Is there an effect of menopause on CHD mortality? Asia Pacific comparisons

Iain K Robertson MMedSci, MBBCh, FRCA and Madeleine J Ball BSc, MD, MRCP, FRCPath

School of Nutrition and Public Health, Deakin University, Malvern, Melbourne, Victoria, and Centre for Health Program Evaluation, Monash University, West Heidelberg, Melbourne, Victoria, Australia

This study examines the mortality rates of men and women from coronary heart disease (CHD) in a number of Asia-Pacific countries with very different incidences of this disorder. In all countries, mortality rates from CHD were higher in men. In women, no unequivocal change in mortality rate from CHD attributable to the menopause could be detected.

Key words: Coronary heart disease, menopause, mortality statistics, Australasian-epidemiology, Asian-epidemiology

Introduction

When the coronary heart disease (CHD) mortality of men and women is compared, mortality in men is higher[1]. It appears that the rise in mortality is delayed in women, and this rise is said to start after the age of the menopause. The conventional interpretation of this is that products of ovarian action protect women from CHD[2], and that after menopause that protection is lost, with women suffering a rise in CHD mortality similar to that of men. As post-menopausal women have higher levels of risk factors than premenopausal women (hypertension, LDL cholesterol and central obesity[3]), many people have accepted that the menopause is the adverse event causing rises in mortality, rather than age.

However, there is a problem with this interpretation. The increase in CHD mortality in both men and women appears roughly exponential (see Figure 1). In cases of exponential increases there are no "take-off points", only a smooth escalation of rate of increase. The process of drawing graphs to illustrate the changes produce a false appearance of a "take-off point". The position of the artificial "take-off point" is highly dependent upon the y-axis scale chosen for the graph. Graphic representation of exponentials must be based on the logarithm of the mortality rate in order to eliminate the visual effect of the exponential. The mortality rate from CHD (semi-logarithmic presentation) in the United States has been described almost 30 years ago[1], but that description seems to have had little impact and would benefit from being re-examined.

This paper presents an analysis of the relationship between CHD mortality and age in men and women from a number of Asia-Pacific countries where such data are available. It includes data from countries with high mortality from CHD as well as countries with relatively low mortality rates. The aim is to detect whether a change in mortality rate exists that is consistent with the hypothesis that the menopause increases the rate of rise of CHD mortality in women.

Figure 1. Relationship between mortality from all coronary heart disease and age in women and men in Australia.
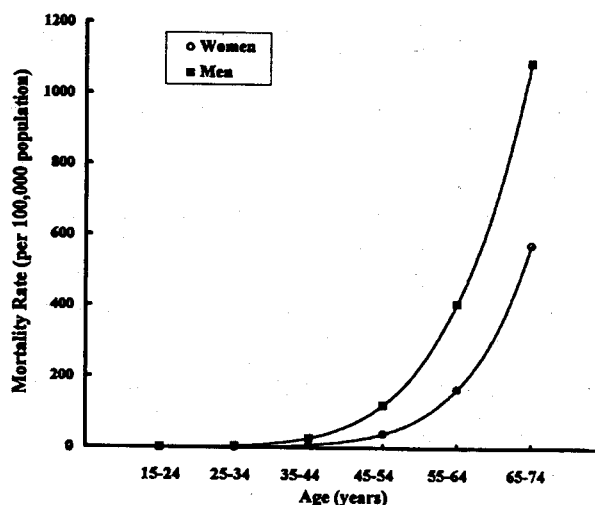
Methods

Mortality and population data were obtained from the WHO publication, World Health Statistics Annual, 1987 to 1994[4]. The number of deaths from CHD (ICD 9 codes 410-414, 410 - acute myocardial infarction, 411-414 other forms of acute, subacute and chronic ischaemic heart disease) were transcribed to a computer spreadsheet, along with the corresponding population figures. The information was recorded by sex and 10 year age groups. The mortality rate per 100,000 population was calculated for each of the countries for each year in which the data were available for each age sex group. The numbers reported are an average of all the year rates that were available in the publications examined. Information was available for the following years

