Published in final edited form as:

Heart. 2015 February ; 101(3): 165–166. doi:10.1136/heartjnl-2014-306921.

Obesity and sudden death: visceral response?

Kyndaron Reinier and Sumeet S Chugh

The Heart Institute, Cedars-Sinai Medical Center, Los Angeles, California, USA

The public health burden of sudden cardiac death (SCD) is high, accounting for about 50% of cardiovascular deaths, and resulting in more years of potential life lost than any single cancer.¹ There is an established association between obesity and SCD²³ which has attained increased importance due to the burgeoning global rise in the proportion of overweight and obese individuals. In the USA, obesity has reached epidemic proportions. A third of the population is obese, with median body mass index (BMI) above 27 kg/m² and age-adjusted obesity prevalence above 35% for both sexes.⁴

Obesity appears to drive overall cardiovascular morbidity and mortality largely by its link to cardiovascular risk factors including diabetes, total cholesterol, low density lipoprotein, and hypertension. Traditionally, BMI has been used in analyses of obesity and outcomes, but there is a growing literature suggesting that the distribution of body fat is important in determining cardiovascular disease (CVD) risk. In particular, abdominal adiposity appears to confer a higher risk for CVD than obesity in general.⁵

OBESITY AS A RISK FACTOR

From a mechanistic perspective, there are several reasons why a detailed examination of obesity as a risk factor for SCD is warranted. Obesity is associated with a variety of ECG abnormalities, including prolonged ventricular repolarisation (QT interval), which increases susceptibility to ventricular arrhythmias. Obesity also increases risk for heart failure, LV hypertrophy and dilatation, sleep apnoea, and altered sympathetic tone, all of which may increase risk of SCD beyond traditional CVD risk factors. Despite these associations, relatively few studies have examined the obesity–SCD association; indicating that the relative contribution and determinants of risk conferred by BMI and abdominal obesity need to be dissected further. An earlier analysis from the Paris Prospective Study reported an association with increased BMI² and a subsequent report highlighted a potential role for sagittal abdominal diameter.³

The interesting findings presented by Adabag and colleagues,⁶ regarding the role of obesity in SCD, have both clinical and research implications. Among nearly 15 000 participants

Correspondence to Professor Sumeet S Chugh, Cedars-Sinai Medical Center, Advanced Health Sciences Pavilion, Suite A3100, 127 S. Vicente Blvd., Los Angeles, CA 90048, USA; sumeet.chugh@cshs.org.

Contributors KR drafted the initial manuscript; SSC made critical revisions; both authors made subsequent revisions and approved the final document.

Competing interests None.

Provenance and peer review Commissioned; internally peer reviewed.

from the Atherosclerosis Risk in Communities (ARIC) cohort, 253 SCDs occurred over a mean follow-up of 12 years. Risk of SCD was significantly associated with all obesity measures (BMI, waist circumference (WC), and waist to hip ratio (WHR)) among non-smokers, when adjusted for age, sex, study centre, and education level. However, the association of BMI and WC with SCD appeared to be largely mediated by cardiovascular risk factors and overt CVD; after adjustment for these factors, including hypertension, lipid profile, prevalent coronary heart disease, heart failure, and LV hypertrophy, BMI and WC were no longer associated with SCD risk. In contrast, WHR remained a significant predictor of SCD risk after adjustment for these factors. Individuals in the highest WHR category (>0.95 for women and >1.01 for men) had a twofold higher risk of SCD than those with normal WHR (HR 2.03, 95% CI 1.19 to 3.46). The authors also found that among the very obese (BMI >35), general obesity also remained a significant predictor of SCD risk.

STUDY STRENGTHS AND WEAKNESS

There are several notable strengths of this analysis by Adabag and colleagues. The ARIC cohort included a large number of individuals from four diverse communities, including 74% white and 26% black participants. SCD was adjudicated by a committee using standardised criteria. A large number of predictor variables were carefully assessed at baseline and at regular follow-ups, including information allowing the calculation of different indices of obesity, including BMI, WC, and WHR. This enabled the authors to compare the relative importance of these measures as predictors of SCD. Interestingly, although both WC and WHR are indirect measures of visceral abdominal obesity and earlier studies have shown both indices to predict cardiovascular outcomes independent of BMI, in this study WHR was more strongly associated with SCD than WC.

