Obesity Alone Increased CHD Death Risk in Men

Study shows 60% higher risk, independent of factors such as hypertension and high cholesterol.

BY JENNIE SMITH

FROM HEART

Being obese may significantly increase the risk of having a fatal coronary heart disease event independent of known obesity-associated cardiovascular risk factors such as high blood pressure and high cholesterol, investigators in Scotland have found.

By contrast, obesity alone was not seen as significantly increasing the risk of nonfatal CHD events.

The findings, derived from the long-term follow-up of a large pharmaceutical trial, and published in the journal Heart (doi:10.1136/hrt.2010.211201), suggest that fatal and nonfatal CHD events could have separate causes – and that CHD death might not be preventable by mitigating traditional cardiovascular risk factors in obese men.

"It's assumed that nonfatal and fatal events occur along an index of severity – but maybe there's something different going on," Dr. Jennifer Logue of the University of Glasgow, the study's lead investigator, said in an interview.

With the fatal events, she said, "we found an almost 60% higher risk from obesity alone." The risk was seen after modeling for obesity-associated cardiovascular risks such as high blood pressure and high cholesterol level, along with factors such as smoking, low socioeconomic status, and medications.

"If you've got a middle-aged man in front of you with a [body mass index] of 35 – and that's not an uncommon sight nowadays – yes, you can treat his blood pressure and cholesterol and help him stop smoking," Dr. Logue said. "But his weight itself is still making him at significant risk."

Dr. Logue and her colleagues examined data from 6,082 men, with a mean age of 55, who had moderate hypercholesterolemia but who were without a history of diabetes or cardiovascular disease. The men had originally been enrolled in a manufacturer-sponsored, 5-year, randomized, placebo-controlled controlled trial to determine the effectiveness of the statin drug pravastatin in preventing cardiovascular events (N. Engl. J. Med. 1995; 333:1301-7), and the follow-up period ran to 15 years.

The researchers excluded from their analysis men who had had a fatal or nonfatal CHD event in the first 2 years of the study, or those who had diabetes. A total of 1,027 nonfatal and 214 fatal CHD events were included in the analysis.

Dr. Logue and her colleagues created two models in an attempt to isolate the role played by obesity alone in the fatal and nonfatal CHD events. One adjusted for age, sex, and statin treatment only. The other adjusted for these factors plus known cardiovascular risk factors, including blood pressure, elevated cholesterol, smoking status, high blood pressure, and use of a host of medications affecting blood pressure or the cardiovascular system. A standard social deprivation score, a measure of socioeconomic status, was also incorporated into the model.

The risk of fatal CHD events, the investigators found, was significantly increased in men with a body mass index of between 30 and 39.9 kg/m^2 in both the minimally adjusted model (hazard ratio, 1.75) and the adjusted model (HR, 1.60). Nonfatal CHD was not seen as independently increased by high BMI.

"This link was not seen for non-fatal CHD events and therefore, owing to large relative numbers of such events, also not seen for composite CHD events," the investigators wrote in their analysis. "In other words, our data suggest that obesity may give greater risk for fatal CHD events than nonfatal events, even after accounting for classical CHD risk factors."

The investigators cautioned that their results were not conclusive, but "should be considered hypothesis generating."

Among the weaknesses of their study, they wrote, was the fact that it evaluated only men, and that the percentage of participants who were obese was relatively small, limiting its statistical power.

Among the study's strengths, they wrote, was "the large cohort with a high number of events; this has allowed significant results to be generated while still allowing participants with events in the first 2 years to be excluded, along with those with known diabetes." A further strength, they wrote, was having details of each death, thanks to standardized government records. "Had we combined fatal and nonfatal CHD events we would have missed this important association."

Dr. Logue and her colleagues cited in their analysis a study highlighting inflammation as a possible culprit in fatal CHD events (PLoS Med. 2009 Aug. 6;6: e1000099) and another exploring the effects of adiposity on inflammation (J. Clin. Endocrinol. Metab. 2010;95:93-9).

"Recent work has shown that inflammatory markers, namely, IL-6, CRP, and fibrinogen, are more strongly related to fatal than nonfatal cardiovascular events. As obesity is increasingly recognized as an inflammatory state, this is a potential etiological pathway to account for the increased risk of fatal CHD events seen with obesity," the investigators wrote.

