Blood pressure and long-term coronary heart disease mortality in the Seven Countries Study: implications for clinical practice and public health

Introduction

High blood pressure is a well-established risk factor for coronary heart disease. Therefore, management of high blood pressure is needed to reduce the burden of coronary heart disease and consequently to increase healthy life-expectancy. Gain in healthy years of life is of importance for both individuals and populations. In clinical practice, treatment of high blood pressure is focused on achieving health benefit for individuals, whereas public health is focused on prevention of high blood pressure in populations.

In clinical medicine, a high-risk strategy is used for coronary heart disease prevention, i.e. detection and treatment of high blood pressure in patients who are most likely to benefit from it. Two components of risk are important for treatment strategies. The absolute risk or absolute rate defines the probability of an individual's developing a disease over a finite period of time[1]. Recent guidelines on the management of hypertension have recommended multifactorial absolute risk as the basis of clinical decision-making, in terms of antihypertensive drug therapy[2–6]. This multifactorial or overall level of risk will often be determined to a greater extent by the presence of other risk factors, such as age, gender, smoking status, total and HDL cholesterol level and family history of premature cardiovascular disease, than by blood pressure level[2]. Consideration of absolute level of risk, in addition to blood pressure level, is mainly aimed at healthy individuals with mild and moderate hypertension, i.e. systolic blood pressures of 140–179 mmHg and/or diastolic blood pressures of 90–109 mmHg. Individuals with severe hypertension and patients with a history of coronary heart disease and in combination with mild or moderate hypertension are already at high risk and are qualified for drug treatment anyway. The relative risk is the ratio of absolute risk for an individual with a defined level of risk (based on one or more risk factors) to that for an individual at a reference level of risk, i.e. either a low or an average level (based on one or more risk factors)[7]. The relative risk provides information about the aetiological significance of a risk factor[1]. A high relative risk implies a strong association between a risk factor and the occurrence of a disease.

To prevent high blood pressure in a public health context, blood pressure-reducing interventions should be selected based on their potential to reduce the incidence of coronary heart disease in the population as a whole[8]. In public health, the population attributable risk is a widely used measure of risk. This population attributable risk is the proportion of all diseased individuals attributable to hypertension[1]. Population attributable risk not only depends on the relative risk, but also on the proportion of the total population that is exposed, i.e. on the prevalence of hypertension.

Epidemiological measures of risk can thus be used as a basis for developing effective strategies for prevention of blood-pressure-related diseases, both in clinical medicine and public health. This hotline editorial deals with such an application of these risk measures, in view of the results of a recently published study on blood pressure and mortality from coronary heart disease in the Seven Countries Study[9]. The study and its main findings are described and the implications for treatment and prevention of hypertension in relation to coronary heart disease are discussed.

The study and its findings

The aim of the study was to compare the mortality rates from coronary heart disease at a given level of blood pressure among different populations. The study also investigated whether the relative risk for death due to coronary heart disease in relation to systolic and diastolic blood pressure was similar in different populations.

The study included 12 031 men aged 40–59 years who were enrolled in the Seven Countries Study between 1958 and 1964 and who were free of coronary heart disease at enrolment. A total of 16 cohorts were examined in the following countries: the United States (US Railroad), Finland (East and West), the Netherlands (Zutphen), Italy (Rome Railroad, Crevalcore and Montegiorgio), Greece (Crete and Corfu), former Yugoslavia (Dalmatia, Slavonia, Zrenjanin, Velika Krsna and Belgrade), and Japan (Tanushimaru and Ushibuka). To increase the power of the statistical analyses the 16 cohorts were

pooled into six populations e.g. the United States, northern Europe (East and West Finland and Zutphen), Mediterranean southern Europe (Crete, Corfu, Montegiorgio, and Dalmatia), Inland southern Europe (Rome, Crevalcore, Slavonia, and Belgrade), Serbia (Velika Krsna and Zrenjanin) and Japan (Ushibuka and Tanushimaru). The criteria for grouping cohorts into one population were similarities among cohorts in coronary heart disease mortality rates and similarities among cohorts in cultural (e.g. dietary patterns) and geographic features[9]. In all cohorts the major cardiovascular risk factors were measured in a standardized way at enrolment and after 5 (except Japan) and 10 years (except U.S.A.)[10,11]. During 25 years of follow-up, 1291 (10·7%) men had died from coronary heart disease.

The main study finding is that, at the same blood pressure level, the mortality rates from coronary heart disease varied substantially among populations. In all populations, however, men whose blood pressure increased a given amount experienced a similar relative increase in risk of dying from coronary heart disease. At systolic and diastolic blood pressure of 140 and 85 mmHg, respectively, 25-year mortality rates from coronary heart disease varied by a factor of more than three among the populations. Rates in the United States and northern Europe were high (approximately 70 deaths per 10 000 person-years), but low in Japan and Mediterranean southern Europe (approximately 20 deaths per 10 000 person-years).

Differences of 10 mmHg in casual systolic blood pressure and of 5 mmHg in casual diastolic blood pressure were associated with, respectively, a 17% and a 13% difference in the risk of death from coronary heart disease. After adjustment for within-subject variability in blood pressure, the relative risk was 1·28 for each of these differences, making the relationship 60% stronger for systolic blood pressure and twice as strong for diastolic blood pressure. A continuous, linear relationship between blood pressure and risk of coronary heart disease mortality, i.e. the lower the blood pressure the lower the risk and vice versa, has also been demonstrated in other larger observational studies[12–15].