It is important to recognise a few weaknesses, particularly since these may present opportunities for future research. First, there was a substantial length of time (mean 12.6 ± 2.5 years) between the measurement of body size and the end of follow-up. As the authors acknowledge, they did not examine potential changes in bodyweight or body fat composition during follow-up. Secondly, smoking status was apparently only considered at baseline. Given that smoking status was obtained by questionnaire at each follow-up study visit, some data regarding changes in smoking prevalence over the 12 year follow-up would have been helpful, particularly because smoking cessation has been associated with weight gain. One aspect of their study that was not fully discussed was the unexpected finding that obesity was 'protective' against SCD among smokers in the fully adjusted model. As the authors mention, this could be an example of the obesity paradox. Finally, echocardiographic measures of LV systolic function were not available. Because LV dysfunction (as measured by LVEF) remains the primary clinical determinant for primary prevention of SCD in the general population, evaluation of whether WHR predicted risk of SCD after accounting for EF would have been ideal but was not possible.

Overall, the findings of Adabag and colleagues suggest that WHR, an estimate of visceral abdominal adiposity, is a better predictor of SCD than BMI. The present results held true among women and blacks, and thus build upon those of Empana and colleagues,³ whose study included only native Frenchmen. Given the large public health burden of SCD and the

staggeringly high prevalence of obesity, more studies to elucidate specific mechanisms by which visceral fat increases SCD risk are warranted.

OBESITY: A 'PAN-INFLAMMATORY' STATE

The epicardial space contains visceral adipose tissue with a similar embryologic origin to abdominal adipose tissue.⁷ Increased epicardial fat, contiguous with atrial and ventricular myocardium, has been associated with an increased risk of atrial fibrillation, and could also promote ventricular arrhythmias. Current evidence suggests that obesity is a 'pan-inflammatory' state and increased visceral fat releases inflammatory cytokines that contribute to coronary atherosclerosis as well as other cardiovascular risk factors.⁷ Visceral adipose tissue is metabolically active, with a constant flux of free fatty acids entering and leaving visceral fat.⁷ We and others have previously reported an association between free fatty acids and SCD.⁸ Experimental models demonstrate that an increased plasma concentration of plasma free fatty acids leads to abnormal lipid deposition within the myocardium, and the resulting increased intracellular triglyceride concentrations lead to cell injury and death.

The good news is that obesity and abdominal adiposity are potentially modifiable risk factors, and weight loss is achievable with lifestyle modification and pharmacologic interventions. In addition, we are learning more about how to implement effective population-level interventions to prevent weight gain across the lifespan. We acknowledge that visceral fat may have a somewhat non-specific association with SCD, given its relation to overall cardiovascular risk factors and non-SCD cardiovascular outcomes.³ However, this represents an opportunity: if reduction in visceral adiposity reduces the incidence of both SCD and other CVD events, such an intervention could prevent premature death and improve the health of many thousands in the USA on an annual basis.

Acknowledgments

Funding Funded in part, by US National Heart, Lung, and Blood Institute grants R01 HL105170 and R01 HL122492 to SSC. SSC is the Pauline and Harold Price Chair in Cardiac Electrophysiology at the Heart Institute, Cedars-Sinai Medical Center, Los Angeles, California, USA

References

1. Stecker EC, Reinier K, Marijon E, et al. Public health burden of sudden cardiac death in the United States. *Circ Arrhythm Electrophysiol*. 2014; 7:212–17. [PubMed: 24610738]
2. Jouven X, Desnos M, Guerot C, et al. Predicting sudden death in the population: the Paris Prospective Study I. *Circulation*. 1999; 99:1978–83. [PubMed: 10209001]
3. Empana JP, Ducimetiere P, Charles MA, et al. Sagittal abdominal diameter and risk of sudden death in asymptomatic middle-aged men: the Paris Prospective Study I. *Circulation*. 2004; 110:2781–5. [PubMed: 15492315]
4. Flegal KM, Carroll MD, Kit BK, et al. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999–2010. *JAMA*. 2012; 307:491–7. [PubMed: 22253363]
5. Zhang C, Rexrode KM, van Dam RM, et al. Abdominal obesity and the risk of all-cause, cardiovascular, and cancer mortality: sixteen years of follow-up in US women. *Circulation*. 2008; 117:1658–67. [PubMed: 18362231]
6. Adabag S, Huxley RR, Lopez FL, et al. Obesity-related risk of sudden cardiac death: the Atherosclerosis Risk in Communities study. *Heart*. 2015; 101:215–21. [PubMed: 25410499]

7. Alexopoulos N, Katritsis D, Raggi P. Visceral adipose tissue as a source of inflammation and promoter of atherosclerosis. *Atherosclerosis*. 2014; 233:104–12. [PubMed: 24529130]
8. Havmoeller R, Reinier K, Teodorescu C, et al. Elevated plasma free fatty acids are associated with sudden death: a prospective community-based evaluation at the time of cardiac arrest. *Heart rhythm*. 2014; 11:691–6. [PubMed: 24418168]