describing the prospective measurement of HR-QOL after incident fractures among elderly patients in Japan or any Asian country.

Recent anti-osteoporosis pharmaceutical therapies can reduce the risk of fragile fractures by up to 50% [11]. However, due to limited health care resources, there is an increased need to demonstrate the cost-utility of these therapies. The influence of fragility fractures on HR-QOL specifically needs to be incorporated into cost-effectiveness analyses [12]. Thus, the present study sought to assess HR-QOL in elderly women following incident hip, vertebral, and wrist fractures using a prospective observational study.

Materials and methods

Patients

For this study, we recruited patients meeting the following criteria: women 45 years old and over who sustained incident clinical fracture of the vertebra, hip, or wrist (distal radius), caused by minor trauma such as falls while standing and who were consecutively treated at one of four hospitals in Tottori Prefecture between 2004 and 2005. Exclusion criteria were pathological fractures resulting from metastatic disease or those resulting from high-energy trauma such as traffic accidents or falls from heights. Incident vertebral fractures were diagnosed by lateral radiographs of the spine as well as physical findings, and the diagnoses were confirmed by magnetic resonance images (MRI) and/or vertebral height loss or sclerotic changes evaluated from subsequent radiographs. Patients with dementia and those who could not complete the questionnaire due to severe cognitive dysfunction were also excluded. All subjects were identified at the time of their first visit or admission and prospectively followed for 1 year.

The study was approved by the local research ethics committee of the Faculty of Medicine, Tottori University and performed in accordance with the Declaration of Helsinki. All enrollments were carried out after obtaining informed consent.

Although informed consent was initially provided, two patients with hip and two patients with wrist fracture withdrew from the study before the evaluation 3 months after the fracture; these four patients were excluded from the analysis. A total of 37 patients with hip fractures (mean age 76.1 years) including 16 with femoral neck and 21 with trochanteric fractures, 35 with vertebral fractures (mean age 72.6 years), and 50 with wrist fractures (mean age 68.6 years) were enrolled and followed in this study (Table 1). Mean patient age was significantly higher, and body mass index (BMI) was significantly lower, in the hip fracture group than in the other two groups. If a patient sustained new fractures during the course of the study, not only second fracture but also other clinical fractures, the HR-QOL evaluation was stopped for that patient. Among the enrolled patients, one in each group was eliminated by new fractures; one of the hip fracture patients dropped out due to a newly developed complication; three of the hip fracture patients, three vertebral fracture patients, and nine wrist fracture patients dropped out due to loss of contact for no specified reason, and one of the hip fracture patients and one of the vertebral fracture patients died during the observational period.

In the hip, the vertebral, and the wrist fracture groups, 5, 8, and 5 patients, respectively, had been diagnosed as having osteoporosis before the fracture. The numbers of patients receiving anti-osteoporosis drugs before and after the fracture are presented in Table 1. It was unclear whether some patients were receiving the medications, since they had been prescribed by other doctors and details could not be obtained. Nine patients in the hip fracture group, 8 in the vertebral fracture group, and 12 in the wrist fracture group had previous fractures. Several patients had comorbidities before the fracture: In the hip fracture group, four patients had cancer, three had stroke, and two had rheumatoid arthritis; there were 2, 3, and 0 in the vertebral fracture group, and 1, 2, and 1 in the wrist fracture group, respectively. Among patients with vertebral fractures, the fracture level was defined at the T9, T11, T12, L1, L2, and L3 vertebra in 2, 3, 8, 11, 7, and 4 patients, respectively. Four patients had prevalent lumbar fractures.

