CHAPTER 1

EPIDEMIOLOGY OF OSTEOPOROSIS

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The epidemiology of osteoporosis is reviewed in this article. Attempts were made to answer the following questions:

1. How should osteoporosis be defined?
2. How can risk factors and BMD measurements be applied to diagnose osteoporosis?
3. How do the rates for osteoporotic fractures vary by country, sex, age and time?
4. What are the cost for osteoporosis in terms of direct and indirect cost, morbidity and mortality?

According to the WHO criteria, osteoporosis can be defined as bone mineral density (BMD) of 2.5 standard deviation or more below the young normal mean. BMD measurements are predictive of fracture risks. Hip fracture is by far the most costly of osteoporotic fracture; and the rates are highest in Caucasians, intermediate in Asians and lowest in Blacks. Risk factors could be used to assist in decision in prescribing BMD measurements.

Research agenda

Further studies aimed at refining the use of risk factors and BMD in predicting fractures.

Further study on the cost-effectiveness of primary and secondary prevention of hip and other fractures.

Studies on the various aspects of epidemiology of osteoporosis in Asian populations.

Summary

Bone mineral density measurements and risk factors can be used to predict osteoporotic fractures. The important osteoporotic fractures are hip fracture, vertebral fracture and forearm fracture. The incidence of hip fracture is highest in Caucasians, intermediate in Asians and lowest in Negroid populations. The incidence of hip fracture increases exponentially with age in both sexes, but remains higher in women than men throughout life. Most vertebral fractures are clinically silent but are associated with much morbidity. Hip fracture is associated with extremely high direct cost in developed countries; and the cost is on the rise in developing countries.

Introduction

Osteoporosis can be defined as a "systematic skeletal disease characterized by low bone mass, and microarchitectural deterioration of bony tissue, with a consequent increase in bone fragility and susceptibility to fractures" [1]. As fragility fractures are the main public health consequence of osteoporosis, diagnostic criteria should be such that they are predictive of fractures.

Definition

In 1994, an expert panel of the World Health Organization recommended thresholds of bone mineral density in women to define osteoporosis [2], that have been widely but not universally accepted by the international

scientific community and by regulatory agencies [3,4,5]. Osteoporosis in postmenopausal Caucasian women is defined as a value of bone mineral density (BMD) or bone mineral content (BMC) more than 2.5 standard deviations below the young average value (Fig 1). Severe osteoporosis (established osteoporosis) uses the same threshold, but in the presence of one or more fragility fractures.

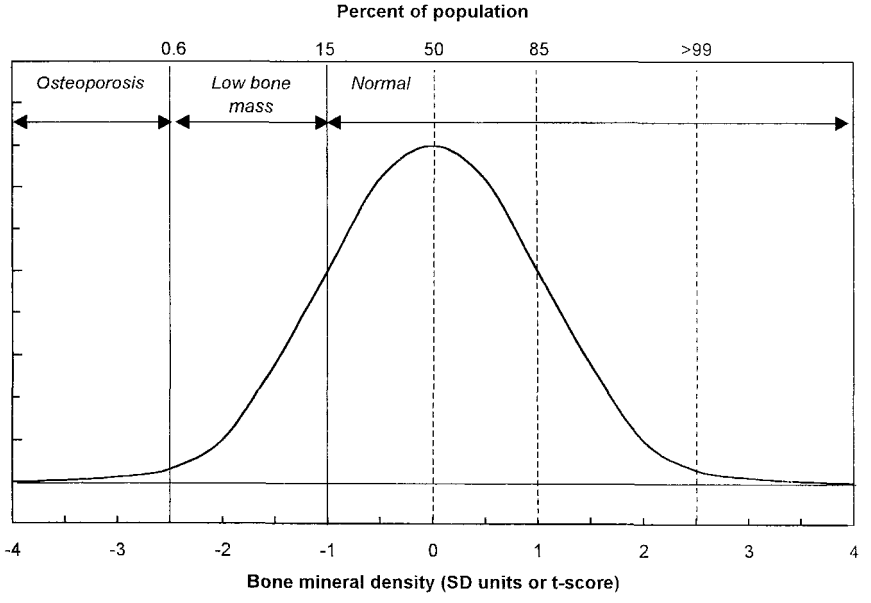

Fig. 1 Diagnostic thresholds for women based on the distribution of bone mineral density in the young healthy female population.

