Journal of the American College of Cardiology
© 2011 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 57, No. 19, 2011
ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2010.10.063

EDITORIAL COMMENT

Excess Visceral Adipose Tissue/Ectopic Fat

The Missing Link in the Obesity Paradox?*

Jean-Pierre Després, PHD

Québec City, Québec, Canada

Although obesity is recognized as a health hazard that has reached epidemic proportions in affluent and emerging economies (1,2), the strength of its relationship with coronary heart disease (CHD) and related mortality has been shown to be variable and inconsistent (3). Two main factors could explain these findings: 1) most of the risk attributed to obesity could be mediated by its related cardiometabolic abnormalities (dyslipidemia, hypertension, insulin resistance and diabetes, inflammation, pro-thrombotic profile, and the like) (4); 2) obesity is most often diagnosed in clinical practice by a simple anthropometric variable, the body mass index (BMI), which is the ratio of weight (in kilograms) over height (in meters squared). Although useful to describe the secular changes in the prevalence of obesity at the population level, the BMI only provides a crude measurement of total adiposity. Furthermore, in all individuals and patients, the BMI is a totally inadequate index of regional body fat distribution, the latter phenotype being critically important in patients with CHD, as nicely shown by the report by Coutinho et al. (5) published in this issue of the *Journal*.

See page 1877

Although prospective studies have shown a univariate relationship between BMI and incidence of a first CHD event and related mortality (6,7), the picture became quite blurry among patients with documented CHD when it was counterintuitively reported that a high BMI was predictive of a reduced mortality risk (8,9). This phenomenon has been commonly referred to as the "obesity paradox" in cardiology (8,9). The report by Coutinho et al. (5) has finally shed some light on this question and should hopefully spur further studies where investigators will consider going beyond the BMI to assess the morbidity/mortality risk associated with excess adiposity in patients with CHD. Indeed, the report provides robust evidence that anthropometric correlates of body shape, such as waist circumference and the waist-to-hip circumference ratio, matter a lot more in cardiology than the BMI, which is only an index of relative body size and not of body composition/fat distribution.

For more than 2 decades, a plethora of studies has clearly shown that the distribution of body fat, especially excess abdominal fat accumulation (which can be crudely estimated by the measurement of waist circumference), is predictive of both prevalent and incident CHD and type 2 diabetes—this relationship being largely independent from the contribution of total body fat to risk (10–15). In their report, Coutinho et al. (5) have meticulously scrutinized the published data and combined individual data from previously published studies with their own unpublished observations. They reached the important conclusion that, although an elevated BMI was indeed associated with reduced mortality risk in patients with CHD, a totally different picture emerged when waist circumference was used as an index of abdominal obesity: an elevated waist circumference and a high ratio of waist over hip circumferences were associated with increased mortality risk in CHD patients.

These results are very important for the field of cardiology, because they will clear the confusion around the prognostic value of obesity and emphasize the need to go beyond the BMI as the preferred anthropometric index of adiposity. From these results, we should also question why, in patients with CHD, a large waistline has a fundamentally different relationship with mortality than relative weight. Furthermore, although waist circumference has been advocated as an index of abdominal obesity, it is important to point out that it should not replace the BMI as the single adiposity index. For instance, when a large population-based sample is examined, considerable variation in the distribution of BMI values is obviously found. In such large and heterogeneous samples, a strong correlation (of about 0.8 to 0.9) between the BMI and waist girth is systematically observed (16). Thus, it has been argued by some that BMI and waist circumference could be interchangeable indexes of adiposity and that there would be no need to measure waist circumference once BMI had been assessed (17–19). Although this is a reasonable point at the population level, Figure 1 shows that waist and BMI are not interchangeable at the individual/patient level. Figure 1 shows median waist circumference values for every individual BMI unit in the subgroup of 64,624 men of the IDEA (International Day for the Evaluation of Abdominal Obe-

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

From the Centre de recherche de l'Institut universitaire de cardiologie et de pneumologie de Québec, Québec City, Québec, Canada and the Division of Kinesiology, Department of Social and Preventive Medicine, Université Laval, Québec City, Québec, Canada. The IDEA study has been funded by Sanofi-Aventis. The work of Dr. Després has been supported by the Canadian Institutes of Health Research. Dr. Després has served as a speaker for Abbott Laboratories, AstraZeneca, Solvay Pharma, GlaxoSmithKline, and Pfizer Canada Inc.; has received research funding from Eli Lilly Canada; and has served on the advisory boards of Novartis, Theratechnologies, Torrent Pharmaceuticals Ltd., and Sanofi-Aventis.

