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Risk factors for osteoporosis in Asia

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The aging society in Asia

The 20th century was the era in which human beings began to experience genuine longevity. In industrialized countries, especially, the trends for a low birth rate and low death rate progress. As a result, the elderly population increases and the average life expectancy has lengthened considerably [1].

Aging of the population is expected to progress globally in all regions and all countries. This is not a phenomenon restricted to industrialized countries, and the aging of the population is also occurring in developing and undeveloped countries. This trend is particularly clear in Asian regions and countries. The total population in Asia is estimated to increase 1.43 times over the period from 1995 to 2025, and will account for 60% of the world's population. The proportion of the population over 65 years of age will increase from 5.3% in 1995 to 9.3% in 2025, which is an approximate 1.8-fold increase [2] (Table 1).

Moreover, the aging of the population in Asian regions is predicted to advance at a remarkable rate. In 2025, Asia will have 57% of the world's population over 65 years of age, up from 49% in 1995. Table 2 shows the changes in and future estimates of the population over 65 years of age in major Asian countries over 100 years from 1950 to 2050. In 2050, all countries will have entered the so-called ultra-aging society, with Japan having aged population of 30.2%, Singapore 23.7%, Korea 21.1%, Thailand 19.0% and China 18.2% [3].

Japan has the highest life expectancy in the world. The rate of aging of Japan's population is unlike that in industrialized Western countries. It took only 24 years for Japan to double its population at age 65 years and over from 7% in 1970 to 14% in 1994. Compared with the 69 years taken in the US, 46 years in the UK, and 82 years in Sweden, the aging of the population in Japan has proceeded at an extremely high speed. What is alarming is that judging from the Japanese experience, other Asian nations are also likely to be confronted with an aging society within a short period of time.

The large-scale and rapid development of an aging society expected in Asian regions and nations also produces a disease structure specific to an aging society. In particular, osteoporosis and its associated fractures are major public health problems that are attracting much concern. Figure 1 shows the number of hip fractures in 1990 worldwide and the projected numbers in 2025 and 2050 according to Cooper et al. [4]. The numbers are increasing rapidly in the Asian region, both in men and women, and more than 200 million women are estimated to suffer from hip fractures in 2050.

Risk factors for osteopenia and osteoporosis

Osteoporosis is a one of the typical diseases that develops from a long-standing lifestyle induced by multifaceted factors. However, to identify the risk factors involved in the development of osteoporosis and the relative contributions of these risk factors in a strict sense is extremely difficult. The main reason for this is that osteoporosis is not a single disease but, rather, is a syndrome (osteoporosis syndrome) with various characteristics, including: (1) a reduction in bone mass; (2) a deterioration of the bone microstructure; (3) an

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Table 1. Population number and percentage of the population over 65 years of age in major world areas, 1995–2025

	1995	2025
World	5716426 (6.5)	8294341 (9.8)
Africa	728074 (3.2)	1495772 (4.2)
Asia	3457957 (5.3)	4959987 (9.3)
Europe	726999 (13.8)	718203 (19.8)
Latin America	482005 (5.2)	709785 (9.7)
South America	292841 (12.6)	369566 (18.1)
Oceania	28549 (9.5)	41027 (13.7)
Asia/World	60.50%	59.80%

Data are taken from the United Nations [2] and show the number of people, with percentages given in parentheses

Table 2. Percentage increase in the population over 65 years of age in Asian countries in the past (1950), present (1995) and future (2050)

	1950	1995	2050
China	4.48	6.11	18.17
Indonesia	3.96	4.31	15.75
Japan	4.94	14.13	30.22
Korea	3.05	5.61	21.05
Philippines	3.59	3.39	13.32
Singapore	2.35	6.74	23.67
Thailand	3.03	4.99	19.04
Vietnam	3.90	4.87	14.58

Data are taken from the United Nations [3]

increase in the fragility of bone tissue as a whole; (4) pain; and (5) susceptibility to fracture. A diagnosis taking into consideration all these factors is virtually impossible. Therefore, to identity all the risk factors for osteoporosis, defined in a strict sense, is impossible at the present stage.

