

An Asian Perspective to the Problem of Osteoporosis

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Abstract

Introduction: Most research into the problem of osteoporosis has been carried out in Caucasian populations. This review highlights emerging data from research on osteoporosis among Asians, and some differences from Caucasian data. **Methods:** A non-systematic review of the English-language literature on various aspects of osteoporosis among Asian populations was carried out. **Results:** Compared to Caucasian populations, epidemiological trends in Asian populations appear to be developing along similar lines, although rates of hip fracture do differ by country and ethnicity, and are generally lower. Bone mineral density (BMD) carries similar relevance with regard to fracture risk, although hip geometry is also believed to have some impact. Risk factors for osteoporosis and fractures are somewhat similar, although dietary factors seem to play a larger role as reported in Asian studies. A uniquely Asian self-assessment tool based on clinical factors has been developed to assist in case-finding of osteoporotic patients. The few intervention trials with hormone replacement, alendronate and parathyroid hormone appear to show similar responses between Asians and Caucasians, although the response to vitamin D analogs in Asians appears better. Some differences in gene polymorphisms between Asians and Caucasians exist, and these may impact on BMD and fractures via different gene-environment relationships. **Conclusions:** Many aspects of osteoporosis in Asia appear similar to the West, but several interesting differences have emerged. These might lead to refinements in the strategies to manage osteoporosis within the Asian context.

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Introduction

Osteoporosis is regarded as an important public health problem in many Caucasian populations.^{1,2} Much of the research on epidemiology, diagnosis, treatment, genetic and molecular aspects has been carried out in the West. However, the body of information on research into various aspects of osteoporosis in Asia is beginning to grow. This review highlights some of the issues of this worldwide problem from an Asian perspective.

Epidemiology

Several projections have suggested that the problem in Asia will escalate over the next 30 to 50 years to epidemic proportions.^{1,2} Already, increases in hip fracture rates have been documented in several Asian countries, notably Singapore³ and Hong Kong,⁴ whose rates are approaching those of the West. Low rates of hip fractures have been reported in more northern Asian populations, but even there, some increase in rates has been observed.⁵ Hip fracture rates in Malaysia and Thailand lie somewhere in between,⁶ but with urbanisation, a similar rapid increase as seen in Singapore and Hong Kong is expected. The real reasons for such secular trends remain obscure, as in the

West.⁷ Ethnic differences in hip fracture rates within the same country have also been reported,^{3,6} but the reasons for this are as yet undetermined. The epidemiology of vertebral fractures appears somewhat different: prevalent vertebral fracture rates already appear similar with the West.^{8,9} The mortality, morbidity and social burden of hip fractures also appears similar to the West.¹⁰

Diagnosis

Large scale epidemiological trials have documented the relationship between bone mineral density (BMD) and fracture risk primarily in Caucasian populations.¹¹ Similar large-scale data in Asians are lacking. However, smaller studies have suggested that fracture risk is increased in Asians with lower BMD,¹²⁻¹⁴ and that the hip site appears able to predict vertebral and hip fractures fairly well.^{14,15} BMD in Asians appears lower than in Caucasians, and this has been attributed to smaller body size.¹⁶⁻¹⁸ Despite this, hip fracture rates remain lower, and there are suggestions that shorter hip axis lengths among Asians may be protective.¹⁹⁻²¹ Because of the differences in BMD between Caucasians and Asians, the use of manufacturer-provided

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T-scores based on Caucasian databases should be avoided. T-scores should preferably be derived from local databases. There are no data to suggest the necessity of a different threshold for osteoporosis for Asians other than the generally accepted T-score of -2.5 standard deviation (SD), although there is some research looking into the cut-off of 70% of the young adult mean for the diagnosis of osteoporosis adopted by the Japanese Society for Bone and Mineral Research.²²

In several Asian studies, biochemical markers of bone turnover have been evaluated, and have shown some clinical relevance, mainly in the setting of monitoring response to therapy.²³⁻²⁶