All patients with hip fractures, 22 of those with vertebral fractures, and 25 of those with wrist fractures were admitted to the hospital for treatment. Mean durations of hospitali-

Table 1 Characteristics of patients

	Hip fracture	Vertebral fracture	Wrist fracture	p-value[a]
Number of patients	37	35	50	
Age(years)	76.1±9.8*	72.6±10.1	68.6±10.3	0.002
Range	49–91	48–91	49–88	
Body height (cm)	148.8±6.2	152.4±7.4	150.5±6.7	0.255
Body weight (kg)	45.8±8.4*	48.7±2.4	52.2±8.0	0.011
Body mass index (kg/m^2)	20.7±3.3*	21.1±2.4	23.0±3.2	0.010
Previous fracture (*n*)	9	8	12	
Surgical treatment (*n*)	37	0	22	
Hospitalized (*n*)	37	22	25	
Receiving anti-osteoporosis drug[b] (*n*)	3, 11 (11), 7 (13)	5, 21 (5), 16 (10)	4, 18 (7), 16 (10)	
Receiving NSAIDS[c] (*n*)	4 (8), 4 (8), 2 (11)	7 (1), 6 (5), 4 (9)	7 (1), 6 (5), 4 (9)	

Data are means±SD

[*] $p<0.05$ vs. wrist fracture by Tukey's test

[a] *p* value was calculated by one-way ANOVA

[b] Each number indicates numbers of patient receiving anti-osteoporosis drug before the fracture, at 6 months, and 1 year after the fracture, respectively (numbers of unknown patients are presented in parentheses)

[c] Each number indicates numbers of patient receiving nonsteroidal anti-inflammatory drug at 3 months, 6 months, and 1 year after the fracture, respectively (numbers of unknown patients are presented in parentheses)

zation for primary treatment were 61.3 days (range 9–157, median 56.0), 25.9 days (7–58, 22.0), and 16.2 days (1–48, 14.0) in the hip, vertebral, and wrist fracture groups, respectively. All patients with hip fractures, none of those with vertebral fractures, and 22 of those with wrist fractures were treated with surgery. The numbers of patients receiving nonsteroidal anti-inflammatory drugs (NSAIDs) are presented in Table 1.

Health-related quality of life

HR-QOL was measured using the EuroQol standard (EQ-5D) [13]. EQ-5D is a generic questionnaire with a visual analogue scale (VAS). Each of the five dimensions or domains of the EQ-5D profile [EQ-5D(profile); mobility, self-care, performance of usual activities, pain/discomfort, and anxiety/depression (not to be confused with clinically diagnosed depression)] is divided into three levels of difficulty: no problem, some problem, or extreme problem. This is expressed as a health profile, and each of the 243 possible health states defined by this profile has been assigned a health utility rating (EQ-5D(utility)) based on data collected from a representative sample of the Japanese general population [14, 15]. The anchor points for EQ-5D(utility) are "perfect health"=1 and "death"=0. Since calculation of the weighted health utility score requires comparison with the general population, we have used the Japanese general population as our comparator. Age-specific normative values (mean±SD) for EQ-5D (utility) have been reported for Japanese women aged 65 to 69 years, 70 to 74 years, 75 to 79 years, 80 to 84 years, and 85 years and over as 0.862±0.167, 0.810±0.187, 0.771±0.182, 0.769±0.173, and 0.684±0.230, respectively [16]. We used these values and calculated the age-adjusted values of EQ-5D (utility) for our patients (since age-specific normative values for Japanese women are available only for those aged 65 and older, age-adjusted QOL values were calculated for patients age 65 years and older).

Baseline questionnaires inquired about prefracture mental status and prefracture comorbidities. When necessary, these questions were asked of patients' relatives. EQ-5D (profile) and VAS (EQ-5D (vas), with "perfect health"=100 and "worst possible health"=0) were prospectively evaluated for the period before the fracture as well as for 2 weeks, 3 months, 6 months, and 1 year after the fracture. Prefracture QOL was evaluated based on the patient's recollection. Questionnaires were self-completed, but assistance was provided by relatives if necessary because of pain or hearing difficulties.

Statistical analysis

Multiple comparisons among groups were performed using Tukey's test after a repeated-measures analysis of variance (ANOVA) for age, body height, body weight, and BMI. Nonparametric multiple comparisons with prefracture values were performed using Dunn's test for EQ-5D (utility). For comparisons between two groups, the Mann–Whitney test was performed. Statistical analysis was performed using SPSS (SPSS II for Windows Version 11.0.1J, SPSS Japan, Tokyo, Japan) and Stat Flex (Version 5, Arteck, Osaka, Japan); $p<0.05$ was considered statistically significant.