Currently, analyses of risk factors have focused on the characteristics of low bone mass, and fractures associated with osteoporosis. Recent studies have clearly shown that not all risk factors for reduced bone mass are necessarily risk factors for osteoporosis. Some factors that are protective factors against a reduction in bone mass may be risk factors for fracture (and vice versa). It is important to understand this possibility when determining strategies for the prevention of osteoporosis or fractures.

Bone mass (or bone mineral density) is unmistakably the most important risk factor for osteoporosis and fracture. Certainly, bone strength, which indicates resistance to fracture, depends strongly on bone mass. However, in addition to bone mineral density, other factors also exert an influence on bone quality or bone strength, and these include the distribution of bone trabeculae and the whole structure of cancellous tissue.

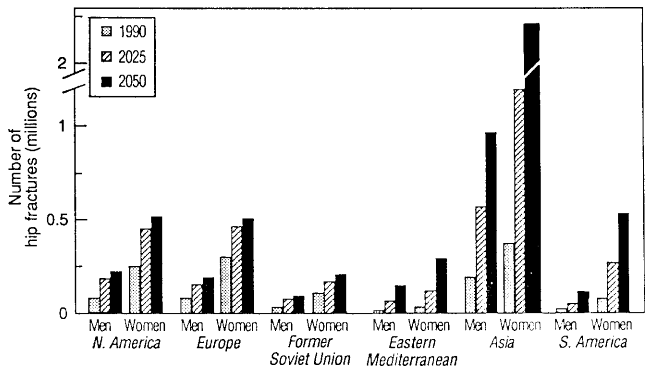

Fig. 1. Estimated number of fractures for men and women in different regions of the world in 1990, 2025 and 2050. Original data are from Cooper et al. [4] and have been modified by the World Health Organization [57]

Table 3. Risk factors for osteoporosis

Individual factors (host factors)
1. Race
2. Heredity and constitution (family history)
3. Sex (female > male)
4. Age (postmenopausal women in particular)
5. Body build (slender, small, and thin persons)

Nutritional factors
1. Calcium deficiency
2. Alcohol and smoking
3. Excessive intake of salt and phosphorus
4. Weight loss due to extreme weight control (inappropriate diet)
5. Insufficient exposure to sunlight, vitamin D deficiency

Physical factors
1. Insufficient exercise (long-term bedridden)
2. Muscle paralysis (by stroke etc.)
3. Decreases in exercise capacity
4. Zero gravity (astronauts)

Disease- or drug-related factors
1. Premenopausal overiectomy, or hypogenitalism
2. Gastrectomy
3. Anorexia nervosa
4. Steroid use

Many factors are known to be risk factors for bone mass reduction. As shown in Table 3, invariable factors, such as sex and age, and variable factors, such as lifestyle, including nutrition and exercise, are involved. These risk factors do not simply affect bone mass in a parallel manner and at constant levels throughout life, but they exert their effects on bone mass in a complicated and intertwoven manner, stronger at times and weaker at others, depending on the life stage or the natural history of bone mass development (Fig. 2). The present article will discuss, in particular, osteoporosis candidate gene polymorphism as a genetic factor and

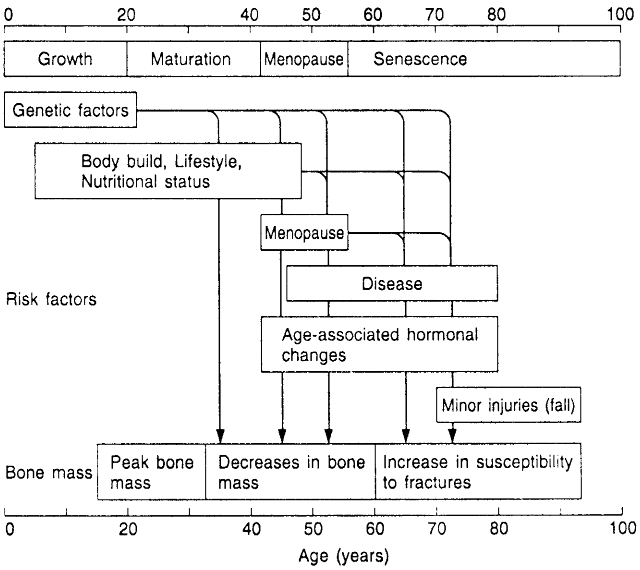

Fig. 2. Accumulation of risk factors for osteoporosis over time. From Suzuki [5], with permission

calcium intake as a lifestyle factor, centering on research in Asia.