Correspondence address: Dr Iain K Robertson, Health Economics Unit, Centre for Health Program Evaluation, PO Box 477, West Heidelberg, Victoria 3081.
Fax. (03) 9496 4424; Tel. (03) 9496 4405
E-mail Iain.Robertson@BusEco.monash.edu.au

in: Australia 1985 to 1992; Japan 1986 to 1993; Singapore 1986 to 1992; Hong Kong 1986 to 1993; New Zealand 1985 to 1992; South Korea 1985 to 1986 and 1988 to 1991; China 1987 to 1990. No population data were available for South Korea for 1988 onwards, so population was extrapolated from previous figures. The mortality figures for China represent results from about 10% of the population.

Semi-logarithmic plots are used in the graphic representation of the results.

Results

Figure 2 shows the mortality rates from CHD in different countries in men and women of different ages. Data from the same source[4] shows that total mortality is higher in men in all countries at all ages. CHD mortality rates of different countries fall roughly into 2 groups: 1) New Zealand, Australia and Singapore; and 2) Hong Kong, China, Japan, South Korea. CHD mortality rates differ by a factor of about 20 between these countries. The populations of these countries are known to differ greatly in their diet, incidence of obesity, smoking rates and exercise patterns, and in the cultural significance of the menopause.

In women, no unequivocal increase in the slope of the mortality rate from CHD occurs following the age of menopause. In women from Hong Kong and Japan, who have the lowest early mortality rates, there is an increase in the exponential curve after the age group 35-44 years, whereas all the other populations show a similar increase in the age group 10 years younger. This pattern would best fit a sigmoid curve, and this argues against a significant effect of the menopause.

Discussion

The ratio of CHD mortality in men compared to women covers a wide range amongst the different Asia-Pacific countries across the age range. A maximum difference between men and women is found in most countries in the age range 35-44 years, following which the difference gradually is reduced but not abolished. The assumption that seems to be made is that male mortality rates represent some fixed normative CHD state that is constant across the age range against which female mortality can be compared. For this ratio of male to female CHD mortality to have any meaning, it would be necessary to postulate that there is some effect that tends to reduce the rate of exponential rise in CHD mortality in older men and women, but that this is precisely counteracted in women by an adverse effect of the menopause. This seems quite contrived, and a better explanation of the observed mortality rates is that the menopause has little adverse effect on those rates.

A more satisfactory explanation for the observed pattern of CHD mortality in these populations is that the CHD mortality increase is governed by an exponential rise whose initial slope is greater in men than in women, and that the rate of rise diminishes at higher absolute mortality rates in both men and women. The data are much more consistent with an adverse effect operating in post-pubertal men explaining the differences in younger men and women, and that the strength of this adverse effect diminishes in older men. Thus the differences appear to be established early in life, either in early adult life or in adolescence. This would be consistent with a specific adverse effect of male sex hormones or a more general effect of various behaviours of young men. It should be noted that the graph presented by

Figure 2. Relationship between mortality from all coronary heart disease and age in women and men in some Asia-Pacific countries.

