Coronary Heart Disease Mortality Among Men Aged 35–44 Years by Prefecture in Japan in 1995–1999 Compared With That Among White Men Aged 35–44 by State in the United States in 1995–1998

— Vital Statistics Data in Recent Birth Cohorts —

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The levels of risk factors for coronary heart disease (CHD) in men in the post World War II (WWII) birth cohort are almost similar between Japan and the USA, except for the considerably higher prevalence of cigarette smoking in Japan and the much higher prevalence of obesity in the USA. The present study evaluated the CHD mortality among men in the post WWII birth cohort by prefecture in Japan in 1995–1999 and then compared the data with those for white men in different states in the USA. There was a greater than 2-fold difference in CHD mortality among men aged 35–44 by prefecture in Japan: 5.3/100,000 in Kumamoto vs 12.6/100,000 in Tochigi. CHD mortality among men aged 35–44 in the top 3 prefectures in Japan is about half that of white men in the USA and is similar to that of white men in the lowest 3 states. The much lower CHD mortality in Japan does not appear to be caused by differences in the classification of causes of death and the results suggest that there may be strong and important protective factors that reduce the risk of CHD in Japan. (*Jpn Circ J* 2001; 65: 887–892)

Key Words: Coronary heart disease; Japan; Mortality; Post World War II birth cohort; USA

Since World War II (WWII), there have been important changes in lifestyle that have had a major impact on the risk for coronary heart disease (CHD), such as the decline in total cholesterol levels, improved treatment of hypertension, and the decline in the prevalence of cigarette smoking, in the United States of America (US) and many other Western countries^{1–3}. At the same time, many non-Western countries, including Japan, have been exposed to the Western lifestyle⁴ and data from national sample surveys in the US and Japan clearly demonstrate that the differences in the levels of cholesterol and blood pressure between the 2 countries have become much smaller during the past decades^{5–10}. In fact, among men in the post WWII birth cohort, the risk factor profiles for CHD (levels of total cholesterol, systolic and diastolic blood pressure) are very similar between white men in the US and men in Japan, except for the considerably higher prevalence of cigarette smoking in Japan and the much higher prevalence of obesity in the US¹¹. In 1988–1994 in the US the mean level of total cholesterol among men aged 20–34 and 35–44 years was 186 mg/dl and 206 mg/dl, respectively⁵ and for

men aged 30–39 years in Japan in 1989 it was 201 mg/dl⁶. The mean systolic and diastolic blood pressures among white men in the US aged 30–39 years in 1988–1991 were 119 mmHg and 77 mmHg⁸, respectively, and for similar aged Japanese men in 1989 they were 127 mmHg and 77 mmHg⁶, respectively. The prevalence of cigarette smoking among white men in the US aged 25–34 and 35–44 years in 1990 was 32% and 34%, respectively⁵, whereas it was 65%¹⁰ among Japanese men aged 30–39 years in 1989. In 1989, about 15% of men aged 20–29, and 20% of men aged 30–39 years in Japan were overweight (body mass index ≥ 25.0)⁹, whereas in the US in 1988–1994, the proportions were 47.5% of men aged 20–34 and 66.5% of men aged 35–44 years⁵.

Nationwide autopsy studies in Japan indicate that extent and severity of atherosclerosis in the coronary arteries of young men became more extensive in the 1990s^{12,13} and the surface involvement of fatty streaks and fibrous plaques was comparable with that among young white men in the US¹⁴. There are limitations in comparing the results because almost all the cases examined in Japan died of non-external causes whereas the study in the US examined cases of death from external causes, and the data were not drawn from nationally representative samples. It is notable, however, that the surface involvement (fatty streaks plus fibrous plaques) among men in their 20s in Japan in 1991–1995 is more extensive than among comparable white men in the US in 1987–1994^{13,14}.