Genetic factors

There are racial differences in bone mass. It is generally considered that the black race has a high bone mass, while Asians, including Japanese, have a low bone mass.

With regard to racial differences in osteoporosis, the incidence of fractures among races has been recognized to be in the order of caucasians > Asians > blacks people [6]. In practice, it is necessary to also consider ethnic differences, such as differences in culture, religion, dietary habits, living environment and geographic factors. When considering risk factors for and the prevention of osteoporosis, ethnic difference is an important factor [7,8].

Even among Asians, bone mineral density has been reported to be higher in Taiwanese than in Japanese or Koreans [9]. A comparative study of the incidence of hip fractures among native Japanese living on Okinawa, Japanese Americans living on Oahu, Hawaii, and various American caucasians has shown that the age-specific and cumulative (age 50–84 years) hip fracture rate among people of Japanese ancestry was approximately half that of caucasians for both sexes [10]. Among the Japanese in this study, although the diet and other cultural attributes of the group living in Oahu, Hawai, have become more westernized than those of people living in Okinawa, there was no significant difference in the hip fracture rate between Oahu and Okinawa Japanese. One of the reasons for this similar and low incidence of hip fractures among Oahu and Okinawa Japanese is likely to be that both groups have a similar genetic constitution. Although the environment for these two Japanese populations is very different, they are relatively homogeneous genetically.

Recently, DNA technology has been used in the analysis of genetic effects on bone mass. Because vitamin D is one of the major regulatory factors for bone formation, polymorphism of the vitamin D receptor (VDR) gene also plays an important role in the genetic regulation of bone mass. Morrison et al. have reported that the pattern of polymorphism of the VDR genotypes (BB, Bb, bb) correlates with bone mass and serum osteocalcin, and that individuals with the BB genotype exhibit a low bone mass, both in twins and in the general population [11]. This work has opened up new possibilities of screening risk factors for osteoporosis from a genetic point of view. However, the frequencies of VDR genotypes, like polymorphisms of other genes, are speculated to have racial differences. In actual fact, the frequency of the BB haplotype that correlates with low bone mineral density is 1%–8% in Japanese, which is markedly lower than that in Caucasians (15%–20%) [12,13]. A study in Korea has also reported a low frequency of the BB haplotype of 1.4%–2.8% among Koreans [14]. Similarly, a frequency of less than 1% was reported in Taiwan [15,16]. The extremely low frequencies of the BB haplotype indicate that, at least in Asians, VDR polymorphism has little significance in terms of bone mass. With regard to the relationship between polymorphism of the estrogen receptor gene and bone mineral density, several studies have been conducted in Japan and Korea, mainly targeting pre- and postmenopausal women. While one study has demonstrated a significant relationship [17], another study in Japan has shown that a direct association could be found only in premenopausal women, but not in postmenopausal women [18]. One study conducted in Korea did not show any significant association [19]. Thus, this aspect remains a matter of controversy. In Japan, many studies have reported an association between bone mineral density and various genes involved in bone metabolism and osteoporosis, including the apolipoprotein (Apo) E phenotype [20], parathyroid hormone gene polymorphisms [21], CA repeat polymorphism of the human interleukin (IL)-6 gene [22], human matrix Gla protein polymorphism [23], and CA repeat polymorphism of the human calcium-sensing receptor gene [24]. The genetic factors that determine bone mass are mostly likely to affect younger subjects to different degrees. In this context, the ratio of the contribution of genetic and environmental factors seems to be subject to change according to the life stage of individuals, and genetic influences become weaker in older subjects.