Results

EQ-5D(utility)

Prefracture values

Mean values of EQ-5D(utility) for patients with hip, vertebral, and wrist fractures were 0.795, 0.882, and 0.934, respectively (Table 2). EQ-5D(utility) for patients with hip fractures was the lowest among the three groups, and there was a significant difference between the hip fracture and wrist fracture groups ($p<0.01$ by Dunn's test). There were no significant differences before the fracture between fracture types (neck and trochanteric) among patients with hip fractures, thoracic or lumbar fractures among patients with vertebral fractures, or surgical and nonsurgical treatment among patients with wrist fractures. Mean value of EQ-5D (utility) for patients with vertebral fractures admitted to hospital was 0.838 (median 0.887) and that for those not admitted was 0.973 (median 1.000), showing a significant difference ($p=0.024$, by Mann–Whitney). There was no significant difference between these two groups for patients with wrist fractures.

Mean (median) values of age-adjusted EQ-5D(utility) in patients aged 65 years and over were 102.1% (100%), 111.7% (119.7%), and 116.9% (123.5%) for the hip, vertebral, and wrist fracture groups, respectively (Fig. 1).

Sequential changes

Mean values of EQ-5D(utility) for patients with hip fractures at 2 weeks, 3 months, 6 months, and 1 year after the fracture were 0.373, 0.635, 0.634, and 0.680, respectively (Table 2). Those for patients with vertebral fractures were 0.531, 0.758, 0.746, and 0.838, respectively. Those for patients with wrist fractures were 0.717, 0.812, 0.873, and 0.881, respectively.

Among the vertebral fracture patients, there was no significant difference between patients with thoracic and lumbar fractures except at 6 months after the fracture, when EQ-5D(utility) was 0.827 for thoracic and 0.695 for lumbar fractures, with a significant difference ($p=0.028$, by Mann–Whitney). There were no significant differences in EQ-5D (utility) throughout the observational period between neck and trochanteric fractures among patients with hip fractures or between surgical and nonsurgical treatment among patients with wrist fractures. In the vertebral and wrist fracture groups, there were no significant differences in EQ-5D (utility) between patients admitted and not admitted to the hospital at any time after the fracture.

Among the hip and wrist fracture groups at 3 months after the fracture, values of EQ-5D (utility) were significantly lower in patients who received analgesics than in those not receiving analgesics ($p=0.023$ and $p=0.012$, respectively, by Mann–Whitney); this was also the case in

Table 2 Sequential changes in EQ-5D scores for patients with incidental fragility fractures

	Duration after fracture				
	Before fracture	2 weeks	3 months	6 months	1 year
Hip fracture					
N	37	37	37	31	30
Mean±SD	0.795±0.174	0.373±0.270	0.635±0.158	0.634±0.184	0.680±0.244
Median (75% tile, 25% tile)	0.768 (1.000, 0.693)**	0.444 (0.587, 0.115)[a,]***	0.649 (0.721, 0.533)[b,#,]***	0.631 (0.693, 0.577)[a,]***	0.640 (0.902, 0.587)[b,#,]***
Vertebral fracture					
N	35	35	35	31	30
Mean±SD	0.882±0.168	0.531±0.173	0.758±0.176	0.746±0.159	0.838±0.171
Median (75% tile, 25% tile)	1.000 (1.000, 0.768)	0.533 (0.649, 0.473)[a,]***	0.749 (1.000, 0.605)[b]	0.724 (0.768, 0.596)[a,]**	0.768 (1.000, 0.693)
Wrist fracture					
N	50	50	50	43	40
Mean±SD	0.934±0.125	0.717±0.137	0.812±0.184	0.873±0.150	0.881±0.148
Median (75% tile, 25% tile)	1.000 (1.000, 0.947)	0.679 (0.775, 0.608)[a]	0.768 (1.000, 0.724)[a]	1.000 (1.000, 0.724)	1.000 (1.000, 0.768)

