Normal-Weight Obesity: A Novel CVD Risk Factor

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COLORADO SPRINGS — As if the obesity epidemic wasn't serious enough already, it turns out more than half of individuals with a normal body mass index have a condition called normal-weight obesity.

Normal-weight obesity—defined by a high percentage of body fat in the presence of a BMI in the normal range of 18.5-24.9 kg/m^2—not only is highly prevalent, but is associated with significantly elevated cardiovascular risk and an increase in metabolic syndrome, Dr. Abel Romero-Corral reported at a conference sponsored by the American Heart Association.

"By screening for high body fat in subjects with a normal BMI, we were able to identify a subset of patients at higher risk for cardiovascular disease. This is very important because self-awareness is always the first step for behavioral modification. Most of the cardiometabolic dysregulation seen in these patients is potentially reversible through diet, physical activity, and possibly pharmacotherapy," said Dr. Romero-Corral of the Mayo Clinic, Rochester, Minn.

He presented a cross-sectional study involving 2,127 adults with normal BMI and a mean age of 41 years who participated in the Third National Health and Nutrition Examination Survey (NHANES-3). All of them underwent body fat composition measurement by bioelectrical impedance, a full cardiovascular and metabolic risk factor assessment, and fasting morning blood tests.

Fifty-five percent of subjects had normal-weight obesity as defined by greater than 20% body fat in men and greater than 30% in women. This would translate into 45 million affected Americans, extrapolating from the NHANES-3 findings using 2006 census data. Although there is no official consensus on criteria for obesity based on body fat, "I think most physicians will agree that 20% and 30% are high," Dr. Romero-Corral said in an interview.

Hispanics had the highest prevalence of normal-weight obesity, at 71%, followed by blacks at 61% and whites at 53%.

Normal-weight obesity is not a benign phenomenon, Dr. Romero-Corral emphasized. After adjusting for age and race, normal-weight obese men had a 68% greater likelihood of meeting ATP-III criteria for metabolic syndrome, compared with men who had normal BMIs and normal body fat. And normal-weight obese women had nearly a threefold increased prevalence of metabolic syndrome compared with women who had normal BMIs and normal body fat.

All of the numerous cardiometabolic parameters measured in this study trended unfavorably in the normal-weight obesity group. Many of these adverse effects achieved statistical significance (see box).

Women with normal-weight obesity were four times more likely to have known cardiovascular disease than were controls.

This study underscores the BMI's drawbacks as a tool for diagnosing obesity. BMI doesn't distinguish between body fat and lean mass, which have very different biologic effects. "We know lean mass is protective because it's related to greater physical activity and a better metabolic profile," the physician noted. ■

Cardiometabolic Abnormalities Associated With Normal-Weight Obesity

	Normal-weight obese	Normal-weight/ normal-fat controls
Dyslipidemia	42.0%	33.9%
Elevated apo B/apo A-I ratio	40.2%	27.2%
Hypertension	27.7%	20.2%
Elevated fasting blood glucose or diabetes	26.6%	16.2%
Low HDL cholesterol	26.2%	22.9%
Elevated leptin	25.6%	7.1%
Elevated C-reactive protein	12.2%	8.7%
Prevalence of metabolic syndrome		
Women	13.0%	2.8%
Men	12.8%	5.4%

Notes: Based on 12-year follow-up data from the Third National Health and Nutrition Examination Survey of 2,127 adults. All differences are statistically significant.

Source: Dr. Romero-Corral

Big Young Men Face Higher Atrial Fib Risk in Later Life

COLORADO SPRINGS — Large body size in youth is associated with increased risk of atrial fibrillation in later life in men, Dr. Annika Rosengren said at a conference sponsored by the American Heart Association.

"If you were tall, or had a lot of muscles … you had more risk of atrial fibrillation. And you could add to this risk further by putting on weight after age 20," said Dr. Rosengren, professor of medicine at Sahlgrenska University Hospital, Goteborg, Sweden.

The implication of this finding from a large Swedish longitudinal study is that the already-high prevalence of atrial fibrillation (AF) in western societies will keep climbing, and the increase won't simply be due to the aging of the population, inadequately controlled hypertension, and worsening obesity epidemic, all well-recognized contributors to AF.

"Each successive generation is bigger in youth. People are not only growing fatter with each succeeding cohort being born, they're also getting taller and larger, independent of obesity. So expect more atrial fibrillation," she said in an interview.