JACC Vol. 57, No. 19, 2011
May 10, 2011:1887–9

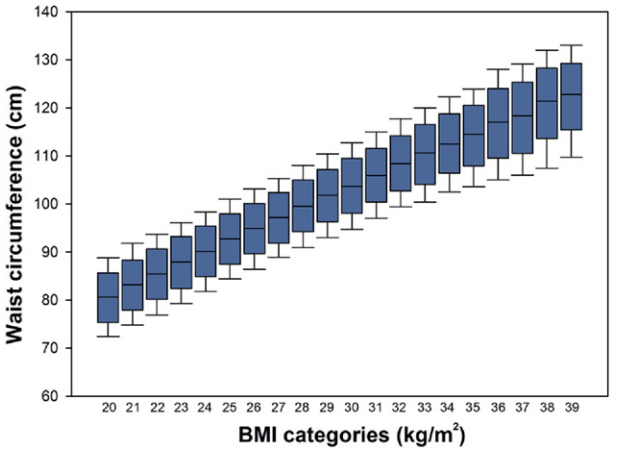

Figure 1 **Waist and BMI Are Not Interchangeable at the Individual/Patient Level**

Box-and-whisker plots showing the distribution of waist circumference values (age-adjusted) per unit of body mass index (BMI) in the subsample of 64,624 men of the IDEA (International Day for the Evaluation of Abdominal Obesity) study (20) who had BMI values ≥20 and <40 kg/m^2. Data shown are medians, quartiles, and 10th and 90th percentiles.

sity) study who had BMI values between 20 and 39 kg/m^2 (20). Although progressively higher median waist values were associated with increasing BMI units, the box-and-whisker plots clearly indicate that, for any given BMI value, the variation in waist circumference was considerable with a mean waist range of 9.43 cm between the 25th and 75th percentiles. Thus, although waist circumference and BMI are strongly correlated at the population level, in clinical practice, cardiologists should expect to find substantial individual variation in waist circumference among their patients with similar BMI values.

The implications of these observations are not trivial: waist circumference should not replace the BMI in cardiology, because it has to be interpreted in the context of the BMI. For example, compare 2 patients who have exactly the same waist circumference value (103 cm): Patient #1 has a BMI of 25 kg/m^2, whereas Patient #2 has a BMI of 30 kg/m^2. Thus, had only the waist been measured, the clinician would have missed tremendously important information: Patient #2 has a large waistline because he has overall obesity, whereas Patient #1 is not obese but clearly has an excess of abdominal fat. This observation could explain why, in the meta-analysis of Coutinho et al. (5), a large waist circumference was particularly predictive of increased mortality among patients with presumably "normal" BMI values. These patients might have less muscle mass, have a poor cardiorespiratory fitness, and most importantly, be characterized by an excess of intra-abdominal (visceral) adipose tissue and by increased ectopic fat deposition for which excess liver fat and epi/pericardial fat are salient features (16). In patients asymptomatic for CHD, it has been shown that excess visceral adipose tissue/liver fat deposition is clearly the adiposity phenotype associated with the most severe diabetogenic and atherogenic metabolic abnormalities (4,16). Although the study by Coutinho et al. (5) only used anthropometric markers of what they referred to as "central obesity," their results question the relevance of only measuring the BMI in cardiology. Clearly, body shape and how regional adipose tissue handles and stores excess dietary energy have tremendous cardiometabolic implications. As suggested by Poirier (21), BMI is now to anthropometry what "total cholesterol" was to lipidology. The report by Coutinho et al. (5) clearly indicates that it is time to move on to better assessment tools. From the work that we have conducted over the last 25 years, it is suggested that further attention should be given to patients who have an exaggerated waistline for their BMI, particularly if this large waistline is accompanied by elevated triglyceride levels as a marker of excess visceral adipose tissue/ectopic liver fat deposition. It is proposed that excess visceral adiposity/ectopic fat identified in clinical practice by "hypertriglyceridemic waist" (22,23) is the clue to what was never an "obesity paradox" but rather a "BMI paradox."

Reprint requests and correspondence: Dr. Jean-Pierre Després, Centre de recherche de l'Institut universitaire de cardiologie et de pneumologie de Québec, Pavilion Marguerite-D'Youville, Fourth Floor, 2725 chemin Ste-Foy, Québec G1V 4G5, Canada. E-mail: jean-pierre.despres@criucpq.ulaval.ca.