◆ Australia ■ New Zealand ▲ Japan ● Hong Kong ◆ Singapore □ Korea ▲ Rural China ○ Urban China
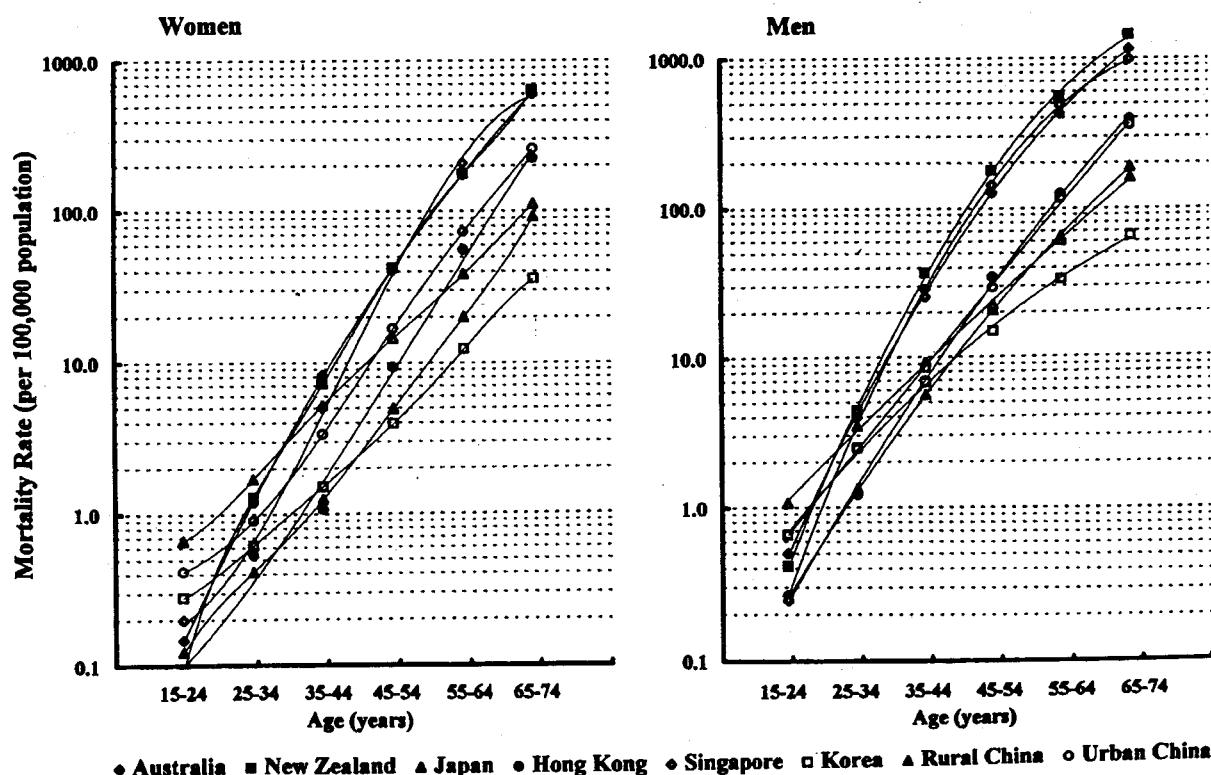
Furman[1] in 1968 and reproduced recently[5] implies a qualitative difference in men between the 25-45 and 45+ age groups. He bases one of the regression lines on two points, which is clearly of limited validity, and seems also to have been limited by the technology available to him (pencil, ruler and paper). Current computer graphics allow accurate interpolation of polynomial regression lines, and these produce much closer fit to the observations.

The putative beneficial effect on CHD mortality of hormone replacement therapy in postmenopausal women must be understood in relation to the natural epidemiology of CHD as demonstrated in this study. No randomised controlled trial has been completed to established this beneficial effect, although at least one has recently been commenced. The benefits rest on the circumstantial evidence of prospective observational and case-control studies[6], which are unable to exclude a healthy-subject effect. If, however, the benefit was established, this would need to be regarded as a pharmaceutical intervention, rather than a "natural" correction of the "pathological condition" of menopause.

Lifestyle factors in later life will have an influence at an individual or population level on the absolute risk of CHD[3,7-9]. The menopause in women may be associated with many changes, and longitudinal data, although sparse, have indicated changes in some established risk factors. However, this must not be over-interpreted to blame the menopause itself for outcomes which may be due to biological and behavioural consequences of aging.

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絕 經 期 對 冠 心 病 死 亡 率 有 影 響 嗎 ？

亞 太 國 家 的 比 較

摘 要

該 文 比 較 了 亚 太 国 家 男 性 和 女 性 的 冠 心 病 〔CHD〕的 死 亡 率， 发 现 差 异 很 大． 在 所 有 国 家 中， 男 性 冠 心 病 的 死 亡 率 较 高， 而 女 性 冠 心 病 的 死 亡 率 较 低． 没 有 发 现 绝 经 期 后 有 明 显 的 改 变．

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