Tall is beautiful and heart-healthy?

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This editorial refers to ‘Short stature is associated with coronary heart disease: a systematic review of the literature and a meta-analysis†, by T.A. Paajanen et al., on page 1802

A large number of studies have assessed the association between stature and coronary heart disease risk in many populations. Within a population, people of short stature seem to have a higher risk of coronary heart disease than taller people. Thus far, these data have not been subjected to a formal meta-analysis. Therefore, the systematic review and meta-analysis on this topic carried out by Paajanen and co-workers1 is well justified 60 years after the first observation2 and the hundreds of other papers which have been published since then on this topic. The results are unequivocal: short stature is associated with increased risk of coronary heart disease. This meta-analysis provides solid proof for this, but, as the authors conclude ‘The possible pathophysiological, environmental, and genetic background of this peculiar association is not known’.1

This systematic review of 52 observational studies comprising >3 million individuals is very impressive, and the full meta-analysis comprised 22 studies. The overall finding shows that short stature is associated with an increased coronary heart disease risk (95% confidence interval 1.37–1.55) compared with the tallest individuals in almost all studies included.1 There are, however, several issues that need to be discussed. First, observational studies are often prone to various confounding effects. Confounding occurs when two factors are associated with each other or ‘travel together’ and the effect of one is confused with or distorted by the effect of the other. A confounder is a variable which is associated with the exposure, and independently of that exposure is a risk factor for the disease. Observational studies are needed for the assessment of effects of factors that cannot be subjected to randomized controlled trials. Stature is in principle modifiable, and it varies between populations and over time, but it cannot be a target of a controlled trial. Short stature is associated with lower socio-economic status that in turn is related to an increased coronary heart disease risk.

Secondly, it is well known that in all populations women have a lower incidence of coronary heart disease compared with men,3 although women are shorter—thus the ‘within population association does not hold’. Since the association between stature and coronary heart disease risk is found within each sex, sex is clearly just an effect modifier. Thirdly, in a between-population comparison, coronary heart disease risk is not higher among those populations that have shorter stature.4 Fourth, it is also important to pay attention to secular trends in both stature and coronary heart disease. For instance, in Finnish men, a linear increase in height of ≈1.3 cm per decade has been reported during the 20th century,5 in keeping with the data from other industrialized countries. However, a continuous increase in coronary heart disease mortality took place until 1970, followed by a steep decrease during the last 40 years both in Finland and in many other western countries.6-7 These discrepant trends indicate that short stature is biologically not causing coronary heart disease.

Is this risk difference really due to short stature or do taller people carry some protective effects that lower their risk compared with their shorter fellow citizens? Very large differences in coronary heart disease incidence were observed between eastern (higher) and western (lower) Finland, especially in the second half of the 20th century.8 As a part of the Seven Countries Study it was noted that men in eastern Finland were shorter. Nevertheless, in both areas, short stature was an independent risk factor for coronary heart disease after the adjustment for major coronary risk factors such as serum cholesterol, blood pressure, and smoking. Interestingly, in taller men (>172 cm) no difference in incidence of coronary heart disease was observed between the two regions (Table 1).5 Thus, something related to short stature must have been involved in the risk of coronary heart disease in men in eastern Finland, and this is not explained by the major coronary risk factors alone.

Various environmental, mainly nutritional, factors influence human growth at all stages of development, starting from the prenatal period, and postnatal conditions also have many effects on growth. It is well known that prenatal factors have a strong influence on foetal growth, in particular trunk growth, whereas legs grow more postnatally than the trunk.10 Intrauterine nutritional problems are related to many health problems in adulthood,

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including coronary heart disease. The length effects of postnatal growth are not simple. It is proposed that leg length is the component that is most sensitive to the early environment, and short leg length but not trunk length is associated with coronary heart disease. Socio-economic adversity in childhood is thus associated with delayed early growth and shorter adult stature. The so-called catch-up growth during the first years of life among children who are born small has negative health effects in adulthood; much of the early growth is due to greater fat accumulation. Thus, it is most likely that short stature is the link to coronary heart disease, and that tallness is not a primary factor in preventing the disease, although it indicates healthy growth. Short stature seems to be a marker of risk. All major biological risk factors for coronary heart disease are inversely correlated to stature. Several studies included in the meta-analysis of Paajanen et al. have adjusted for other risk factors in their original analyses, but interactions between stature and other risk factors for the development of the disease still remain unknown.

