Cardiovascular Prevention: A Compelling Reason?

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The relative risk is the measure most commonly used in etiologic studies to determine the magnitude of the association between a risk factor and a disease, and it is an essential measure for the evaluation of causality. Nevertheless, once this has been established coherently and in agreement with scientific knowledge, other measures of association exist that have greater relevance when deciding what it is more important to do when faced with a particular health care problem. One of these measures is the population attributable fraction (PAF), or excess proportion of cases due to a certain risk factor in a particular population. In other words, the fraction of avoidable disease in a specific period if the risk factor would be completely eliminated, assuming that the association is causal and that the other risk factors remain constant.[1] Although the relative risks of the various classic risk factors for ischemic heart disease are usually very similar across different populations, provided that the studies producing these figures were designed correctly and similarly, the risks and the attributable fractions are not similar. This is due to the diverse distribution and prevalence of the risk factors across populations, which result in different incidences of disease.

The estimation of the PAF of the risk factors for ischemic heart disease is not new.[2] One of the more recent and better known studies is INTERHEART,[3] a case-control study of patients with a first acute myocardial infarction admitted to coronary care units or other cardiology units and different types of controls. This study provided a worldwide view of the impact of the risk factors. In Spain, the PAF for smoking and for alcohol have been published,

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based on routine mortality data. In this issue of the *Revista Española de Cardiología*, Medrano et al[4] attempt to quantify the impact of the various coronary risk factors in the Spanish population, using data from 4 published studies. The relative risks are those from a 5-year follow-up study of the population assigned to 8 primary care centers in Zaragoza (ZACARI, n=6124). The prevalence of cardiovascular risk factors for the crude calculation of the PAF comes from a meta-analysis of 48 Spanish cross-sectional studies involving a total of 130 945 subjects, carried out by the same authors. To adjust the calculation for other risk factors, the authors use the prevalence rates of 2 secondary prevention studies in patients with myocardial infarction admitted to coronary care units, PRIAMO-II and PREVESE-2.

The results show that overweight (body mass index ≥25) is the factor that has the most population impact, followed by smoking. The association between obesity and coronary disease has been established. Studies such as the Framingham study[5] and the Nurses Health Study,[6] as well as others, show that obesity and overweight are predictors not only of coronary heart disease, but also of cardiovascular events in men, whereas in women they are only predictors for effort angina. Obesity is associated with other factors as well.[7] The finding by Medrano et al is coherent with the MONICA study, which showed 7 years ago that obesity was the risk factor that had experienced the greatest increase, together with the increase in the incidence of infarction in Catalonia.[8] It was moteworthy that the incidence of coronary heart disease that is potentially by eliminating just 1 single risk e.g. overweight (42.5% of the men and 36.5% of the women in the adjusted calculation; 51% of the men and 45% of the women in the crude data). This level of impact corresponds with that found in other studies for the combination of several different risk factors. Thus, in the first National Health and Nutrition Examination Survey NHANES-I/NHFS,[9] the PAF for the combination of smoking, hypertension, hypercholesterolemia, and diabetes in men aged 35 to 74 years was 41.2%. In the Framingham study, after a follow-up of 44 years,

the attributable fraction of overweight by itself was 20% of hard coronary events (acute myocardial infarction or coronary death) in men and 4% in women.[5]

Let us see what factors might be able to explain these different estimations. Calculation of the PAF involves 2 parameters, the prevalence of the risk factors and the relative risks, though the prevalence is usually more decisive. The meta-analysis used comprised an age interval ranging from 2 to 75 years and it included studies in both the general population and in working populations, primary care patients, the elderly, and schoolchildren. Although at the time the results were broken down for the general population studies, the prevalences of the risk factors used in this article are those of the whole set of studies, even though the general population studies do carry a greater weight. The prevalence of overweight was 48% in the women and 67% in the men. Comparison of these figures with those of any other study is impossible because of the mixture of populations and ages mentioned earlier. As an example, in the American national survey the prevalence was 42% and 53.5%, respectively, in the pool of SEEDO 2000 studies[10] (48% in women and 58% in men aged 25 to 60 years) and in the MONICA-Catalonia study[11] (68% in women and 66% in men aged 25 to 64 years). The prevalence of the PREVESE-2 study was used to calculate the PAF adjusted for overweight. However, 63% of the clinical histories in this study failed to note the weight and height, and the body mass index could not therefore be calculated. Among those records that did include these data, the prevalence of overweight was 46% in the men and 38.3% in the women, values that are clearly lower than those provided in the tables of the article, which appear to correspond more to the prevalence of overweight in the EUROASPIRE-2 study[12] rather than that of the PREVESE-2 study. A similar observation can be made concerning the relative risks of overweight and the ratio of low-density lipoprotein cholesterol to high-density lipoprotein cholesterol in the ZACARI study, which were only calculated in subgroups of the study, as the data referring to body mass index and lipoproteins was missing in more than 30% of the subjects. Moreover, these relative risks are greater and statistically more unstable than those of the Framingham study, due to the nature of the study from which they are derived. Taken together, the limitations mentioned above lead us to question the robustness of these calculations of the PAF. In fact, their wide confidence intervals, which are even negative for some factors, leaves the true magnitude of the impact of the coronary risk factors uncertain.

The PAF is a theoretical calculation and is especially useful to illustrate the potential impact of a preventive measure. Nonetheless, it has certain inconveniences, such as assuming that other risk factors remain constant. In practice, however, it would be difficult for 1 risk factor to disappear completely with no resulting change in any of the other factors. Coronary heart disease is a multifactorial disease and preventive interventions to reduce it must also be multifactorial. This concept has already been incorporated into the clinical setting, with varying degrees of success, using tables evaluating cardiovascular risk. The Public Health authorities must also take this qualitative leap and future attempts to estimate the impact of cardiovascular risk factors should not just be made taking the combined prevalences of various risk factors, but also they should be based on genuine studies in the general population. The users of primary care are not representative of the general population. Although it is estimated that 80% of the Spanish population attend a health center at least once a year, this percentage varies greatly according to age and sex. The estimations of risk and the validations of the equations of risk based on this type of patients fail to reflect adequately the true epidemiologic situation, although they are nevertheless respectable attempts to approach the problem.[13] Perhaps the time has come to combine efforts and carry out studies that are more sound methodologically and with sufficient statistical power to establish the magnitude of the cardiovascular risks in our country. Additionally, we must not forget that the question asked by the planners and decision-makers in matters of health is not just whether an intervention or program is desirable, but also what degree of intervention is needed in order to eliminate or minimize a health problem.

In spite of all these observations, overweight and obesity are undoubtedly highly prevalent in the Spanish population and are increasing. This demands a much more decisive clinical and Public Health intervention,[14] in addition to the fight against smoking, to control the cardiovascular epidemic.

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