*$p<0.05$
**$p<0.01$
***$p<0.001$ vs. wrist fracture
#$p<0.05$ vs. vertebral fracture (by Dunn's test)
[a]$p<0.01$
[b]$p<0.05$ vs. values before fracture (by Dunn's test)

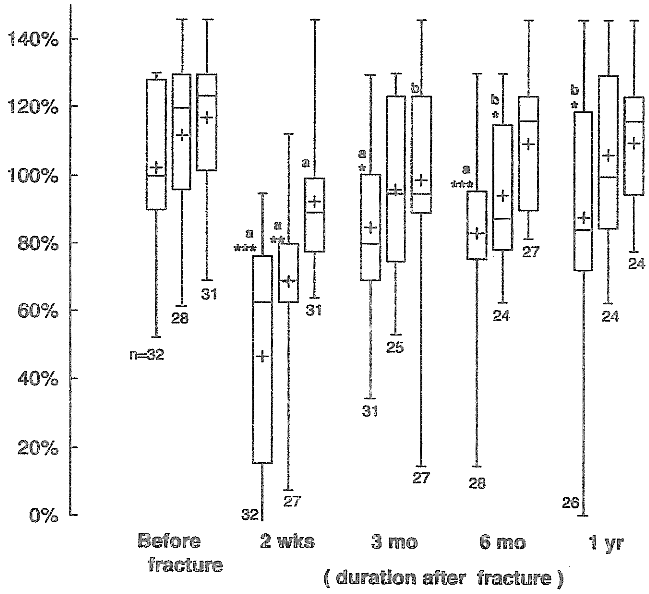

Fig. 1 Sequential changes in age-adjusted EQ-5D (utility) for patients aged 65 years and over. *Left box* represents hip fracture group, *middle box* represents vertebral fracture group, and *right box* represents wrist fracture group at each observational point (before fracture, at 2 weeks, 3 months, 6 months, and 1 year after the fracture). Data points represent EQ-5D (utility) age-adjusted to values for the Japanese general population aged 65 years and over. The *vertical bars* indicate the range (maximum and minimum), and the horizontal boundaries of the *boxes* represent the first quartile, median, and third quartile. +indicates mean values. *$p<0.05$, **$p<0.01$, ***$p<0.001$ vs. wrist fracture (by Dunn's test). *a* $p<0.01$, *b* $p<0.05$ vs. values before fracture (by Dunn's test)

the vertebral fracture group at 1 year after the fracture ($p=0.031$). However, there were no significant differences at the other observational points from 3 months to 1 year after the fracture. There were no significant differences in EQ-5D (utility) throughout the observational period between patients administered and not administered anti-osteoporosis drugs in all fracture groups.

Percent changes (means±SD) of EQ-5D(utility) from baseline (before fracture) for patients with hip fracture at 2 weeks, 3 months, 6 months, and 1 year after the fracture were −55.1±32.9% (range from −112.9% to 0%), −19.1±22.8 (−55.6 to 10.6), −16.6±24.8 (−80.5 to 31.9), and −12.9±33.1 (−99.6 to 70.4), respectively. Those for vertebral fractures were −37.5±23.6 (−94.8 to 0.0), −13.8±22.3 (−54.1 to 30.2), −13.2±25.7 (−42.3 to 87.6), and −7.8±17.3 (−40.4 to 30.2), respectively. Those for wrist fractures were −22.2±16.2 (−54.1 to 30.2), −12.9±19.4 (−88.5 to 29.2), −5.9±18.2 (−39.2 to 38.1), and −5.8±15.9 (−36.9 to 44.3), respectively.

The reduction of EQ-5D(utility) during the observational period was greatest in the hip fracture group. In the wrist fracture group, EQ-5D (utility) at 6 months after the fracture showed recovery; however, values in the hip and vertebral fracture groups were significantly lower than before the fracture. One year after the fracture, EQ-5D (utility), values were not significantly different from prefracture values in the vertebral and wrist fracture groups, but remained significantly lower in the hip fracture group (Table 2).