What are the reasons for the variation in adult height? It is becoming increasingly clear that adult height as an end-result of a multitude of genetic and environmental factors is highly poly- morphic. There is no doubt that adult height is a genetically determined trait, well illustrated by population comparisons and a similar adult height among healthy identical twins. Heritability estimates suggest that within a population at least 80% of variation in height may be genetically determined. Despite the high heritabi-

Can information on human height be used for the prevention of coronary heart disease and other chronic diseases linked to short stature? The answer is clearly ‘yes, it can’. Full-term babies who are born small are likely to be short as adults. They should receive preventative attention early on. The primordial prevention of chronic diseases should start during foetal life, and health promotion should be targeted to all pregnant women with the aim of healthy development of the foetus. Low birth weight and some other birth characteristics can reveal potential problems during this period of life. After that, in babies with low birth weight, it is important to avoid excessive catch-up growth, i.e. early-life fatness. However, in adult life it is not easy to discover the best practices and evidence-based approaches to prevent coronary heart disease in those of short stature. It is likely that they would benefit from more aggressive risk factor reduction. Currently, no algorithms exist to include height in risk prediction scores, and whether they should be population/ethnicity specific, but only a few populations have proper prospective data to develop such risk algorithms. This makes the practical use of short stature in preventive cardiology very difficult, but most of us know approximately our own height ranking, and, if we are at the low end, we should take coronary risk factor control more seriously. On the other hand, tall people are not protected against coronary heart disease, and they also need to pay attention to the same risk factors as shorter people.

Conflict of interest: none declared.

References


People's corner: Prize awarded

Gabriela Kania, MSc, PhD

The successful research of Gabriela Kania has resulted in two recent awards: Maria Heim-Vögltin Prize in late 2009, a Swiss National Foundation grant for women in science; Cardiovascular Biology Prize 2010 from the Swiss Society of Cardiology. Currently, Gabriela is working as an independent research associate in the Division of Cardioimmunology, Department of Cardiovascular Research at Zurich University. She completed her biology studies at Jagiellonian University in Cracow, Poland, in 1998 and a PhD thesis in early embryology in 2001 at the Department of Animal Reproduction, National Institute of Animal Production in Cracow, Poland. At that time, she was highly involved in research (1999–2001) cooperating with PienGen Biomedical Corporation, Knoxville, TN, USA, in two main projects: cloning in cattle and cats. After finishing her PhD, she decided to broaden her scientific interests and moved to Gatersleben, Germany, to the laboratory of Professor Anna M. Wobus to study the differentiation potentials of embryonic and adult stem/progenitor cells. To deepen her knowledge further, she opted to cross-talk between stem/progenitor cell research and the heart regeneration/pathological remodelling in the inflammatory cardiomyopathy mouse model of Professor Urs Eriksson’s group in Basel. In April 2009, she moved with Eriksson’s group to Zürich and joined the excellent Cardiovascular Research Department (University of Zürich) headed by Professor Thomas F. Lüscher. There she leads projects, raises funds for herself and the projects’ costs, actively participates in scientific meetings, and has successfully established national and international collaborations. Gabriela's scientific interests focus on heart regeneration. She identified the pool of stem/progenitor cells within the inflamed heart, and studied the role of these progenitors in heart remodelling in the mouse model of inflammatory cardiomyopathy. Gabriela strongly believes that the local cytokine milieu determines the fate of progenitor cells recruited to the injured heart. She recently showed that the micro-environment of the inflamed heart disables myocardial regeneration from cell progenitors, and instead promotes pathological tissue remodelling leading to cardiac fibrosis. Therefore, for the near future, myocardial fibrosis is an expected target in the battle against heart disorders. Gabriela said, ‘My dream is to design stem cell-based therapies that attenuate myocardial fibrosis and promote the heart reparative processes instead’. She is a member of the Swiss Stem Cell Network and a junior member of the Zurich Centre for Integrative Human Physiology (ZIHP). As a mother of two small girls (1 and 3 years old), she believes it is a real challenge to combine a successful scientific carrier with family responsibility.

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