Lifestyle factors

Calcium intake and exercise (or physical activity) are typical and representative lifestyle factors that affect bone mass.

Although many epidemiological studies have been conducted to examine the relationship between calcium intake and bone mass, the results are not necessarily concordant [25]. A lack of reliable methods for the evaluation of calcium intake, problems with sample bias and sample size, and inappropriate handling of confounding factors are the main causes of the inconsistent results obtained in different studies.

In addition, most studies of the relationship between bone mineral density and calcium intake have been conducted in Western countries, and the study populations either had an average daily calcium uptake of more than 800 mg, or consumed milk and dairy products as 50% of the source of calcium uptake. These background factors do not apply to Asian populations. In Japan, for example, the major source of calcium intake is composed of a large variety of foods, such as vegetables, soybeans, fish and shellfish, cereals, and seaweeds [26]. Studies in Asian countries require more than simply investigating the consumption of cow's milk-based milk and dairy products, and analyses of more complicated intake patterns are necessary.

Low calcium intake in Asian populations has been well documented. The daily consumption is always less than 600 mg/day in Japan [26], 640 ± 240 mg/day in Taipei (Taiwan) [16], and 390–500 mg/day in Hong Kong Chinese [27,28], all showing a markedly lower intake compared with Western countries. The consumption of calcium in mainland China is 230–724 mg/day, with regional differences [29]. In Korea, although the recommended daily allowance (RDA) is 700 mg/day, the actual intake has been reported to be 70–80% of the RDA [30]. Most studies on the relationship between calcium intake and bone mineral density in Asia, a region of low calcium intake, are intrapopulation epidemiological surveys [31]. However, one study conducted in China has shown that bone mineral density at the proximal radius is significantly higher in one of the pastoral counties with a higher calcium intake than in the non-pastoral counties [29]. Other intrapopulation studies have shown no significant association between calcium intake and bone mass.

Most studies that report a significant relationship between physical activity and bone mineral density have been conducted in Western countries. Clinical research into the effects of calcium supplementation and exercise on bone mineral density in Hong Kong Chinese reported a 5% increase in bone mineral density in patients with hip fractures [33]. In a study on Japanese elderly subjects using water exercise as an intervention, the bone mineral density in lumbar vertebrae was 0.92% in the control group and a maximum of 2.16% in the intervention group, showing an increase in bone mass [34].

Epidemiology of fracture: incidence, prevalence, and risk factors

Vertebral fractures

Although vertebral fractures are the most common fractures related to osteoporosis, there are relatively few epidemiological and or comparative studies that have examined their incidence and prevalence. One of the reasons for this is that surveys conducted in medical facilities cannot represent the whole picture of the problem. Vertebral fractures may be mild or even asymptomatic, and all patients who have had vertebral fractures do not necessarily visit a medical facility.

Another reason is that there are no internationally recognized or standardized diagnostic criteria for vertebral fractures. Vertebral fractures are conventionally diagnosed by visually assessing vertebral X-ray images. However, diagnosis based on this kind of visual assessment is not only subject to errors between investigators, but is also prone to variations even when examined by the same investigator (repeat assessment after a period of time). Due to the lack of reproducibility, this method is not necessarily suitable for epidemiological studies of regional comparisons or longitudinal studies.

Morphometric diagnosis based on X-ray images of vertebral fractures is available [35,36]. This method determines the index from measured values of the heights of the anterior margin, center of the body and posterior margin of the vertebra. Diagnosis is made based on specific cut-off points for individual nations or regions. Although this kind of quantitative diagnosis has the merit of being objective and reproducible, there are problems over the specificity and sensitivity of diagnosis. Moreover, distinction between vertebral deformity due to fracture and deformity due to spondylitis deformans is extremely difficult.

Prevalence. The prevalence of vertebral fracture in Taiwanese Chinese aged 65 years or older has been reported to be 18% in women and 12% in men [16]. The prevalence in Hong Kong Chinese is high, reaching 30% [37]. After standardizing the definition of vertebral (body) fracture on X-ray, Hong Kong Chinese have the same prevalence of fractures as caucasians in the US [38]. In elderly Singaporean women with compression fractures of the spine, the bone mineral density and vertebral body index were significantly reduced in comparison with normal premenopausal women [39].