Risk Factors

Large epidemiological studies have delineated the risk factors for osteoporosis,²⁷ falls²⁸ and fractures^{29,30} predominantly in Caucasian populations. Several studies in Asian populations, albeit with smaller numbers, have reported on a range of risk factors for osteoporosis³¹⁻³³ and fractures.³⁴⁻³⁹ The risk factors for hip fractures which were similar to Caucasian populations included a previous history of fracture, sedative use,^{36,37} taller stature, physical inactivity and cigarette smoking.³⁶ Other important risk factors for hip fractures in Asian populations include a history of stroke,³⁵⁻³⁷ excessive alcohol intake^{36,37} and the use of thyroid medication.³⁶ Of interest is the relatively greater impact of calcium intake on osteoporosis and fractures demonstrated in Asian populations^{31-34,36-38} compared to the West; possibly related to generally lower calcium intake throughout life in Asians. Also, increased physical activity seems more protective in Asian populations against hip fractures.^{34,36,37} The relevance of patterns of falls to fractures¹² and the risk factors for falls among Asians, such as various visual and motor incapacities,^{40,41} appear similar to those in the West.²⁸

Although the osteoporosis epidemic is anticipated in many Asian countries, devices to measure BMD in these countries are relatively scarce, expensive and inaccessible. Strategies which enhance the judicious and appropriate use of BMD devices, such as the Osteoporosis Self-assessment Tool for Asians (OSTA),⁴² have been developed to facilitate the case-finding approach to detecting osteoporosis.

Lifestyle

Calcium supplementation and exercise appear to be beneficial in Asians,⁴³ with milk being an effective dietary calcium source, even among Asians.⁴⁴ Although the mean dietary calcium intake in Asian populations is generally low compared to the West, ranging from 350 to 500 mg/day,³⁶ fracture rates remain lower than in the West. One reason for this might be more efficient calcium absorption among Asian women,⁴⁵ and this may be related to the more

common vitamin D receptor polymorphisms among Asians.⁴⁶ The effects of low dietary calcium may also be offset by other nutrients more commonly found in the Asian diet. Observational studies have demonstrated skeletal benefits of dietary phytoestrogens, of which soy-based products are a major source,⁴⁷⁻⁴⁹ fish consumption³⁵ and fermented soybean, a rich source of vitamin K2.⁵⁰ However, paradoxically, an omnivorous diet appears to be more beneficial than a vegetarian or lacto-vegetarian diet.⁵¹

Treatment

Intervention studies on osteoporosis among Asians are limited. Early studies on therapy for osteoporosis centered on the effectiveness of vitamin D analogs, particularly alfacalcidol, in Japan,⁵²⁻⁵⁴ in contrast to inconsistent experience in the West with the other vitamin D analog, calcitriol. However, direct comparisons of alfacalcidol with other drugs such as hormone replacement therapy⁵⁵ and the bisphosphonate, alendronate,²⁴ have revealed clear differences in efficacy favouring the latter drugs.

As in the West, hormone replacement therapy,⁵⁶ alendronate⁵⁷⁻⁵⁹ and intermittent parathyroid hormone injections⁶⁰ are effective in maintaining or improving bone density. It appears that Asians demonstrate a similar BMD response to alendronate as Caucasians.^{61,62} However, to date, no data exist on the anti-fracture efficacy of these drugs specifically in Asian populations.

Genetics

Fairly extensive studies have revealed differences in the various receptor gene polymorphisms between Asian and Caucasian populations with differing impacts on bone density and fractures. The pattern of polymorphisms of the vitamin D receptor are similar between Koreans,⁶³ Japanese,⁶⁴ Chinese⁶⁵ and Thais,⁴⁶ but different from Caucasians, and the correlation with BMD appears less. Polymorphisms may affect BMD via gene-environment relationships resulting in increased bone loss,⁶⁶ differences in gastrointestinal handling of dietary calcium⁴⁶ or response to oestrogen.^{67,68} Other polymorphisms which have been found to be related to BMD include those of the oestrogen receptor,^{69,70} parathyroid hormone receptor,⁷¹ osteocalcin gene,⁷² calcitonin gene,⁷³ transforming growth factor β -1 gene⁷⁴ and peroxisome proliferator-activated receptor- γ gene.⁷⁵ The clinical applicability of these findings remains to be determined.

Conclusions

For the most part, many aspects of osteoporosis in Asia appear similar to the West. However, as more research is undertaken, several interesting differences have emerged which might lead to refinements in the strategies to manage osteoporosis in the Asian context.

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