Comparing the CHD mortality rate among men in the post WWII birth cohort (ie, those aged 35–44 years) may better reflect recent changes in risk factors than comparing the age-adjusted rate or rate among men in an older age

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group because alterations in risk factors would emerge more rapidly in younger groups, as has been observed in the US and other countries.^{15,16} Also, taking into account the opposite direction of the changes in risk factors for CHD between the US and Japan, comparing the age-adjusted mortality may be misleading because of the cohort effect.

It is possible that the CHD mortality in Japan has been underestimated because heart attack may be reported as acute heart failure and the cause of death may be then misclassified as heart failure.¹⁷ The Ministry of Health and Welfare in Japan added the instruction for death certificate

coding 'Do not put heart failure as a cause of death when it is a manifestation of the terminal state of disease' when the 10th revision of the International Classification of Diseases (ICD-10) was introduced in 1995. As a result, from 1990–1992 to 1995–1997 the mortality among men aged 35–44 years from heart failure decreased by 68% and that from CHD rose by 65%.¹⁸

We recently reported a 3-fold difference in the CHD mortality among white men aged 35–44 years by state in the US.¹⁹ Mortality in the top 3 states was almost as high as that in Poland, which has one of the highest rates in Europe, whereas mortality in the lowest 3 states in the US was less than that in France, which has one of the lowest rates in Europe and the world.

We hypothesized that there would be a 2- to 3-fold difference in mortality from CHD among men aged 35–44 years by prefecture in Japan, and that the CHD mortality in the top prefecture would be much higher than that among white men in the lowest state in the US. We investigated the mortality from CHD, and from the subcategories of heart diseases, among Japanese men, and compared the data with those for similar aged white men in some states of the US and in some other countries.

Methods

The number of deaths by sex, age group, prefecture, and ICD code from 1995 to 1999 was obtained from the Vital Statistics Division, Statistics and Information Department, Ministry of Health, Labor, and Welfare in Japan. The population by sex, age group, and prefecture from 1995 to 1999 was obtained from the Statistics Bureau and Statistics Center in Japan. Mortality data in the US from 1995 to 1998 (the latest available data) were obtained from the CDC Wonder database (<http://wonder.cdc.gov/>), maintained by the Centers for Disease Control and Prevention, which enabled data on mortality to be extracted by age group, race, sex, state, underlying cause of death by the ICD-9 code, etc. The mortality data by country, age group, sex, year, ICD code, etc were obtained from the World Health Organization Statistical Information System (WHOSIS; <http://www.who.int/whosis/>), maintained by the World Health Organization (WHO). Countries selected were Australia, Canada, Finland, France, Greece, Hungary, Poland, and the United Kingdom (UK). Data were available for most of the countries for the year of 1996 or 1997 and by ICD-9 code.

For CHD, codes I20–25 in ICD-10 and codes 410–414 in ICD-9 were used. For diseases of heart, codes I01–51 in ICD-10 and codes 390–429 in ICD-9 were used. Diseases of heart is a cumulative grouping recommended by the WHO for the tabulation of mortality data and is much more reliable in comparing mortality among industrialized countries than CHD because of the heterogeneity of recording the cause-of-death.¹² For heart failure, code I50 in ICD-10 and code 428 in ICD-9 were used.

Results

Mortality rates from CHD, heart failure, and diseases of heart among Japanese men aged 35–44 years from 1995 to 1999 were 8.7/100,000, 5.2/100,000 and 18.7/100,000, respectively. Fig 1 shows the variation in mortality from these 3 conditions by prefecture. In 13 prefectures, the number of deaths from CHD was small and the data could

Fig 1. Mortality from coronary heart disease (CHD), diseases of heart, and heart failure (/100,000) among men aged 35–44 years in 1995–1999 by prefecture in Japan. Values in parentheses indicates that the number of CHD deaths in that prefecture was small and the CHD mortality data could be unreliable.

