EVIDENCE BASED MEDICINE

Shorter people are more likely to have coronary heart disease

Source: Christopher P. Nelson, et. al., Genetically Determined Height and Coronary Artery Disease. NEJM April 8, 2015. DOI: 10.1056/NEJMoa1404881

Epidemiological studies over the years have shown that there is a well established link between short stature and the risk of coronary artery disease (CAD). Shorter people were also found to have a higher incidence of high blood pressure, high levels of low-density lipoprotein (LDL) cholesterol, and diabetes (risk factors for CAD) when compared with those who were taller. Poor nutrition, educational level and other behavioural patterns that could be associated with short stature could not account for this association and hence the exact cause was not clear. This study has shown that genetic pathways that are associated with short stature were also associated with an increased risk of CAD. In other words, those with a short stature were genetically predisposed to CAD irrespective of other factors.

The researchers used a genetic approach and looked at 180 genetic variants in around 193,000 people (65,066 cases and 128,383 controls). 73.8% of the cases and 49.8% of the controls were men. The average age was 57.3 years (range, 42.4 to 75.6). The researchers performed two kinds of analyses. First, they looked at the association between height-related genetic variants and several established and potential cardiovascular risk factors. In the second analysis (genetic pathway analysis), they studied genetic pathways that were associated with short stature and with atherosclerosis.

Results:

This study found that there was a significant association between the height-associated genetic factors and CAD (odds ratio, 0.88; 95% CI, 0.82 to 0.95; P<0.001). For every 6.5cm or 2.5 inches decrease in height (one standard deviation), the risk of CAD increases by 13.5%.

There was a small but significant association between genetically determined height and an adverse lipid profile (high LDL and high Triglyceride levels). Though the association between short stature and CAD was significant in men, it was not significant in women. Whether this was a genuine difference or whether it was due to a smaller sample size was not clear.

One possible explanation for the association between short stature and CAD could be that smaller people have coronary arteries of smaller diameter (established in earlier studies). However, women also have smaller-caliber arteries than men, independent of body size and height and in this study the risk of CAD was not significantly higher in women, which argues against this as an explanation.

The second analysis (genetic pathway analysis) showed that there were overlaps between the genetic pathways associated with short stature and the pathways associated with atherosclerosis. Taken together, these findings suggest that several overlapping and complex biologic pathways on the one hand influence development and height and on the other hand influence the risk of atherosclerosis through an effect on vascular biology and function.

Author's conclusions:

- There is an inverse association between genetically determined shorter height and an increased risk of CAD. Part of this is because short stature is associated with an adverse lipid profile.
- There are overlapping genetic pathways between those associated with short stature and atherosclerosis this could partly explain the association.