Ross et al. have examined the prevalence of vertebral fracutres among US caucasians, native Japanese and Japanese immigrants in Hawaii. They found that the prevalence of vertebral body fracture or vertebral deformity was 25% in the 70–74 year age group and 43% in the 80–84 year age group in native Japanese [40]. This prevalence was higher than that in caucasians or Japanese immigrants in Hawaii. The prevalence in native Japanese was 1.8-fold higher than that in Japanese Americans and 1.2-fold higher than that in US caucasians. Although the prevalence of vertebral fractures is greater among women in Japan, compared with caucasians in the US, the incidence of hip fractures is much lower in Japanese women than in caucasian women. This clear contrast indicates that the risk factors responsible for these two osteoporotic fractures may be different. Another epidemiological study has revealed that the prevalence of vertebral body fracture in age categories in Japanese women living in rural districts was reported to be 2.1% in women aged in their 40s, 10.2% in women aged in their 50s, 14.0% in women aged in their 60s and 44.9% in women aged in their 70s [41]. Huang et al. conducted an international comparative study of the prevalence of vertebral fractures in native Japanese and Japanese–Americans living in Hawaii. They found that the prevalence in native Japanese was higher in all age groups, and this trend was particularly remakable in the advance old-age groups [42].

In Japan, the incidence of thoracic vertebral fractures is decreasing in men and women who were born in more recent years. The incidence is reduced by 0.5 in males and 0.6 in females for each 10-year decrease in the year of birth [43]. Changes in lifestyle, especially dietary habits, in postwar Japanese women is having great effect on their physical build and the menarcheal age or menopausal age, which has probably caused a decrease in the incidence of vertebral fracture. Concerning the lifetime risk of vertebral fractures in Japanese populations, women are estimated to have a 37% risk of having vertebral fractures, and men a 22% risk over their lifetime [44].

Hip fractures

Femoral neck fractures (hip fractures) are the most serious fracture associated with osteoporosis, and are a cause of immobility and a bedridden condition that greatly decrease the quality of life of the elderly. Many epidemiological studies have been performed, including international comparisons, on the incidence and risk factors associated with hip fracture.

In Asia, the incidence of hip fracture is increasing, especially in urbanized areas. In Hong Kong Chinese, the incidence had increased more than two-fold within 20 years [45] (Table 4). In Japan, nationwide surveys on hip fracture were conducted in 1987, 1992, and 1997, and the incidence according to sex and age has been reported [46–48] (Fig. 3). The annual number of hip fractures was 53 000 in the 1987 report, which increased to 76 600 after 5 years in 1992, and further increased to 92 400 in the 1997 survey, showing an increase of 1.7-fold within 10 years. The data for incidence according to sex and age showed great increases in 1992 compared

Table 4. Age-specific hip fracture rates in Hong Kong per 100 000 population (in 1966, 1986, and 1991)

Age group (years)	Men			Women		
	1966	1985	1991	1966	1985	1991
40–49	6	13	9	7	11	6
50–59	16	28	27	22	32	26
60–69	67	54	73	54*	135	112
70–79	224	339	321	173*	501	581
>80	321**	1156	1191	716*	1521	1916*

* $P < 0.05$ compared with 1985 rates
** $P < 0.01$ compared with 1985 rate
Data from Lau [45]