Predicting fracture risk

The association of BMD values and fracture risk has been studied in several large cohort studies. DEXA measurements of the hip, spine, forearm and calcaneus predict the risk of any fragility fracture in older women similarly, each with a relative risk (RR) for any fracture of 1.5, per age-adjusted standard deviation decrease. It is important to note that

the risk of specific types of fractures, especially hip fractures, is more strongly predicted by measuring bone density at that site. The results of the Study of Osteoporotic Fracture showed that the RR for hip fracture is 2.6 for each standard deviation decrease in age-adjusted BMD at the femoral neck, while the RR is 1.5 for mid-radius [6].

BMD measurements are less accurate in predicting absolute risk than the relative risk of fracture, for absolute risk changes marked with age [7]. Absolute risks are important for decision making on therapeutic interventions.

The National Osteoporosis Foundation (NOF) has issued clear guidelines concerning the use of risk factors in predicting fracture [8]. It was stated that risk factors for low bone density have limited value in estimating a women's actual bone density [8]. However, risk factors for fracture can be useful in identifying women at high risk of fractures [9-12].

Five factors were selected by the NOF workgroup as being especially useful in a clinical setting, because they are easily assessible and are relatively common [8]. They were:

- Low bone mineral density;
- History of a prior fracture after age 40;
- History of a fracture at the hip, wrist, or vertebra in a first-degree relative ("family history");
- Being in the lowest quartile in weight;
- Current cigarette smoking.

A simple counting method was recommended by the NOF, in which practitioners will only need to determine whether a woman has had a prior fracture, and then count whether she has none, one, two or more of the remaining three clinical risk factors: family history of fracture, relatively low body weight, and smoking [8]. This method is practicable.

There is a general lack of longitudind data on the relationship between BMD measurements, risk factors and the risk of hip fracture among Asian populations. However, cross-sectional studies demonstrated that risk factors for hip fracture are similar to Caucasian [13]. Moreover, the relationship between the relative risk of hip fracture

and diminishing BMD in Hong Kong Chinese were found to be similar to Caucasians [14]. Hence much of the above recommendation in Caucasian is probably applicable to Asian populations.

Fracture epidemiology

There is no universal definition of osteoporotic fractures. It is logical to consider low energy fractures as being osteoporotic, for osteoporotic individuals are more likely to fracture than their normal counterparts [15]. Fractures of the hip, vertebra and forearm are considered to be osteoporotic fractures. They share common epidemiological features: the incidences are higher in women than in men, increases exponentially with age, and occur at sites with a large proportion of trabecular bone [16].

It is increasingly being recognized, however, that osteoporosis can lead to fracture at other sites. These include fracture of the humerus, ribs, tibia (in women), pelvis and other femoral fractures. Exclusion of such fractures would lead to considerable underestimates in studying the cost of osteoporosis.

Hip fracture

A. Geographical pattern

There is pronounced geographical variation in the incidence of hip fracture, with rates being highest in Caucasians living in North Europe, followed by rates in Caucasian living in North America. The rates are intermediate in Asians and lowest in Black populations (Table 1) [17]. Moreover, the female to male ratio for hip fracture was 3:1 in Caucasians, but 1:1 in Chinese and Bantu.

Table 1. Age-adjusted rate* of hip fracture per 100,000 population for females and males, by ethnic group and year of study

Ethnic group	Site	Year of study	Female	Male	Female to male ratio
Blacks	Maryland, USA	1979-1988	345	191	1.8
	California, USA	1983-1984	241	153	1.6
	Johannesburg, SA	1950-1964	26	29	1.3
Hispanics	California, USA	1983-1984	219	97	2.3
	Texas, USA	1980	305	128	2.4
Asians	Hong Kong	1985	389	196	2.0
	Hong Kong	1965-1967	179	113	1.6
	Tottori, Japan	1986-1987	227	79	2.9
	Okinawa, Japan	1984-1985	325	86	3.8
	California, USA	1983-1984	383	116	3.3
	Hawaii, USA	1979-1981	224	66	3.4
	New Zealand	1973-1976	212	121	1.8
	Singapore	1955-1962	83	111	0.7
Caucasian	Sweden	1972-1981	730	581	1.3
	Kuopio, Finland	1968	280	107	2.6
	Malmo, Sweden	1950-1960	468	153	3.1
	Norway	1983-1984	737	298	2.5
	Edinburgh, Scotland	1978-1979	529	174	3.0
	Oxford, England	1983	603	114	5.3
	California, USA	1983-1984	617	215	2.9
	Hawaii, USA	1979-1981	645	205	3.1
	New Zealand	1973-1976	466	139	3.4

* Rates were age- and gender-adjusted to the 1990 US non-Hispanic Caucasian population.