Changes in age-adjusted EQ-5D (utility) for patients aged 65 years and over are presented in Fig. 1. The reduction of age-adjusted EQ-5D (utility) during the observational period was greatest in the hip fracture group; mean (median) values of percent changes from baseline at 2 weeks, 3 months, 6 months, and 1 year after the fracture were 46.9%(62.8%), 84.8%(80.1%), 83.2%(83.1%), and 88.1%(84.4%), respectively.

EQ-5D (profile)

Among the groups, the proportion of patients reporting problems in each of the five health domains of EQ-5D (profile) was higher in the hip fracture group than in the other two groups (Fig. 2). The difference between the hip fracture and other groups was most evident in the "mobility" and "usual activity" domains.

EQ-5D (vas)

Changes in EQ-5D (vas) were similar to those in EQ-5D (utility) (Fig. 3). There were no significant differences in EQ-5D (vas) between neck and trochanteric fractures among patients with hip fractures, between thoracic and lumbar fractures among patients with vertebral fractures, or between surgical and nonsurgical treatment among patients with wrist fractures throughout the observational period.

Discussion

The present study demonstrates that among clinical fragility fractures, hip and vertebral fractures have the highest impact on patients' HR-QOL. HR-QOL indices of these two fractures did not return to prefracture levels even one full year after the fracture occurrence. These findings are in accordance with previous reports [9, 17–19]. This is the first report to describe the prospective measurement of HR-QOL in Asian patients with incident fragility fractures.

Measurement of the effects of diseases on HR-QOL is of importance, since it allows a broad assessment of health domains not always captured in standard clinical or disease-specific assessments [20]. The EQ-5D is a generic measure of health status developed by the EuroQol Group and was originally standardized for use in England and Northern Europe. Translations have been undertaken in several languages; the official Japanese version of the EQ-5D instrument was developed in May 1998 (Japanese EuroQol Translation Team, 1998) [15]. EQ-5D is a self-completed,