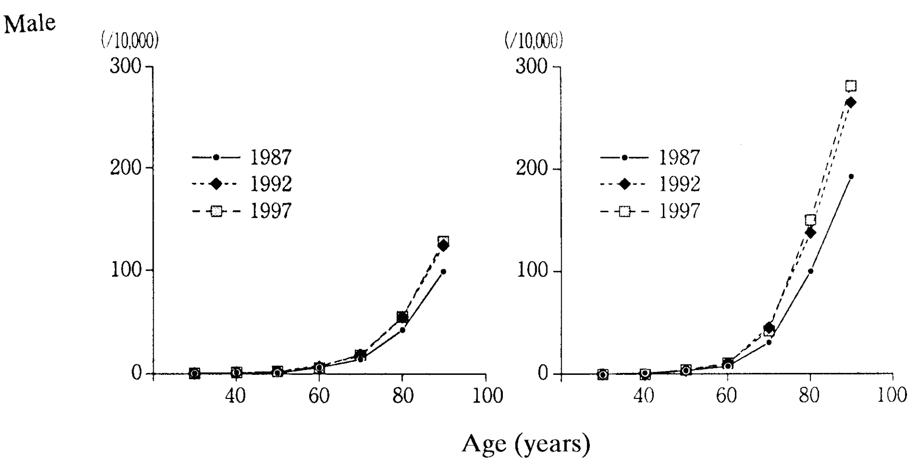

Fig. 3. Incidence of hip fractures in Japan, 1987–1997. From Orimo et al. [48], with permission

with 1987 for both sexes and in all age groups. However, the only increase in 1997 compared 1992 was in the advanced old-age group, aged 80 and above. In Japan, the standardized incidence ratio (number of reported cases/number of expected cases) of hip fracture has been calculated for each district. The ratio was high in western Japan and lower in eastern Japan (Fig. 4). One of the determinants of this regional difference in hip fracture incidence in the Japan is speculated to be the habit of eating *natto* (fermented soybeans), which is rich in vitamin K.

International comparisons of hip fractures have been reported by Schwartz et al. (Table 5). Compared with caucasians and Hispanics, the fracture incidence in Chinese living in Beijing and Hong Kong is low [49]. Considering also the incidence in Japanese women discussed above, the incidence of hip fractures among Asians can be said to be low.

Furthermore, the ongoing Asian Osteoporosis Study has reported that the incidence (per 1000 population) of hip fractures in industrialized cities/nations, such as Hong Kong (3.8) and Singapore (3.9), is higher than that in Thailand (2.5) and Malaysia (1.4) [50].

Risk factors for hip fractures

Numerous risk factors are known for hip fractures. These risk factors are classified by various ways accord-

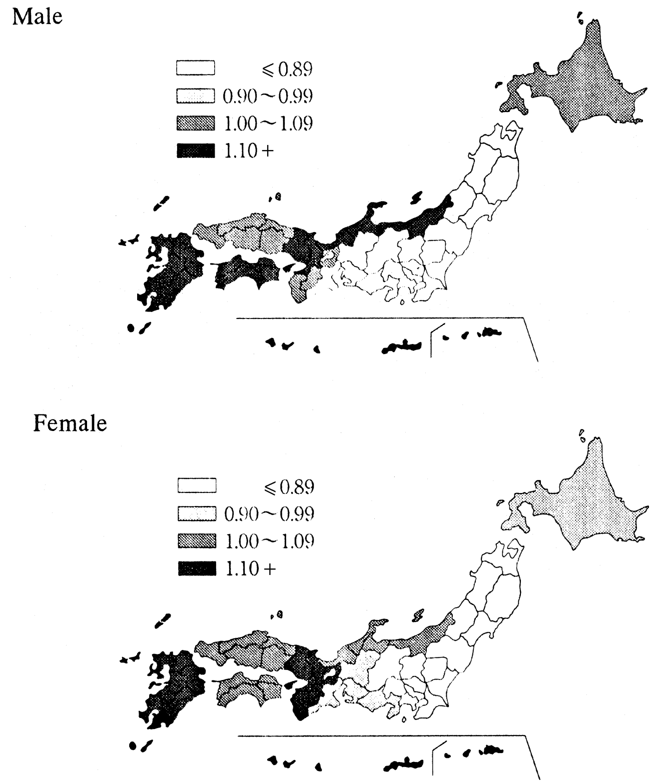

Fig. 4. Differences in the satandardized incidence ratio among districts in the 1997 survey in Japan. From Orimo et al. [48], with permission

Table 5. Hip fracture incidence rates[a] according to age (≧60 years old), gender and study site