Dr. Logue said in an interview, however, that the culprit was far from clear. "It could be inflammation," she said. "But there's also upcoming evidence around structural changes to the heart caused by obesity, which could mean your heart can't cope as well when you're having a heart attack." But more important in any case, she said, is to learn whether the risk of a fatal CHD event is mitigated by weight loss.

"I'd rather see the resources put into looking to see if we can get people's weight down and preventing people getting to this weight in the first place," Dr. Logue said.

The pravastatin trial and the first 5 years of follow-up were funded by the drug's manufacturer, Bristol-Myers Squibb and Sankyo. The final years of follow-up and Dr. Logue and her colleagues' analysis were funded by the Scottish government and a grant from Scotland's Chest, Heart, and Stroke Association, respectively. Dr. Logue and her colleagues said they had no financial disclosures. ■

Extreme BMI Tied to Deep Intracerebral Hemorrhage

BY SHERRY BOSCHERT

FROM THE INTERNATIONAL STROKE CONFERENCE

LOS ANGELES – A body mass index of less than 18.5 or greater than 30 kg/m^2 was associated with increased risk for deep intracerebral hemorrhage in a case-control study of 772 adults.

The findings differed by sex, with an increased risk seen in males with a BMI of less than 18.5 or greater than 30 kg/m^2 but only in females with a BMI greater than 30 kg/m^2, Dr. Jonathan Rosand said at the meeting.

VITALS

Major Finding: A BMI of less than 18.5 kg/m^2 or greater than 30 kg/m^2 in men and a BMI of greater than 30 kg/m^2 in women were associated with an increased risk for deep intracerebral hemorrhage.

Data Source: Case-control study of 384 consecutive patients with ICH (188 lobar ICH and 196 deep ICH) and 388 controls matched for age and ethnicity.

Disclosures: Dr. Rosand said he had no relevant financial disclosures.

There appeared to be no association between BMI and risk for lobar intracerebral hemorrhage (ICH), said Dr. Rosand, director of the neuroscience intensive care unit and of the division of neurocritical care and emergency neurology at Harvard Medical School, Boston.

Intracerebral hemorrhages routinely get categorized based on whether they occur in the cortical or subcortical regions (lobar ICH) or in the deep brain structures or brain stem (deep ICH). Extremes of BMI have been associated with an increased incidence of ICH in previous studies.

Dr. Rosand and his associates studied the effect of BMI on the risk of the subtypes of ICH by comparing consecutive patients with either lobar (188) or deep ICH (196) who were admitted to Massachusetts General Hospital, Boston, with a control group of 388 individuals matched for age and ethnicity.

All patients were older than 18 years. CT imaging at the time of admission determined the ICH location. Investigators calculated the BMI based on subjects' height and weight at enrollment and divided subjects into four BMI quartiles: less than 18.5, 19-24, 25-30, and greater than 30.

Male sex, a BMI less than 18.5, and a BMI greater than 30 were significantly associated with an increased risk for deep ICH in both univariate and multivariate analyses. Some traditional risk factors for deep ICH – hypertension and consumption of more than 3 ounces of alcohol per day – also were associated with a significantly increased risk in the two analyses. Diabetes mellitus was a risk factor in only univariate analysis.

The risk for deep ICH was 34% higher in males, nearly twice as high in patients with either a BMI of less than 18.5 or greater than 30, four times higher in patients with hypertension, and nearly three times higher in patients consuming more than 3 ounces of alcohol per day, compared with patients without those characteristics, in a multivariate analysis.

A subsequent sex-stratified analysis found a 75% higher risk for deep ICH in females with a BMI greater than 30, compared with females with a BMI of 19-24.

The risk for deep ICH was 81% higher in males with a BMI greater than 30 and nearly three times higher in males with a BMI less than 18.5, compared with males with a BMI of 19-24.

"There does appear to be, at least in these data, a difference in the effect of BMI on risk of deep ICH in men compared with women," Dr. Rosand said at the conference, which was sponsored by the American Heart Association.

Risk for lobar ICH did not vary significantly based on BMI in either a univariate or multivariate analysis.

The association of deep intracerebral hemorrhage with hypertension, BMI, and possibly diabetes raises the possibility that deep ICH is linked to the metabolic syndrome, but this hypothesis requires further study, he said, adding that the study was limited by its size and by the fact that it did not match controls to patients by sex. ■