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The incidence of hip fracture also varies between subjects of the same origins but living in different countries. In Europe, the incidences of hip fracture vary more than 7 folds from one country to another [18,19].

There is some evidence that the incidence of hip fracture is raising rapidly in developing Asian countries. For instance, in Hong Kong, a highly urbanized city in China, the incidence of hip fracture had increased by 200% in the last 3 decades [20]. A recent multi-national study conducted in four Asian countries showed the incidence of hip fracture to be directly proportional to economic developments. The adjusted rates in Hong Kong and Singapore were almost identical to American Caucasians (at 19 per 10,000), while the rate in Thailand and Malaysia were 2/3 and 1/2 of the Hong Kong rates respectively [21]. With rapid economic development and aging of the population, hip fracture will be a major health problem in Asia.

Indeed, Cooper et al [22] had projected that, by the year 2050, more than half of all hip fractures in the world would occur in Asia. The projected number of fractures will be 6.3 million, with 3.2 million in Asia.

B. Secular trends

Recent research suggested that the incidence of hip fracture has experienced either a leveling off or a slightly downturn in North America and Europe. In Malmo, Sweden, Gullberg described a leveling off of hip fracture incidence during the mid 80's [23]. Nungu reported that the age-adjusted incidence of hip fracture remained at around 6/1000 population in the Uppsala country of Sweden in the same period [24].

In the Canton of Vaud, Switzerland, Jequier et al found a slight increase in hip fracture incidence in Swiss men, but not in women, from 1986 to 1991[25]. In Siena, Italy, the incidence of hip fracture increased slightly in men, but not in women from 1980 to 1991 [26].

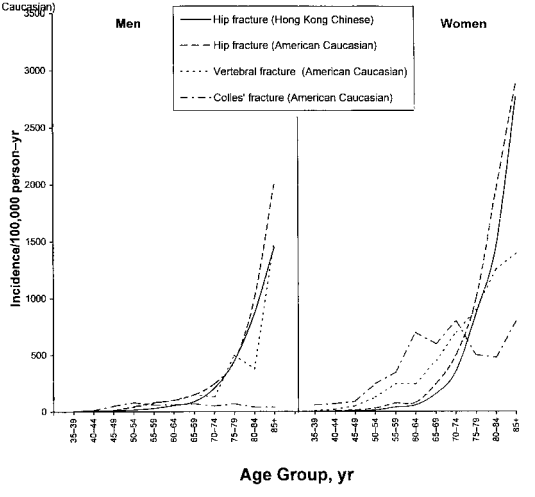
The time trends for hip fracture in the UK from 1968 to 1986 was studied by Spector et al, using data from the Hospital In Patient Enquiry [27]. The standardized admission rates for hip fracture increased tremendously from 1968 to 1980 in both sexes, after which the rates

leveled off. A more recent study by Evans et al confirmed these results [28].

Similar trends have been observed in North America. Melton et al reported a downturn in hip fracture incidence in Rochester Minnesota, between 1984 and 1987 [29]. It is not known if such changes are due to health education, lifestyle changes; or cohort effects. Assuming no increase in hip fracture incidence, the number of hip fracture patients will continue to rise in all continents, as a result of population ageing.

C. Incidence by sex and age

As shown in Figure 2, the incidence rates for hip fracture increased exponentially with ageing in both sexes [30]. The incidence in Rochester rises from 2 per 100,000 person-years among women less than 35 years old to 3,032 per 100,000 for women 85 years old and over [30]. Although the annual incidence among young men was similar to young women, the rates in elderly men were only half of those in elderly women [30]. These patterns were representative of those in Caucasian populations.



(Data for American Caucasians are reproduced with permission from Cooper & Melton, Ref 16)
(Data for Hong Kong Chinese are from: Lau EMC, unpublished data)

Fig. 2 Estimated numbers of hip fractures in 8 geographic regions in 1990, 2025 and 2050.