Age group (years)	Age-specific incidence rates				Age group (years)	Age-specific incidence rates: Porto Alegra[b]	
	Beijing[b]	Budapest[b]	Hong Kong[c]	Reykjavik		Low estimated[d]	High estimated[d]
Men							
60–64	84.3	128.6	93.1	100.4	60–69	65.6	106.3
65–69	88.2	158.3	126.5	132.7			
70–74	132.5	240.0	254.2	287.2	70–79	97.9	158.5
75–79	160.5	280.2	494.3	563.5			
80–84	281.9	728.3	1014.2	1495.7	80–89	381.5	618.1
85–89	327.8	1498.9	1473.2	1263.8			
90–94	445.2	1872.7		3091.9	90+	705.9	1143.5
95+				6397.0			
Women							
60–64	56.2	84.4	75.0	199.1	60–69	51.7	83.8
65–69	91.2	193.0	194.0	402.5			
70–74	164.1	288.1	438.8	838.0	70–79	327.9	531.2
75–79	141.0	564.8	823.6	1311.1			
80–84	224.2	1100.5	1588.1	1945.3	80–89	779.5	1262.7
85–89	219.2	1652.6	2572.9	3791.9			
90–94	401.0	2217.3		3732.9	90+	1390.2	2252.1
95+				5300.4			

[a] Per 100000 population. Corrected for coding errors, transfers and undercounts in the discharge lists
[b] Census data available only for the 90+ year age group; [c] Census data available only for the 85+ years age group
[d] Low estimate is based on 270 hip fractures confirmed by medical record review, with an 8% increase for hospital without any review; the high estimate includes information from the review of the odds ratio logs
Data are modified from that in the report of Schwartz [49]

Table 6. Comparison of risk factors for hip fractures with the standardized MEDOS questionnaire in Europe and Japan

	Europe[a]	Japan[b]
Area	14 centers from 6 European countries	Three centers in Japan
Period	Over 1 year	1 year
Subjects	Women aged 50 years or more	Men and women in the 65–84 year age group
Cases	2086 cases (mean age 78.1 years)	249 cases (mean age 78.6 years)
Controls	3532 controls (mean age 77.1 years)	498 controls (mean age 78.6 years)
Protective factors (categories)	BMI (>25 kg/m^2) Recreational physical activity (any) Sunlight exposure (>median) Milk intake (highest 90%) Tea consumption (any) Menarche (<12 years) Menopause (>44 years) Mental score (perfect score)	BMI (≧23.1 kg/m^2) Less coffee drinking (≦2 cups/day) Eating fish (≧4 times/week) Moderate alcohol intake (<27 g/day) Type of bed (Japanese *futon*)

MEDOS, Mediterranean Osteoporosis Study
BMI, body mass index
[a] From Johnell et al. [51]
[b] From Suzuki et al. [52]

Table 7. Comparison of risk factors for hip fractures in the recent (1997) two major population-based studies in Japan

	Fujiwara et al. [53]	Suzuki et al. [52]
Area and subjects	Atomic bomb survivors in Hiroshima and Nagasaki 1586 men and 2987 women (mean age 58.5 ± 12.2 years)	Ordinary elderly people from three centers in Japan 129 men and 618 women (mean age 78.6 years)
Method	Cohort study	Case-control study (249 cases and 498 controls)
Survey year	Baseline survey in 1978–1980 Outcome survey in 1992	1994–1995
No. cases	55 (6 men, 49 women)	249 (43 men, 206 women)
Preventive factors (categories)	Large BMI Moderate intake of milk (2–4 drinks/week) No alcohol intake No vertebral fracture	Large BMI (≧23.1 kg/m^2) Less coffee drinking (≦2 cups/day) Eating fish (≧4 times/week) Moderate alcohol intake (<27 g/day) Type of bed (Japanese *futon*)

BMI, body mass index

ing to the prevention strategy for hip fracture, such as "factors capable of improvement", "invariable factors", or "bone-related factors" and "fall-related factors". In actual fact, various factors intertoven in a complicated way to case fractures.