Fig 2. Mortality from coronary heart disease (CHD) and diseases of heart among men aged 35–44 years in the highest and lowest 3 prefectures in Japan in 1995–1999, among white men aged 35–44 years in 1995–1998 in the highest and lowest 3 states in the United States, and among men aged 35–44 years in 1994 in some other countries. Mortality rates from CHD and diseases of heart in Hungary in 1998 were 82.6/100,000 and 116.4/100,000, respectively.

be unreliable, but even after excluding these prefectures, there was a greater than 2-fold difference in mortality from CHD: 5.3/100,000 in Kumamoto vs 12.6/100,000 in Tochigi. There was an almost 2-fold difference in mortality from diseases of heart: 14.4/100,000 in Kanagawa vs 25.7/100,000 in Ehime. The proportion of mortality from diseases of heart in categories other than CHD among Japanese men aged 35–44 years was 53.5%, and by prefecture, it ranged from 27.0% in Osaka to 71.8% in Kumamoto. Mortality from heart failure ranged from 2.1/100,000 in Osaka to 10.3/100,000 in Ehime. The proportion of mortality from heart failure in mortality from diseases of heart (mortality from heart failure/mortality from diseases of heart) among Japanese men aged 35–44 years was 27.7% and by prefecture it ranged from 10.8% in Osaka to 46.7% in Hiroshima.

Fig 2 shows the mortality from CHD and diseases of heart among 35–44-year-old Japanese men and white men in the US and other countries, in addition to the highest and lowest 3 prefectures in Japan and the highest and lowest 3 states in the US. Mortality from CHD among Japanese men aged 35–44 years in the lowest 3 prefectures was much lower than among white men in the lowest 3 states in the US, whereas in the top 3 prefectures it was similar to that among white men in the lowest 3 states: 12.6/100,000 in

Fig 3. Proportion by country of mortality assigned to other than coronary heart disease (CHD) in the category of diseases of heart.

Fig 4. Proportion of mortality from coronary heart disease (CHD), ill-defined description and complications of heart (IDC), heart failure (HF), and others in the category of diseases of heart between men aged 35–44 years in Japan in 1995–1999 and white men in the US in 1995–1998.

Tochigi, 12.4/100,000 In Kagawa, and 12.2/100,000 in Osaka, vs 13.7/100,000 in Washington, 12.0/100,000 in New Mexico, and 10.4/100,000 in Maryland. Mortality from CHD among Japanese men aged 35–44 years in the highest 3 prefectures in Japan was still lower than in France, where the mortality from CHD is one of the lowest among industrialized countries (15.1/100,000), and mortality from diseases of heart in this cohort in the highest 3 prefectures was much lower than that among white men in the lowest 3 states in the US: 22.0/100,000 in Tochigi, 22.5/100,000 in Kagawa, and 19.5/100,000 in Osaka, vs 33.6/100,000 in Maryland, 30.0/100,000 in Washington, and 28.5/100,000 in New Mexico. Mortality from diseases of heart in the highest 3 prefectures in Japan was lower than in France (25.1/100,000).

Fig 3 shows the proportion of mortality from diseases of heart in categories other than CHD in Japan and the other countries. The proportion ranged from 16.7% in Greece to 53.5% in Japan. Less than one-fifth of deaths from diseases of heart among men aged 35–44 years in Greece were not CHD whereas more than half of the deaths from diseases of

heart among Japanese men were diagnosed as other than CHD.

Fig4 shows the proportion of mortality from CHD, ill-defined descriptions and complications of heart disease (IDC) (ICD-10 code: I-51, ICD-9 code: 429), heart failure (HF), and diseases of heart other than CHD, IDC or HF among men aged 35–44 years in Japan from 1995 to 1999 and white men aged 35–44 years in the US from 1995 to 1998. More than a quarter of deaths in diseases of heart among the Japanese men were coded as heart failure, which represented less than 2% among the white men in the US. Approximately 12% of diseases of heart among US white men were coded as ill-defined descriptions and complications of heart disease, whereas this proportion was very small in Japan. Most of the deaths in the ill-defined descriptions and complications of heart disease ($\approx 80\%$) among white men in the US were coded as arteriosclerotic cardiovascular disease (ASCVD; ICD-9 code 429.2).