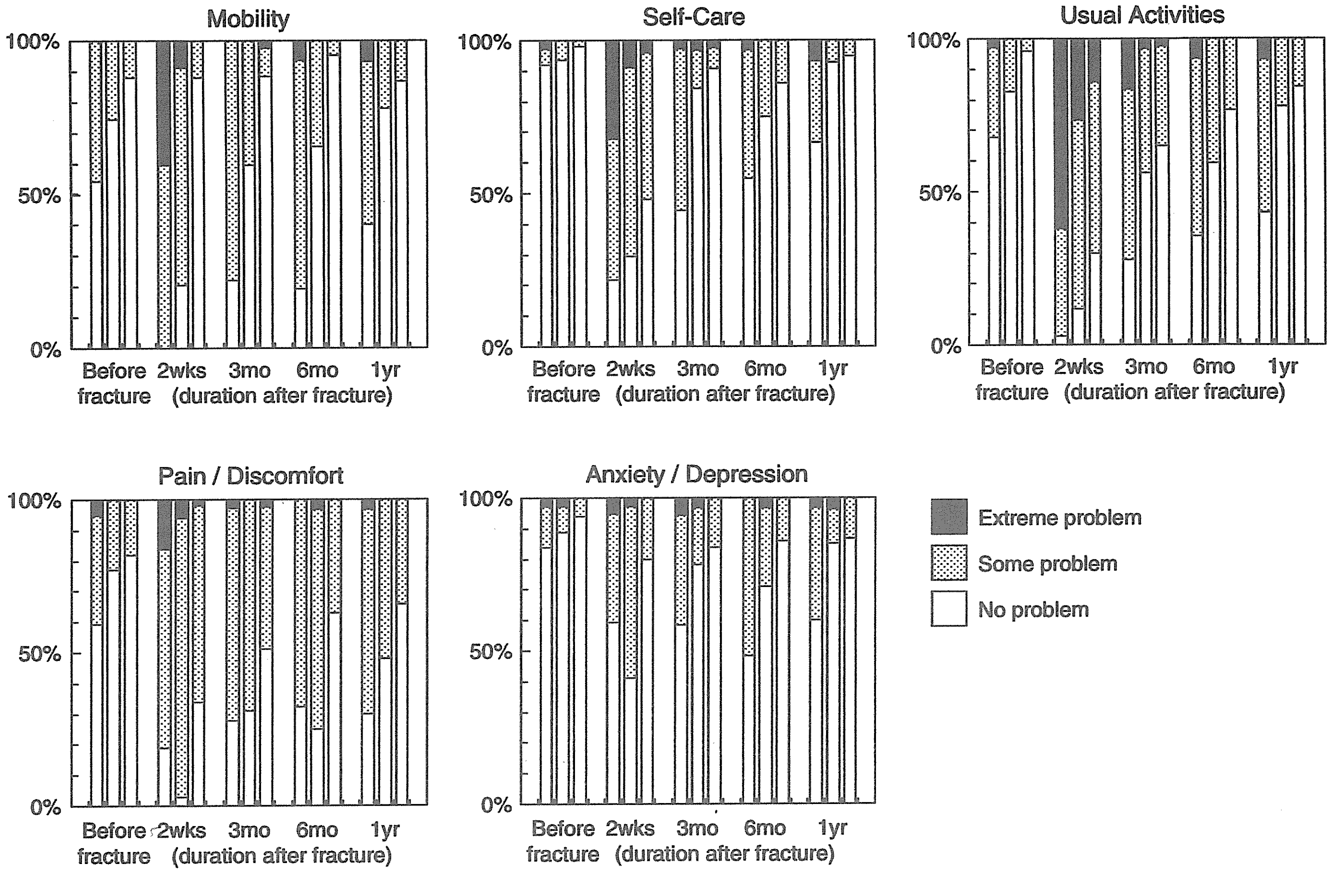

Fig. 2 Sequential changes in health profile. *Left box* represents hip fracture group, *middle box* represents vertebral fracture group, and *right box* represents wrist fracture group at each observational point (before fracture, at 2 weeks, 3 months, 6 months, and 1 year after the fracture). Data points represent the percentage of patients reporting no problem, some problems, or extreme problems in each domain of EQ-5D profile

easy-to-use questionnaire that provides a health profile with a VAS [20]. Because this study targeted aged patients, we adopted EQ-5D for its simplicity and ease of use. EQ-5D also allows measurement of health utility, which forms the basis for estimation of quality-adjusted life years (QALY) [13].

Hip fractures cause acute pain and loss of function and nearly always require surgery. Recovery is slow and rehabilitation is often incomplete. We reported that the ratio of patients who could go out with assistance was 69% before hip fracture, whereas only 40% could go out at 1 year after the fracture [21]. Therefore, a considerable reduction of HR-QOL, as well as impairment of physical function, occurs after hip fractures [8, 9, 22–24]. A prospective, case-control study showed significant reductions of HR-QOL in the SF-36 domains: −51% for Physical Function, −24% for Vitality, and −26% for Social Function at 3 months after fracture [25]. Tidermark et al. demonstrated that EQ-5D scores decreased from 0.78 before the fracture to 0.59 at 4 months after surgery, and further decreased to 0.51 at 17 months after surgery, in relatively healthy elderly patients treated with internal fixation [10]. Our data from before and 3 months after fracture were very