REFERENCES

1. Ford ES, Mokdad AH. Epidemiology of obesity in the Western Hemisphere. J Clin Endocrinol Metab 2008;93:S1–8.
2. Poirier P, Giles TD, Bray GA, et al. Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss: an update of the 1997 American Heart Association Scientific Statement on Obesity and Heart Disease from the Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. Circulation 2006;113:898–918.
3. Bogers RP, Bemelmans WJ, Hoogenveen RT, et al. Association of overweight with increased risk of coronary heart disease partly independent of blood pressure and cholesterol levels: a meta-analysis of 21 cohort studies including more than 300 000 persons. Arch Intern Med 2007;167:1720–8.
4. Després JP, Moorjani S, Lupien PJ, Tremblay A, Nadeau A, Bouchard C. Regional distribution of body fat, plasma lipoproteins, and cardiovascular disease. Arteriosclerosis 1990;10:497–511.
5. Coutinho T, Goel K, Corrêa de Sá D, et al. Central obesity and survival in subjects with coronary artery disease: a systematic review of the published data and collaborative analysis with individual subject data. J Am Coll Cardiol 2011;57:1877–86.
6. Manson JE, Willett WC, Stampfer MJ, et al. Body weight and mortality among women. N Engl J Med 1995;333:677–85.
7. Willett WC, Manson JE, Stampfer MJ, et al. Weight, weight change, and coronary heart disease in women. Risk within the 'normal' weight range. JAMA 1995;273:461–5.
8. Romero-Corral A, Montori VM, Somers VK, et al. Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies. Lancet 2006;368:666–78.
9. Lavie CJ, Milani RV, Ventura HO. Obesity and cardiovascular disease: risk factor, paradox, and impact of weight loss. J Am Coll Cardiol 2009;53:1925–32.
10. Canoy D, Boekholdt SM, Wareham N, et al. Body fat distribution and risk of coronary heart disease in men and women in the European Prospective Investigation Into Cancer and Nutrition in Norfolk

cohort: a population-based prospective study. Circulation 2007;116: 2933–43.
11. Lapidus L, Bengtsson C, Larsson B, Pennert K, Rybo E, Sjöström L. Distribution of adipose tissue and risk of cardiovascular disease and death: a 12 year follow up of participants in the population study of women in Gothenberg, Sweden. Br Med J 1984;289:1257–61.
12. Larsson B, Svardsudd K, Welin L, Wilhelmsen L, Björntorp P, Tibblin G. Abdominal adipose tissue distribution, obesity, and risk of cardiovascular disease and death: 13 year follow-up of participants in the study of men born in 1913. Br Med J 1984;288:1401–4.
13. Ohlson LO, Larsson B, Svardsudd K, et al. The influence of body fat distribution on the incidence of diabetes mellitus: 13.5 years of follow-up of the participants in the study of men born in 1913. Diabetes 1985;34:1055–8.
14. Rexrode KM, Carey VJ, Hennekens CH, et al. Abdominal adiposity and coronary heart disease in women. JAMA 1998;280:1843–8.
15. Yusuf S, Hawken S, Ounpuu S, et al. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. Lancet 2005;366:1640–9.
16. Després JP, Lemieux I, Bergeron J, et al. Abdominal obesity and the metabolic syndrome: contribution to global cardiometabolic risk. Arterioscler Thromb Vasc Biol 2008;28:1039–49.
17. Bouchard C. BMI, fat mass, abdominal adiposity and visceral fat: where is the 'beef'? Int J Obes (Lond) 2007;31:1552–3.
18. Farin HM, Abbasi F, Reaven GM. Body mass index and waist circumference correlate to the same degree with insulin-mediated glucose uptake. Metabolism 2005;54:1323–8.
19. Kiernan M, Winkleby MA. Identifying patients for weight-loss treatment: an empirical evaluation of the NHLBI obesity education initiative expert panel treatment recommendations. Arch Intern Med 2000;160:2169–76.
20. Balkau B, Deanfield JE, Després JP, et al. International Day for the Evaluation of Abdominal Obesity (IDEA): a study of waist circumference, cardiovascular disease, and diabetes mellitus in 168,000 primary care patients in 63 countries. Circulation 2007;116:1942–51.
21. Poirier P. Adiposity and cardiovascular disease: are we using the right definition of obesity? Eur Heart J 2007;28:2047–8.
22. Lemieux I, Pascot A, Couillard C, et al. Hypertriglyceridemic waist. A marker of the atherogenic metabolic triad (hyperinsulinemia, hyperapolipoprotein B, small, dense LDL) in men? Circulation 2000;102: 179–84.
23. Lemieux I, Poirier P, Bergeron J, et al. Hypertriglyceridemic waist: a useful screening phenotype in preventive cardiology? Can J Cardiol 2007;23:23B–31B.

Key Words: central obesity ■ coronary artery disease ■ mortality ■ waist circumference ■ waist-hip ratio.