Discussion

We observed a 2-fold difference in mortality from CHD and diseases of heart by prefecture among Japanese men aged 35–44 years. We had previously reported that in the US, differences by state in CHD mortality among white men aged 35–44 years were most likely attributable to differences in levels of risk factors, rather than to differences in medical services because most of the CHD deaths in this age group were sudden and not in hospital.¹⁹ Unfortunately, there are no age- and sex-specific data on the risk factors for CHD by prefecture or by state and further investigations are needed to elucidate the cause of the variations in CHD mortality.

In spite of the similar levels of risk factors for CHD between Japan and the US for men in the post WWII birth cohort, the mortality from CHD among Japanese men in the top 3 prefectures was much lower than for white men in the US and was similar to that among white men in the lowest 3 states. The mortality from diseases of heart in the top 3 prefecture was also much lower than that in the lowest 3 states in the US.

We compared the proportion of mortality from disease of heart other than CHD and found that the proportion was highest among the men in Japan, followed by white men in the US, suggesting that the mortality from CHD is underestimated in both countries. We further examined the mortality from subcategories of diseases of heart among these men and found that in the US, approximately 10% of the deaths in the diseases of heart were coded by coroners as ASCVD (ICD-9 code: 429.2) to denote CHD that falls somewhat short of definitive evidence of a myocardial infarction, but was separate from the rest of codes for CHD in ICD-9.²⁰ Such deaths were coded 412.4 under the ICD-8 and, therefore, in the US, mortality from ASCVD should be added to mortality from CHD. This proportion was negligible among the Japanese men aged 35–44 years. The proportion of mortality from heart failure in this age group in Japan was still much higher than for white men in the US, in whom death from heart failure was rarely coded, even after the instruction by the Ministry of Health in Japan in 1995. It is likely that the mortality from CHD among these men in Japan is still underestimated.

The death certificates of cases of cardiovascular diseases in Japan have been validated with the WHO MONICA criteria.²¹ After the re-evaluation, however, a substantial

proportion were categorized as either sudden death of unknown origin or insufficient data. These studies^{22–25} examined people aged 15–24 years, or 25–74 years and the number of deaths among men aged 35–44 years is too small to draw any inferences on the post WWII birth cohort. In addition, these studies were conducted before 1995, when the Ministry of Health and Welfare added the instruction for death certificates concerning heart failure. Baba et al evaluated the death certificates of cases of CHD, heart failure, other heart diseases, stroke, and others, which may contain CHD deaths, among people aged 25–74 years in Suita, Japan from 1984 to 1986 using clinical and police records²² and found that approximately 4% of cases of stroke (ICD-9 codes: 430–438) by death certificate were actually from CHD after re-evaluation. They concluded that CHD deaths could be underestimated by 11%. However, approximately 30% were classified as either sudden death of unknown origin or insufficient data or were not re-evaluated. Naruse et al evaluated the death certificates of cases of CHD and heart failure among people aged 15–74 years in rural areas in Japan from 1987 to 1990 using clinical records²³ and concluded that CHD deaths could be underestimated by 7.7%, although approximately 35% were classified as insufficient data after the evaluation. In the Oita Cardiac Death Survey (OCDS), Saito et al evaluated the death certificates of cases of CHD, heart failure, other heart diseases and others, which may contain CHD deaths, among people aged 25–74 years in Oita, Japan from 1992 to 1993 using clinical and police records²⁴ and they concluded that the CHD deaths could be underestimated by 30%; approximately 30% were classified as either sudden death of unknown origin or insufficient data after the evaluation. Recently, Saito et al compared the mortality from CHD among men and women aged 35–74 years in the OCDS with the data from the Atherosclerosis Risk in Communities Study²⁵ and reported that when sudden deaths were counted as CHD deaths, the differences in mortality from CHD were not as great as suggested by vital statistics, and the ratio of mortality from CHD among men (US/Japan) fell from 5.9 to 4.7.