In the Asian Osteoporosis Study, a multicenter study conducted in five Asian countries, load-bearing activity (relative risk (RR) = 1.5; 95% confidence interval (CI) = 1.1–1.2) and a low dietary calcium intake (RR = 1.4; 95% CI = 1.0–2.0 for the lowest quartile) have been reported as risk factors for hip fracture [50].

Table 6 shows the results of a case-control study using a common questionnaire for Japan and European countries Mediterranean Osteoporosis Study (MEDOS) as a part of an international collaborative study [51,52]. The only risk factor common to Japan and the European countries was body mass index (BMI); the larger the BMI, the lower the risk of hip fracture. This result indicates that, with background of geographic and cultural differences between Japan and Europe, there exist also great differences in lifestyle as a risk factor for hip fracture.

Recently, two large-scale population-based studies on the risk factors for hip fracture were conducted in Japan [52,53]. Table 7 compares the findings of the two studies. Once again, BMI is a common protective factor. Alcohol consumption has double effects. Alcohol consumption at an appropriate amount decreases the risk of fracture, while drunkenness due to excessive alcohol consumption increases falls and increases fractures.

Table 8. Results of multiple logistic regression analysis for experiencing falls (≧2) over 5 years

Significant independent variables	χ^2	*P*	Odds ratio	95% CI
Fall experience within 1 year preceding baseline (yes = 1, no = 0)	23.785	0.0001	3.80	2.22–6.49
Preferred walking velocity (m/s)	10.921	0.0010	0.20	0.08–0.52
Skinfold thickness (cm)	7.038	0.0080	0.97	0.94–0.99

Independent variables: sex, age, fall experience within 1 year preceding baseline, self-rated health, Tokyo Metropolitan Institute of Gerontology (TMIG) Index of Competence, eyesight, using glasses, height, weight, body mass index, skinfold thickness, bone mineral density at lumbar spine (L_{2-4}), grip strength, one foot standing time with eyes open and closed, preferred and maximum walking velocity, finger-tapping speed
CI, confidence interval

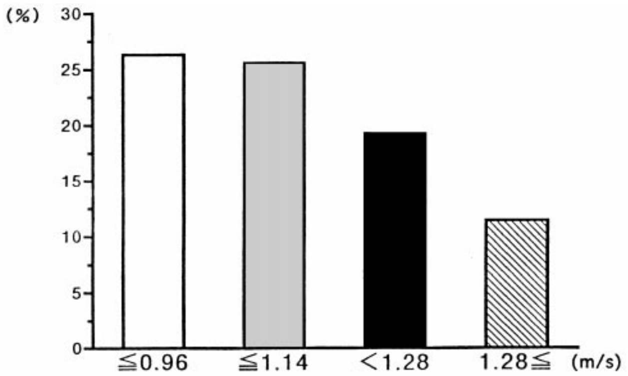

Fig. 5. Association between an experience of falls (≧2) during 5 years (%) and baseline preferred walking velocity (m/s) by quartile. From Suzuki et al. [56], with permission

Various studies conducted in Japan on the risk factors for hip fracture have indicated that the Japanese lifestyle may contribute to prevent fractures [52,54]. This includes sitting and standing on *tatami* mats, sleeping in *futon* beds, eating of fish, the consumption of plant flavonoid-containing *tofu* and vitamin K-rich *natto*.

Falling is the most important direct cause of hip fractures. Research on the risk factors for falls is in progress in the rapidly urbanizing Asian region. In a study of Hong Kong Chinese, a RR of 1.9 (95% CI = 1.2–2.0) has been reported in people who had a history of falls within 1 year compared with those with no such history [45].

In an international comparative study on the frequency of falls among community-dwelling elderly in Japan and Hawaii, the frequencies were similar for both native Japanese and Japanese Hawaiians, and the frequency of caucasians was approximately two-fold higher [54].

From a recent prospective study in Japan, which followed 527 general community-dwelling elderly citizens for 5 years, the risk factors are shown in Table 8. Apart from confirming that a history of falls is an important risk factor, this study also showed that reduced walking speed as a result of a deterioration of physical ability is an extremely significant risk factor for falls [56] (Fig. 5).

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