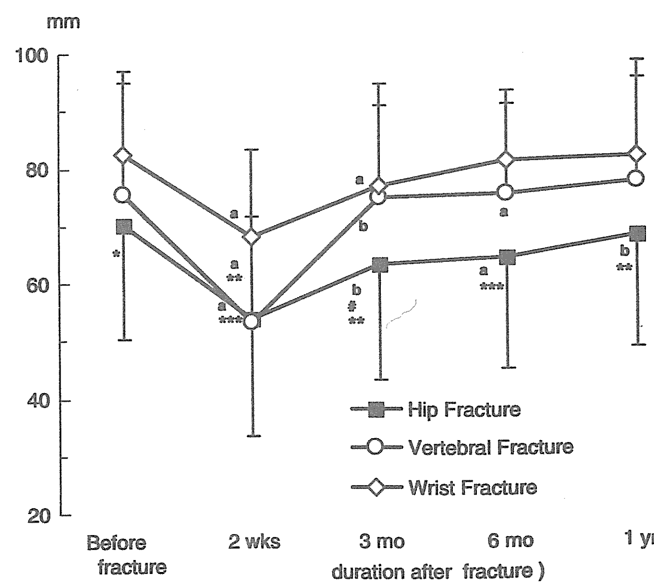

Fig. 3 Sequential changes in VAS. Data represent means±SD. *$p<0.05$, **$p<0.01$, ***$p<0.001$ vs. wrist fracture, #$p<0.05$ vs. vertebral fracture (Dunn's test). *a* $p<0.01$, *b* $p<0.05$ vs. values before fracture (Dunn's test)

close to the scores of Tidermark et al. from before and 4 months after fracture, indicating that the impact of hip fracture on HR-QOL dose not differ much between the two populations in spite of the cultural differences.

The morbidity of vertebral fractures varies from mild cases, with only slight pain, to severe and multiple fracture cases with acute pain and many reoccurrences. Several studies have investigated the impact of prevalent or incident vertebral fractures on HR-QOL. A progressive worsening trend in HR-QOL with an increasing number of prevalent fractures has been observed [26]. Incident vertebral fractures have an adverse impact on HR-QOL regardless of symptomatology, and QOL score changes for patients with subclinical (absence of symptoms) vertebral fractures were intermediate between those for patients with clinical (symptomatic) vertebral fractures and patients without incident vertebral fractures [19]. The adverse health impact was most marked among patients with incident fractures who had a prevalent vertebral fracture, suggesting that the effect of multiple fractures on HR-QOL is cumulative [19, 27]. In the current study, only clinical fractures were evaluated, and we did not find any difference in the impact on HR-QOL between patients with and without prevalent vertebral fractures. This might be due to the small number of patients; only four patients presented with prevalent vertebral fractures. We showed a statistical difference in HR-QOL between patients with thoracic and lumbar fractures that is in agreement with previous studies [26]. This difference occurs because lumbar fractures are more often symptomatic than thoracic fractures, due to stabilization of the thoracic spine by the rib cage.

Wrist fractures cause pain and loss of function, but fracture healing and regain of function are usually favorable. Dolan et al. observed considerable loss in the first 3 months, but recovery was fast, and the HR-QOL impairment was small [28]; these findings are compatible with our observations.

In a previous study, each of the five dimensions or domains of the EQ-5D (profile) were collected from a representative sample of the Japanese general population aged 65 years and over [16]. The percentages reporting "some" or "extreme" problems were 29.2% and 0.8% for mobility, 6.0% and 1.5% for self-care, 21.5% and 3.4% for usual activity, 40.3% and 2.0% for pain/discomfort, and 15.5% and 1.1% for anxiety/depression, respectively. Compared with these data, the percentage of patients complaining of "some" or "extreme" problems in each domain seemed to recover to normal levels by 6 months in the wrist fracture group, and by 1 year in the vertebral fracture group; however, in the hip fracture group, a substantially higher percentage of patients complained of "some" or "extreme" problems in all domains throughout the observational period.

In North America, QALY loss in the first year after hip fracture was 0.4681, mainly due to the hospital and nursing home stay, whereas the QALY loss after a vertebral fracture with severe pain was up to 0.5000 [29, 30]. This type of analysis is indispensable, but has not been done in Japan, since to date, there have been no data available to estimate QALY loss after fragility fractures among the Japanese population. The data presented in this study could make possible a cost-utility analysis of osteoporosis therapies.

This study had several limitations. First, the number of the subjects was limited, which might introduce some sampling biases. In this study, patients who could not complete the EQ-5D questionnaire were not enrolled, which could lead to overestimation of HR-QOL scores for hip and vertebral fracture patients. Second, the dropout rate could have affected the results. Most patients who dropped out were in the wrist fracture group; many of them fully recovered and thereafter lost contact. This could have led to underestimation of HR-QOL scores. Third, the severity of the fracture may affect QOL status, i.e., patients with more severe fractures may become more pessimistic, while patients with slight fractures may be more optimistic even at the time of recollection. Therefore, patients with more severe disabling fractures may overestimate prefracture quality of life. Hospitalization or residence at the evaluation point might affect the HR-QOL scores: hospitalized patients showed lower prefracture QOL scores for vertebral fractures, and patients who received analgesics tended to have lower QOL scores. The findings could represent possible biases in the pre- and postfracture QOL assessment. Finally, further studies are required to assess the influence of comorbidity on HR-QOL scores in patients with osteoporosis-related fractures.