A much higher incidence rate of type 1 diabetes mellitus (IDDM) and CHD as cause of death in the US account to some extent for the difference. Traven et al investigated CHD mortality and sudden death among people aged 35–44 years in Allegheny County, USA²⁶ and of the CHD deaths during 1984 to 1989, 20% had IDDM. The incidence of IDDM among children aged 0–14 years in Japan has been reported as 1.82/100,000²⁷ which is one-quarter to one-fifth as low as that in the US.²⁸ The Diabetes Epidemiology Research International Mortality Group reported that cardiovascular/cerebrovascular-disease-specific mortality among patients with IDDM comprised only 2% of all deaths in Japan, compared with 10% in the US.²⁹

Even when these factors are taken into account, however, mortality from CHD among men aged 35–44 years in Japan is still much lower than that among comparable white men in the US, and in the top prefecture in Japan the rate is similar to that of white men in the lowest state in the US. Assuming that 20% of CHD deaths (ICD-9 codes: 410–414, 429.2) among white men in the US are caused by IDDM and thus excluded from CHD for the comparison, the mortality from CHD among white men in the US would be 21.6/100,000. Assuming that all the cases of CHD (ICD-10 codes: I20–25) on death certificate are true cases of CHD, and that 50% of cases from heart failure (ICD-10

code: I50) on death certificate are in fact from CHD, and 5% of cases of stroke (ICD-10 codes: I60-69) are from CHD, the estimated CHD among men aged 35–44 years in Japan would be still 12.0/100,000. When the same assumptions were applied to prefecture-specific mortality from 1995 to 1999 and to state-specific mortality from 1995 to 1998, the estimated CHD mortality in the top 3 prefectures in Japan is 16.0/100,000 to 16.8/100,000, whereas that in the lowest 3 states is 14.4/100,000 to 15.2/100,000.

Study Limitations

First, the mortality data are based only on vital statistics in both Japan and the US. Second, the assumptions are not based on mortality validation studies in men aged 35–44 years, other than the studies in Allegheny County, USA. Third, diagnostic practice is likely to differ not only by country, but also by region within a country (ie, by prefecture in Japan, and by state in the US).

Even with these limitations, this study is likely to overestimate the true rate of CHD mortality in Japan because all the cases of CHD by death certificate were assumed to be true cases of CHD, which is very unlikely.^{22–25} We also believe that the CHD mortality in the US is likely to be overestimated because we assumed that 20% of CHD deaths were due to IDDM and were thus excluded from comparison. This figure (20%) was based on the mortality validation study carried out in Allegheny County, which has one of the highest incidence rates of IDDM within the US.²⁸

The present data imply that among the post WWII birth cohort of men aged 35–44 years, mortality from CHD is still much higher in white men in the US than that among men in Japan, in spite of the very similar traditional risk factor profiles, other than the considerably higher prevalence of cigarette smoking in Japan and the much higher prevalence of obesity in the US. If true, differences in genetic factors would be unlikely to explain the differences in mortality because studies of Japanese male migrants to the US clearly illustrate an increase in the morbidity and mortality from CHD.^{30–32} There may be several reasons for the much lower CHD mortality among the men in Japan: (1) higher levels of high density lipoprotein cholesterol;^{33–35} (2) higher consumption of soy products;³⁶ (3) higher polyunsaturated/saturated fat ratio;³⁷ (4) higher alcohol consumption;³⁸ (5) higher fish consumption;^{39,40} (6) a time lag between the increase in levels of cholesterol and the increase in mortality from CHD;⁴¹ and others.^{42–44} The identification of these factors would be extremely valuable for the prevention of CHD, so there is a clear need for monitoring trends in morbidity and mortality from CHD and atherosclerosis, as well as the trends in risk factors among men in the post WWII birth cohort.

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