The age-specific rates of hip fracture in Hong Kong Chinese in 1995 are also presented in Fig 2 (Lau, unpublished data). The changes in the incidence of hip fracture with age are similar to those observed in Rochester. While the incidence were similar in young men and women, an exponential rise was seen in women from 65 years onwards and in men from 70 years old onwards. The rates in elderly women remained to be twice as high as in elderly men. In general, the incidence rates for hip fracture in elderly Chinese men were 75% of those observed in Rochester, while the rates in elderly women approached 90% of those observed in Rochester.

Vertebral fracture

Epidemiological studies on vertebral fractures are hampered by the lack of universally accepted criteria for the definition of vertebral fracture. Moreover, a substantial proportion of vertebral deformities are clinically silent.

A. Geographical pattern

According to radiographic studies, 19-26% of postmenopausal women have a vertebral deformity [31-34]. Vertebral fractures are as frequent in Asians as in white women [35,36]. However, vertebral fractures are less common in African-American [37] and Hispanic population [38].

The incidence of new vertebral fracture has been estimated to be around three times that of hip fracture, with the female to male ratio to be 2:1 [39].

B. Temporal trends

The temporal trends for vertebral fracture are not as well studied as for hip fracture, and the results are mixed. According to Bengnèr et al [40], the prevalence of vertebral fracture increased in Sweden between the periods 1950-1952 and 1982-1983.

Nevertheless, the temporal trend was found to be stable in Rochester, USA, from 1950 to 1989 [41].

Distal forearm fracture

The change in incidence with age for distal forearm fracture is different from fractures of the hip and vertebra. Study results from the Mayo clinic suggested that incidence rates increased linearly from age 40-65 years and then stabilized [30]. However, in men, the incidence remained relatively constant between 20 to 80 years. The female to male ratio for forearm fracture was 4 to 1. This ratio was much larger than that of 2 to 1 for vertebral and hip fracture.

The reasons why the incidence of forearm fracture plateaus with age are unknown. Nevitt and Cummings [42] proposed that elderly women have a slower gait and impaired neuromuscular coordination, and are hence more likely to fall backwards to land on their hip. On the other hand, younger women tended to fall on their outstretched arms. The changes in the incidence of forearm fracture with age concur with the pattern of age-related bone loss [43].

The international pattern for forearm fracture is not well described. There is some evidence to suggest that forearm fracture is much less frequent in Asian [44] and Black [45] population than Caucasians.

Socio-economic impact of osteoporosis

Mortality

The mortality attributable to osteoporosis results largely from hip fractures. Hip fracture causes a 12% to 20% reduction in expected survival [46]. Hospital-based studies showed that mortality rate was higher in men, older patients and in non-white populations [46]. Such observations can be explained by the difference in the prevalence of co-morbidity in population subgroups [47].

Morbidity and quality of life

Osteoporotic fractures cause varying degrees of morbidity. Colles' fractures have only short-term consequences, while hip fracture causes much disability. Many hip fracture patients become permanently disabled. Up to a third of hip fracture patients become totally independent, necessitating institutionalization [48].

The morbidity caused by vertebral fracture varies with the frequency of fractures. Multiple fractures typically cause the most pain and disability. Ettinger et al, demonstrated that vertebral fracture caused significant back pain, disability and height loss in Americans [49,50].

The effects of vertebral fracture on back pain and low morale were consistently demonstrated in Chinese men and women [51].

Costs of osteoporosis

Studies in various countries showed that the costs of osteoporosis are very substantial. Hip fracture is a major cause of hospital admission in the elderly. The acute care cost associated with hip fracture is tremendous in all developed countries. In the USA, the direct cost of hip fractures was around US$13.8 billion in 1995 [52]. In the UK, the direct for hip fracture was £942 million per year in 1998 [53]. The predicted annual treatment costs in Australia for atraumatic fractures occurring in subjects ≥60 yeas was A$779 million (or approximately A$44 million per million of population per annum) [54]. The majority of direct cost (95%) were incurred by hospitalized patients and related to hospital and rehabilitation cost [54]. In 1996, the acute hospital care cost of hip fracture per annum amounted to 1% of the total hospital budget, or US$17 million, for Hong Kong with a population of 6 million (Lau, unpublished data).

In the United States of America, the average nursing home care cost for each hip fracture patient was as much as US$3,875 in 1995 [52]. This approximated 28% of the total cost for hip fracture. As death due to hip fracture occurs mainly in the elderly, the indirect cost due to reduced productivity is much lower than for other chronic disorders such as

ischaemic heart disease; stroke or breast cancer. However, the direct cost is comparable.

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