Dr. Rosengren reported on 6,903 Swedish men who were a mean of 52 years old in the early 1970s when they enrolled in the Swedish Primary Prevention Study. They were followed until 2004, for a maximum of 34 years. During follow-up, 18% of the men were diagnosed with AF.

The participants' body surface area at age 20 was strongly related to risk of AF, based on a Cox regression analysis adjusted for midlife body mass index and other potential confounders. They turned 20 during 1935-1945, when "obesity was virtually non- existent in Sweden," she noted.

In the adjusted regression analysis, men in the second quartile of body surface area at age 20 had a 42% greater risk of later developing AF as did men in the lowest quartile. Men in the third quartile had a 58% increase in risk, and those in the top quartile for body surface had a 200% greater risk. Body weight at age 20 showed a virtually identical association with subsequent AF.

"If you're big … there's a high likelihood of having large atria [which] are more prone to develop atrial fibrillation," she said.

Weight gain between age 20 and midlife was also independently tied to higher AF risk. A 5%-15% weight gain was associated with a 13% greater rate of AF, compared with no weight gain. A 16%-35% gain was associated with a 33% increase in AF rate, and a gain of more than 35% was linked to a 61% increase in risk. ■

Stroke Risk Jumps Substantially in Atrial Fib Patients Aged 85 and Older

COLORADO SPRINGS — The stroke risk without warfarin therapy in atrial fibrillation patients aged 85 years and older who have no other stroke risk factors is more than double that of patients aged 75-84 years, according to new data from the ATRIA study.

Moreover, the absolute reduction in stroke risk achieved with warfarin in the 85-plus age group seems substantially greater than in younger atrial fibrillation (AF) patients, study investigator Dr. Daniel E. Singer reported at a conference sponsored by the American Heart Association.

These findings from the National Institutes of Health–sponsored Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) study indicate a need to revisit current national guidelines, which allow aspirin rather than warfarin for AF patients aged 75 years and up with no stroke risk factors other than their advanced age.

"These data suggest that looking at old people with just a single age cut-off at 75 misses the fact that those who are aged 85 and older are at considerably heightened risk. The risk in the rapidly growing oldest old population shouldn't be confused with that of the younger old population aged 75-84. Those aged 85 and up should be considered strong candidates for warfarin," said Dr. Singer, professor of medicine and epidemiology at Harvard Medical School and chief of the clinical epidemiology unit at Massachusetts General Hospital, both in Boston.

Dr. Singer also is the principal investigator in ATRIA, a study to assess the impact of warfarin in usual care that has enrolled 13,559 northern California patients with nonvalvular AF. In effect, ATRIA is a real-world postmarketing study of a 60-year-old drug.

The 4,330 ATRIA participants who had no additional stroke risk factors at baseline have accumulated 16,000 person-years of follow-up. During that period, those aged 75-84 years who were not on warfarin had a 1.41% annual stroke rate, compared with a 3.31% annual rate in the 643 patients aged 85 and up with no other stroke risk factors who were not on warfarin.

Those aged 75-84 years who were on warfarin had a 0.53% annual stroke rate, and those aged 85 years and older had a 0.86% event rate on warfarin, indicating a substantially greater absolute benefit for warfarin in the oldest group. The caveat, he stressed in an interview, is that ATRIA was not a randomized trial, so the main focus should be on the core stroke risk off warfarin—impressively greater in patients aged 85 and older.

The intracranial hemorrhage rate in patients aged 85 years and older with no stroke risk factors other than age was 0.60% a year on warfarin and 0.58% a year in those not taking it. "When you get into these older age groups, the intracranial hemorrhage rate is quite substantial. But the fact is, it's high on or off warfarin."

The widely used CHADS2 stroke risk scoring system for AF patients awards one point each for congestive heart failure, hypertension, age over 75 years, and diabetes, and two points for a history of stroke.

The ATRIA findings suggest that age 85 years or greater ought to receive more weight—perhaps two points—although this has to be viewed as a tentative conclusion, because ATRIA is the first study to show a substantially greater stroke risk in the oldest old, Dr. Singer stressed.

There was considerable hope in the 1990s for aspirin as a safer alternative, but its impact proved to be quite small. And aspirin turned out to be particularly poor at preventing severe or fatal strokes, he said. ■