

# Obesity and the heart: The impact of obesity beyond the body mass index

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Obesity is a public health concern all over the world. The incidence has tripled since 1975 and in 2016 an estimated 39% of all adults worldwide were either overweight or obese.<sup>1</sup> Overweight and obesity are traditionally defined by body mass index (BMI). Obesity comes with a multitude of morbidities and is associated with pre-mature all-cause and cardiovascular disease-related mortality.<sup>1</sup> One of the recognised effects of obesity is heart failure, both with and without preserved ejection fraction.<sup>2</sup> The prevalence of heart failure increases with aging and is estimated to be around 7.5% in adults aged 75 years and over.<sup>3</sup> Generally, overt clinical heart failure is preceded by years of subclinical decline in ventricular function. Conditions leading to heart failure include coronary heart disease, hypertension, diabetes mellitus and obesity. The negative health impact of obesity is likely related to the amount of abdominal fat. Easy anthropometric tools such as waist circumference and the waist to hip ratio are used to quantify excess abdominal fat. Imaging methods that are able to evaluate body composition and to differentiate between subcutaneous abdominal fat (subcutaneous adipose tissue (SAT)) and visceral abdominal fat (visceral adipose tissue (VAT)) are gaining popularity. A recognised method to measure abdominal fat is computed tomographic examination of the fat area.<sup>4</sup>

Sawada et al. addressed the relation between abdominal fat distribution and subclinical ventricular dysfunction in healthy volunteers at the University of Tokyo Hospital in Japan. The hospital provides an extensive health check-up for the general population to promote health and prevent cardiovascular disease. These systems are called 'Kenshin', and are common in Japan. In the current study 340 individuals were included who voluntarily underwent an extensive cardiovascular health check-up. Assessment comprised measurement of BMI, subcutaneous versus visceral abdominal fat with an abdominal computed tomographic examination, and cardiac function including left ventricular global longitudinal strain and right ventricular free-wall longitudinal strain with speckle-tracking echocardiography. VAT was significantly related with a decrease in left and right ventricular strain, independent

of classic cardiovascular risk factors, whereas SAT was not. Serum adiponectin, an anti-inflammatory adipokine, was correlated to left ventricular strain, with higher values indicating lower strain.

The results of Sawada et al. are interesting, as the relation between abdominal fat distribution and subclinical heart failure is not yet studied widely in a healthy population. Given the substantial impact on health, it is important to recognise the determinants of heart failure in an early stage. Several publications are in line with the findings of Sawada et al.

In the Atherosclerosis Risk in Communities Study, including individuals from four communities in the USA aged 66 years and over, an increase in BMI and waist circumference were found to be associated with an increase in left ventricular stiffness. Moreover, body fat percentage was strongly related to ventricular stiffness, independently of BMI. Ventricular stiffness has been related to the development of heart failure, and specifically heart failure with preserved ejection fraction.<sup>5</sup>

Neeland et al. included 2710 healthy individuals in the Dallas Heart study, a multi-ethnic population cohort, and found that VAT was independently associated with concentric left ventricular remodelling and a reduced cardiac output.<sup>6</sup> A recent study in the UK, including 4590 individuals, found that VAT was associated with a decrease in ejection fraction in men. The authors suggest that VAT might be more related to left ventricular remodelling than general obesity.<sup>7</sup>

In the Multi-Ethnic Study of Atherosclerosis, one standard deviation increase in VAT resulted in a hazard ratio (HR) of 2.24 to be hospitalised for heart failure with preserved ejection fraction. On the

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contrary, there was no relation between SAT and heart failure. Both BMI and waist circumference were also related to hospitalisation for heart failure, but with weaker associations than VAT.<sup>8</sup>

To summarise, within the spectrum of overweight and obesity, VAT is the component that seems to be mainly responsible for the adverse impact on cardiac structure and function. This is not surprising as there is a wealth of evidence on the adverse metabolic effects of VAT. Adipose tissue functions as an endocrine organ and secretes multiple adipokines, some with pro-inflammatory, and others with anti-inflammatory, capacity. A group from the Netherlands showed that VAT, and not SAT, resulted in an increase in pro-inflammatory adipokines, and a decrease in anti-inflammatory adipokines.<sup>9</sup> Last year a review described the development of heart failure and the pro-inflammatory effects of VAT through the leptin-aldosterone-nephrilysin axis. Adiposity, and especially VAT, increases the leptin receptor, which in turn results in activation of the renin-angiotensin system and the sympathetic nervous system. Plasma volumes are expanded with cardiac fibrosis and remodelling initiated. Nephrilysin, a pro-inflammatory adipokine, is upregulated. This promotes adipogenesis and adipocyte dysfunction.<sup>10</sup> Sawada et al. touched on the metabolic pathway as they measured total serum adiponectin, an anti-inflammatory adipokine, the expression of which is decreased in obesity. Adiponectin was correlated to both left and right ventricular strain, but lost its significance following multivariable adjustment. It might be the case that serum adiponectin alone is not enough to understand the influence of adipokines on heart structure and function, as acknowledged by the authors. Measurement of other adipokines and adiponectin isoforms might be needed to increase our understanding of the influence of VAT on cardiac structure and function.

Sawada et al. did not analyse the relation between BMI and ventricular strain nor did they adjust for BMI in their models, so it is unclear what the incremental value of abdominal fat assessment is over BMI in their study. However, considering all the evidence on BMI, waist circumference and body composition effects on cardiac structure and function, there is a strong indication that anthropometric measurements alone do not tell the whole story.

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