Other investigators contest this viewpoint and suggest that systolic blood pressure is not related to a risk of all-cause and cardiovascular disease death for all pressures lower than an age- and sex-dependent threshold[16]. For a 40-year-old man, they suggest that the threshold for systolic blood pressure should be about 140 mmHg, and for a 60-year-old man about 150 mmHg. However, their end-points were different and their numbers were smaller. More

studies are needed to draw definite conclusions about this issue.

Clinical implications

The large differences between the coronary heart disease death rates in the U.S.A. and northern Europe and those in Japan and Mediterranean southern Europe among men with similar blood pressure levels have implications for the treatment of hypertension in different parts of the world. It emphasizes the limited usefulness of hypertension as a diagnostic category in clinical decision making, and the importance of an individual's total risk of developing coronary heart disease. In the 1998 recommendations of the Joint Task Force of European Societies on prevention of coronary heart disease in clinical practice, a 10-year multifactorial coronary heart disease risk greater than 20%, or in young persons a risk exceeding 20% if projected to age 60, is arbitrarily defined as a risk sufficiently high to justify the selective use of antihypertensive drug therapy in healthy individuals[6].

In populations with high coronary heart disease mortality rates, a large proportion of individuals has a high absolute level of risk. Our results show that at each level of blood pressure, this 'absolute risk' criterion is passed more often in the U.S.A. and northern Europe than in Japan and Mediterranean southern Europe. Thus, according to the 'absolute risk' criterion, a higher percentage of men in the U.S.A. and northern Europe with mild and moderate hypertension would be treated for this condition than in Japan and the Mediterranean.

In the recommendations of the Joint European Task Force, risk stratification charts derived from Framingham risk functions are used to estimate an individual's multifactorial absolute risk[6]. Although these risk charts predict absolute risk reasonably well in high-risk populations, e.g. the U.S.A. and northern Europe, they overestimate the risk in low-risk populations, e.g. Japan and the Mediterranean[17,18]. This means that, in the latter, an excess of people would be treated by drugs using the Framingham risk function based charts. These findings indicate the importance of developing and comparing risk functions derived from prospective population-based studies carried out in different parts of Europe, with different coronary heart disease mortality rates. For this purpose, the SCORE project was started in 1997[17].

Of course, the definition of 'high risk' status, with regard to need for antihypertensive therapy is not solely based on considerations from observational epidemiology and clinical trials. Cost-effective issues

also play a role[19]. In addition, due to limitations in professional and financial resources, the need to establish priorities in health care may play a role in targeting risk groups for drug treatment. Because these aspects may vary in different countries, the definition of 'high risk' status may vary from country to country.

Public health implications

In clinical medicine, a high risk approach to coronary heart disease prevention is used. Mainly patients with severe hypertension and patients with mild or moderate hypertension who have a high short-term absolute risk of developing coronary heart disease, e.g. within 10 years are treated. Most individuals have, however, average, mildly or moderately elevated blood pressure levels and a low short-term absolute coronary heart disease risk. Most of these individuals will be not included in the high risk strategy.

In a public health context, the aim of coronary heart disease prevention is to reduce the incidence of coronary heart disease in the population as a whole. Viewed from a population perspective, the potential benefit of blood-pressure reducing interventions is determined by the population attributable risk. The population attributable risk depends both on the relative risk and on the proportion of individuals with blood pressure levels above optimal, e.g. a systolic blood pressure above 120 mmHg and/or a diastolic blood pressure above 80 mmHg. In the present study, we found that any increase in blood pressure was associated with an increase in the relative risk for coronary heart disease mortality, irrespective of an individual's blood pressure level. These positive associations and the large number of individuals with blood pressure levels above optimal (who will not be targeted by clinicians) indicate that the total burden of coronary heart disease among this group is considerable[13,15]. A population strategy, aimed at blood pressure reductions in the population as a whole, will therefore theoretically result in a much larger absolute decline in the number of coronary heart disease cases than a high risk strategy, even at moderate blood pressure reductions[8]. Small population-wide reductions of blood pressure may be achieved by stimulating lifestyle changes, such as increased physical activity and changes in diet, in the total population[20–24]. An advantage of such lifestyle interventions is that they also have a beneficial effect on other coronary heart disease risk factors such as total cholesterol[8,20,23]. Furthermore, they may prevent 'medicalization' of the population by avoiding the need for, or reducing the intensity of, antihypertensive drug therapy[25,26].

An important role of lifestyle factors in reducing the burden of coronary heart disease is suggested by the results of the present study. The observed differences in coronary heart disease mortality rates between populations at similar levels of blood pressure could not be explained by the major causal coronary heart disease risk factors: prevalence of diabetes was very low in all cohorts and coronary heart disease death rates were adjusted for age, smoking status and total cholesterol level. Although there may be some residual confounding, other factors such as genetic susceptibility for coronary heart disease, biological factors such as low HDL-cholesterol and coagulation factors, and lifestyle factors, should thus be considered. Dietary patterns differed greatly between the populations. Compared with the northern European and U.S. diets, the Mediterranean diet at baseline contained less meat and dairy products but more olive oil, fish, fruits, vegetables, and wine[27]. Lifestyle factors, such as diet, are therefore suggested to be major determinants of differences in coronary heart disease death rates.

Conclusion

From a public health perspective, the high risk and the population strategy with respect to prevention of coronary heart disease are complementary. Adequate treatment of patients at high risk is needed because they will benefit most. This is, however, not enough to reduce the population burden of coronary heart disease and should be complemented by a population approach in order to obtain maximal benefit of coronary heart disease prevention.

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