In conclusion, HR-QOL data obtained in this study showed that loss of quality of life is more severe after hip or vertebral fractures than after wrist fracture. HR-QOL was not completely restored in patients suffering from hip fracture. Collectively, these data suggest that prevention of osteoporotic fractures is of the utmost importance for maintaining quality of life.

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Conflicts of interest None.

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Comparison of outcomes and costs after hip fracture surgery in three hospitals that have different care systems in Japan

Akiko Kondo[a,*], Brenda K. Zierler[b], Yayoi Isokawa[c], Hiroshi Hagino[d,e], Yayoi Ito[f]

[a] Department of Nursing, College of Life and Health Sciences, Chubu University, 1200 Matsumoto-cho, Kasugai-city, Aichi-ken 487-8501, Japan
[b] Department of Biobehavioral Nursing and Health Systems, University of Washington, School of Nursing, Seattle, WA, USA
[c] Orthopedic Department, Juzenkai Hospital, Nagasaki, Japan
[d] Department of Fundamental Nursing, School of Health Science, Faculty of Medicine, Tottori University, Yonago, Japan
[e] Rehabilitation Division, Tottori University Hospital, Yonago, Japan
[f] Neurological Surgery, Tokyo Labour Welfare Hospital, Tokyo Japan

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ABSTRACT

Hip fracture is a medical and socioeconomic problem among the 65 years and older population in Japan. Length of hospital stay in Japan is much longer than other developed countries, and the Japanese government has tried to reduce length of stay in order to reduce medical expenditures.

The objective of this study was to compare outcomes and costs of health care services for patients with hip fracture surgery among three hospitals with different care systems in Japan. Medical records of patients who were 65 years or older, who had hip fracture surgery within the past 2.5 years were reviewed. A questionnaire was sent to patients and/or their family members to ask patients' health outcomes and approximate costs of care after discharge. Initial hospitalization costs, costs of subsequent transitional care hospital, elders' care services and family's salary loss were estimated and compared among the three hospitals after adjusting for patients' characteristics and treatments.

The response rate of the questionnaire was 70% ($n = 149/211$). Patients' outcomes (mortality and ambulatory ability) after discharge were comparable. Hospitals that had shorter lengths of stay reduced costs to themselves, but did not reduce overall costs including care after discharge; however, costs were even higher because patients stayed in subsequent hospitals longer and/or used more elders' care services. Reducing the length of stay in the initial acute care hospitals could be just a method of cost-shifting to subsequent care services and is unlikely to bring an overall cost-savings to the Japanese health care system.

1. Introduction

Hip fracture is a medical and socioeconomic problem among the 65 years and older population in Japan, and the numbers of hip fractures are rapidly increasing [1]. In Japan, the national medical care expenditures have been increasing each year with the aging of the population, which has affected the national economy [2,3]. The average lengths of stay (LOS) for hip fractures in acute care hospitals including rehabilitation in Japan was 68 days in 2002 [4], compared to the acute care LOS of 6.2–6.9 days in the United States (U.S.) [5] and the LOS including rehabilitation of 23 days in the United Kingdom [6]. Therefore, the Japanese government has deemed the LOS to be unnecessarily long, and

* Corresponding author. Tel.: +81 568 519054; fax: +81 20 46635779.
E-mail addresses: fwjh1872@yahoo.co.jp (A. Kondo), brendaz@u.washington.edu (B.K. Zierler), yayoinosoraha@hotmail.com (Y. Isokawa), hagino@grape.med.tottori-u.ac.jp (H. Hagino), tokyoh-nurse@tokyoh.rofuku.go.jp (Y. Ito).

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