Selected Summaries

Waist–hip ratio: A thrifty phenotype?

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SUMMARY
In the second report of the Interheart study, Salim Yusuf and colleagues have reported on the associations between different obesity measures and myocardial infarction. In a case–control study of over 27,000 men and women belonging to many different ethnic groups in 52 countries, they found that the waist–hip ratio (WHR) has a much stronger association with myocardial infarction than the body mass index (BMI) or the waist circumference. Of the two measures of central size, waist circumference was predictive than the body mass index (BMI) or the waist circumference. The authors and an accompanying leader in the Lancet suggest that the BMI is an inappropriate risk factor for myocardial infarction and that it should be replaced by waist and hip measurements.

COMMENT
The Interheart study is a marvellous achievement in collaborative epidemiology, and the number of myocardial infarctions (more than 12,000) must be one of the largest ever studied. However, a cross-sectional case–control design does not establish causality, and ‘obesity’ has a number of metabolic, mechanical and other risks, which may or may not be captured by one measurement. Further studies are necessary before we can say that BMI should be replaced in clinical practice, but doctors should now start using a measuring tape in addition to a weighing scale, height stadiometer and the stethoscope. More efforts are necessary to standardize the measurement of waist and hip circumferences, which are somewhat difficult because of anatomical reasons and social inhibitions.

BMI is the most frequently used index of obesity, and has the advantage that it is easily measured. WHO has provided ‘normal’ values and guidelines on the diagnosis of ‘undernutrition’ and ‘overnutrition’, and these dictate current clinical practice. Over the past few years there is a growing concern that the WHO criteria for the diagnosis of ‘overweight’ and ‘obesity’ may not be universally appropriate, and that body composition rather than size may be the more relevant risk factor for non-communicable diseases (NCD). Thus, Asian Indians have a high risk of type 2 diabetes at a low BMI. Such considerations led to new ‘population-specific’ recommendations for ‘public health action points’ of BMI. The differences in the risk of a given BMI in different populations are partly due to differences in ‘adiposity’ (body fat percentage) and its distribution. Thus, Asian Indians have a higher adiposity for a given level of obesity, and it is more central than compared with other populations. The suggested BMI cut-off point for Asian Indians is 23 kg/m², which is lower than that for other populations. On the other hand, Pacific Islanders have a larger body frame and are muscular; the cut-off point for them is 27 kg/m².

Jean Vague, a French physician, first suggested that cardiovascular and metabolic risk in women is more closely related to ‘android’ (upper body or abdominal) than to ‘gynoid’ (lower body) obesity. Thus, ‘apples’ suffer more than ‘pears’. A real boost for this idea came after the publication of prospective follow up reports from Sweden, which showed that higher WHR predicted incident type 2 diabetes, cardiovascular events and death in Swedish women and men. The first report of the association between WHR and hyperglycaemia in Indians was from Pune.

Per Bjorntorp and Rosmond elaborated the concept of central obesity and proposed that the risk was related to ‘visceral’ (rather than subcutaneous) fat which drained in the portal circulation. This produces morphological (steatosis) and metabolic derangements in the liver causing insulin resistance, abnormal lipid metabolism and a pro-coagulatory, pro-thrombogenic and pro-inflammatory state. These arguments were supported by newer imaging techniques (CT and MRI), which allowed separation of abdominal fat into subcutaneous and ‘visceral’ compartments. However, it is still debated if subcutaneous abdominal or visceral fat carries a higher risk for NCD.

The conventional explanation for the metabolic and vascular risks of adiposity has revolved around the role of fatty acids that cause insulin resistance by metabolic competition (Randle ‘glucose–fatty acid’ cycle). In addition, fatty acids are vasculotoxic and are ligands for nuclear factors which have a profound effect on metabolism (for example, peroxisome proliferator-activated receptors, PPARs). Fat tissue is now recognized as the largest ‘endocrine’ organ, secreting a number of protein molecules (‘adipokines’) which affect intermediary metabolism (leptin, resistin and adiponectin), inflammation (interleukin-6), thrombosis (plasminogen activator inhibitor-1), etc. It is not clear how adipose tissue in different parts of the body behaves differently.

Understanding the factors that influence deposition of lean and fat tissue is thus of paramount importance. Body fat of the human foetus is influenced by maternal adiposity, metabolism and nutrition. Maternal glycaemia (even in the normal range) is a well known risk factor for foetal adiposity and subsequent obesity and type 2 diabetes; maternal lipids may be equally important. On the other hand, low birth weight and thinness (‘thrifty phenotype’) have also been associated with increased risk of NCD. This apparent paradox was resolved when low birth weight babies were shown to be ‘thin but fat’, and to grow into ‘obese’ children and adults. There is as yet little information on the specific genetic and maternal nutritional factors that influence foetal body composition, and it is interesting to note...
that there are few, if any, paternal determinants of foetal adiposity. Recently, we have shown that an imbalance in maternal vitamin B$_2$ and folate nutrition could programme adiposity and insulin resistance in Indian babies. Rapid childhood growth (presumably due to abundant nutrition) increases the risk of central adiposity.

What might be the evolutionary advantage of ‘central adiposity’ for the developing foetus? Post partum, the fat provides energy and helps thermoregulation. The driving force for fat deposition may be the need for brain preservation, a requisite for species survival. The brain is composed mostly of fat, and the requisite nutrients are supplied by diversion of blood flow to the preductal circuit, depriving the ‘caudal’ structures (heart, liver, kidneys, pancreas and legs). Short legs, representing ‘caudal diminution’ predict diabetes and cardiovascular disease. Higher WHR thus represents an exaggerated thrifty phenotype due to rapid nutritional transition: small hips represent foetal deprivation and large waist the subsequent abundance. Thus, prevention of cardiovascular disease may depend on the use of appropriate measures during foetal life and childhood, whereas measures targeting adults will probably be much less effective.

REFERENCES