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European Society of Cardiology

'Fitness and fatness': Not all obese people have the same prognosis

Second study sheds light on the 'obesity paradox'

People can be obese but metabolically healthy and fit, with no greater risk of developing or dying from cardiovascular disease or cancer than normal weight people, according to the largest study ever to have investigated this, which is published online today (Wednesday) in the *European Heart Journal* [1].

The findings show there is a subset of obese people who are metabolically healthy – they don't suffer from conditions such as insulin resistance, diabetes and high cholesterol or blood pressure – and who have a higher level of fitness, as measured by how well the heart and lungs perform, than other obese people. Being obese does not seem to have a detrimental effect on their health, and doctors should bear this in mind when considering what, if any, interventions are required, say the researchers.

"It is well known that obesity is linked to a large number of chronic disease such as cardiovascular problems and cancer. However, there appears to be a sub-set of obese people who seem to be protected from obesity-related metabolic complications," said the first author of the study, Dr Francisco Ortega (PhD). "They may have greater cardiorespiratory fitness than other obese individuals, but, until now, it was not known the extent to which these metabolically healthy but obese people are at lower risk of diseases or premature death."

Dr Ortega is currently a research associate affiliated to the Department of Physical Activity and Sport, University of Granada (Spain), and at the Department of Biosciences and Nutrition, Karolinska Institutet (Stockholm, Sweden); but the project and investigation took place at the University of South Carolina (Columbia, USA) under the direction of Professor Steven Blair, who is responsible for the long-running "Aerobics Center Longitudinal Study" (ACLS) which provided the 43,265 participants for this current analysis.

The participants were recruited to the ACLS between 1979 and 2003. They completed a detailed questionnaire, including information on their medical and lifestyle history, and they had a physical examination that included a treadmill test to assess cardio-respiratory fitness and measurements of height, weight, waist circumference, and their percentage of body fat. Body fat percentage (BF%) was measured either by calculating the amount of water displaced when the person was completely submerged (the method that is considered the most accurate), or by taking the sum of seven skin fold measures (when folds of skin are pinched between measurement callipers). Blood pressure, cholesterol and fasting glucose levels were also measured. The study participants were followed until they died or until the end of 2003.

Dr Ortega and his colleagues found that 46% of the obese participants were metabolically healthy. After adjusting for several confounding factors, including fitness, the metabolically healthy but obese people had a 38% lower risk of death from any cause than their metabolically unhealthy obese peers, while no significant difference was seen between the metabolically healthy but obese and the metabolically healthy, normal weight participants. The risk of developing or dying from cardiovascular disease or cancer was reduced by between 30-50% for the metabolically healthy but obese people, and there were no significant differences observed between them and the metabolically healthy, normal weight participants.

"Our study suggests that metabolically healthy but obese people have a better fitness level than the rest of obese individuals. Based on the data that our group and others have collected over years, we believe that getting more exercise broadly and positively influences major body systems and organs and consequently contributes to make someone metabolically healthier, including obese people. In our study, we measure fitness, which is largely influenced by exercise," said Dr Ortega.

"There are two major findings derived from our study. Firstly, a better cardio-respiratory

fitness level should be considered from now on as a characteristic of this subset of metabolically healthy obese people. Secondly, once fitness is accounted for, our study shows for the first time that metabolically healthy but obese individuals have similar prognosis as metabolically healthy normal-weight individuals, and a better prognosis than their obese peers with an abnormal metabolic profile."

The researchers say their findings have important clinical implications. "Our data suggest that accurate BF% and fitness assessment can contribute to properly define a subset of obese individuals who do not have an elevated risk of CVD [cardiovascular disease] or cancer," they write.

Dr Ortega added: "Physician should take into consideration that not all obese people have the same prognosis. Physician could assess fitness, fatness and metabolic markers to do a better estimation of the risk of cardiovascular disease and cancer of obese patients. Our data support the idea that interventions might be more urgently needed in metabolically unhealthy and unfit obese people, since they are at a higher risk. This research highlights once again the important role of physical fitness as a health marker."

A second study [2], which analysed data from over 64,000 patients on the Swedish Coronary Angiography and Angioplasty registry, has provided further evidence for a phenomenon known as the "obesity paradox", whereby once someone has developed heart disease, they have a reduced risk of dying if they are overweight or obese, while underweight and normal weight patients have an increased risk.

The researchers looked at 64,436 patients who had developed acute coronary syndromes (ACS) such as unstable angina and myocardial infarction (heart attacks) and who underwent coronary angiography (a specialised x-ray test to discover detailed information about the condition of a patient's coronary arteries) between May 2005 and December 2008.

Dr Oskar Angerås, consultant cardiologist and PhD student at the Sahlgrenska Academy, University of Gothenburg (Gothenburg, Sweden) who led the research, explained: "We found that patients who were underweight with a body mass index (BMI) of less than 18.5 kg/m2 had the greatest risk of dying. Their risk was double that of normal weight patients, who had a BMI of between 21 and 23.5 kg/m2. Compared to the group with lowest risk – those with a BMI of 26.5 to 28 kg/m2, they had three times the risk of death."

The researchers found that the relation between BMI and mortality was U-shaped. "Those with the lowest risk of death were overweight and obese patients with BMIs ranging from 26.5 to about 35 kg/m2. The highest risk was found among underweight and morbidly obese patients, that is those with a BMI above 40 kg/m2," said Dr Angerås.

It is well known that maintaining a healthy weight is one of the ways to avoid developing heart problems. However, the researchers say that advice to lose weight has been extended to overweight and obese patients who have already developed heart problems, despite limited scientific evidence that this helps. As a result of their findings, the authors write: "We believe that no evidence exists that proves weight reduction in itself has a positive prognostic value after ACSs. Actually some evidence suggests that weight loss after ACSs might in fact have a negative effect. We believe that given the current state of our knowledge, obesity paradox requires much more attention and deserves to be recognized in the guidelines."

In an accompanying editorial on both papers [3], Stephan von Haehling, Oliver Hartmann and Stefan Anker conclude: "The available studies, together with previously published study data, permit the conclusion that weight loss in patients with chronic illness and a BMI <40 kg/m2 is always bad, and in fact not a single study exists to suggest that weight loss in chronic illness makes patients live longer. In this context, fat tissue has several beneficial effects, for example in its action as an endocrine organ, but also, nevertheless, as an aid in protecting against hip fracture. Obesity may carry benefit up to a certain degree, and it should be recognized that obesity is not necessarily associated with abnormal metabolic function."

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Notes:

[1] "The intriguing metabolically healthy but obese phenotype: cardiovascular prognosis and role of fitness," by Francisco B. Ortega, Duck-chul Lee, Peter T. Katzmarzyk, Jonatan R. Ruiz, Xuemei Sui, Timothy S. Church, and Steven N. Blair. *European Heart Journal*. doi:10.1093/eurheartj/ehs174.

[2] "Evidence for obesity paradox in patients with acute coronary syndromes: A report from the Swedish Coronary Angiography and Angioplasty Registry", by Oskar Angerås, Per Albertsson, Kristjan Karason, Truls Råmunddal, Göran Matejka, Stefan James, Bo Lagerqvist, Annika Rosengren, and Elmir Omerovic. *European Heart Journal*. doi:10.1093/eurheartj/ehs217.

[3] "Does obesity make it better or worse: insights into cardiovascular illnesses", by Stephan von Haehling, Oliver Hartmann, and Stefan D. Anker. *European Heart Journal*. doi:10.1093/eurheartj/ehs237.

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