Commentary: Does the presence of asthma increase the incidence of coronary heart disease?

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The prevalence of asthma has increased markedly over the last 50 years in many countries, and asthma is now a major cause of morbidity in all age groups. In the UK approximately one-third of children aged 12–14 years have symptoms suggestive of current asthma and 4% of these children have frequent night time waking because of wheeze. The widespread introduction of inhaled corticosteroids and long acting beta-agonists has led to marked improvements in the morbidity attributable to asthma, and possibly also a decrease in mortality. As the asthma epidemic matures, however, there is a need to consider other features of the condition, and one aspect of particular interest to people with asthma is the potential for co-morbidity associated with the diagnosis.

In this edition of the International Journal of Epidemiology Iribarren et al. report the results of a historical cohort study of 151,620 people who were members of the Californian Kaiser Permanente Health Plan. The median duration of follow-up was 27 years and because members of the health plan were encouraged to attend for voluntary health checks, data were available on a number of potentially important confounding variables. Among men with asthma, 17% were either admitted to hospital or died as a result of coronary heart disease (CHD) compared with 19% of men without asthma. The corresponding figures for women were 13% and 11%. In the multivariate analyses the rate ratio for CHD in people with asthma compared with those without asthma was 0.99 (95% CI: 0.93, 1.05) for men and 1.22 (95% CI: 1.14, 1.32) for women.

There are a number of drawbacks with the study design that may explain the findings and the authors acknowledged some of these. Information on the CHD outcomes was derived from hospital discharge data and so is likely to be valid, but asthma was defined in part on the basis of self-reported diagnosis and so some random error may be present here. In addition, there may be some systematic bias in the diagnosis of asthma since smokers with respiratory symptoms tend to be diagnosed with asthma if they are female and chronic obstructive pulmonary disease if they are male. Given these limitations it would be interesting to see the impact on the analyses of trying to increase the specificity of the asthma diagnosis by looking at people with more severe disease, perhaps by stratifying according to the number of hospital admissions for asthma. In addition, residual confounding may be present since the simple classifications of smoking status and socioeconomic status recorded at entry to the study are unlikely to capture all of the impact of these important exposures. There may also be ascertainment bias if women tend to use health care resources more than men in general and therefore have more opportunities to receive diagnoses of asthma and CHD. Thus it would be reassuring to know that the severity of CHD outcomes was similar for men and women.

If the findings of Iribarren et al. are true, then why does asthma increase the incidence of CHD, and why is this effect present in women but not men? The authors speculate that the increased risk of CHD among people with asthma may result directly from the chronic inflammatory nature of asthma. Data to support this hypothesis come from the follow-up of the Dutch Vlagtwedde-Vlaardingen study in which eosinophilia was a predictor of cardiovascular death. Further circumstantial evidence is provided by the fact that adult women with asthma tend to have more severe disease than adult men with asthma, and so presumably have more systemic inflammation. Other explanations need consideration, however. It is possible that the drugs used to treat asthma may precipitate acute coronary events. Beta-agonists are commonly used as bronchodilators in people with asthma and two of the early preparations, isoprenaline forte and fenoterol, have been implicated in the epidemics of death amongst people with asthma in New Zealand during the 1960s and 1970s. Another possible explanation for the findings is that the association between CHD and asthma is mediated by lung function. Adults with asthma tend to have a lower forced expiratory volume in one second (FEV1) than those without asthma, and FEV1 has been shown to be an important predictor of CHD, particularly in women. Thus a simple explanation for the findings of Iribarren et al. is that in their study a diagnosis of asthma is merely acting as a proxy marker of FEV1. There are a number of reasons why FEV1 may be a good predictor of CHD. In absolute terms lung function is dependent on lung size and hence growth. Thus FEV1 is closely correlated with adult height, and FEV1 more completely captures the impact of early life exposure on growth. Alternatively this may reflect the more complex nature of FEV1 since lung function, to a far greater extent than adult height, may be impaired by a number of environmental exposures acting in adult life which are also risk factors for CHD, such as cigarette smoking and poor diet. The reason why in relative terms FEV1 appears to have a greater influence on the risk of CHD in women than men is not clear, but in one study the association between quintile of adult height and CHD was...
marginally stronger in women than men, suggesting that early life influences may be important. Adult women are more likely than men to have bronchial hyper-responsiveness and incident asthma however, and so other mechanisms acting later in life may also be important.

In summary, because asthma is now so common even a small increase in the relative incidence of CHD associated with a diagnosis of asthma would have a significant adverse public health impact. It is therefore important that we understand fully the relationship between asthma, FEV1, and CHD and to do this we need further cohort studies. In order to provide definitive answers these cohorts will require include information on serial measurements of lung function and objective markers of asthma, as well as early life exposures affecting growth and more traditional adult risk factors for CHD.

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References