

Moderately Large Waist Measurements Matter

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COLORADO SPRINGS — Marginally increased waist circumference is strongly associated with prevalent hypertension in normal-weight and overweight adults, according to data from a large National Institute of Neurological Disorders and Stroke-sponsored study.

The finding is likely to change practice and guidelines, Dr. Deborah A. Levine predicted in reporting the results at a conference of the American Heart Association.

"As a practicing general internist, I do not routinely measure waist circumference as well as I should," conceded Dr. Levine of Ohio State University, Columbus. "And I certainly don't do it in persons with normal [body mass index] at this time. But these data have prompted me to reconsider that practice."

The data indicate a need to revise current U.S. guidelines regarding how waist circumference measurement is used as a cardiovascular risk assessment tool.

Current NIH guidelines include a less-than-forceful recommendation to consider measuring waist circumference—a guide to central adiposity—in individuals with normal BMIs. But the new data presented by Dr. Levine indicate that waist circumference measurement is a valuable indicator of risk in patients with normal BMIs.

The U.S. guidelines define normal waist circumference as less than 80 cm in women and 94 cm in men, and el-



evated waist circumference as more than 88 and 102 cm, respectively. The middle zone of marginally elevated values—80-88 cm in women and 94-102 cm in men—is a gray area that's largely disregarded by physicians and researchers alike. But this needs to change.

"Our data suggest that we should be treating waist circumference as a continuous risk factor and not a categorical variable where the middle category is actually ignored in practice and in studies," Dr. Levine said.

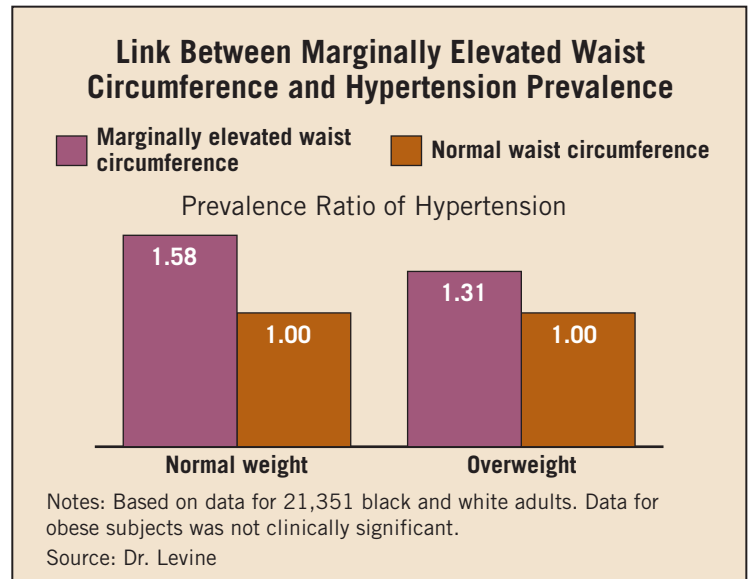
In light of the new findings, she said, the current International Diabetes Federation guidelines make far more sense. In the IDF guidelines on metabolic syndrome, the group defines any waist circumference that's above normal as elevated, period.

Dr. Levine presented an analysis of waist circumference and prevalent hypertension in 21,351 black and white adult community-dwelling participants in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, a population-based study whose primary goal is to identify explanations for the excess stroke mortality in the so-called "stroke belt."

The prevalence of baseline hypertension was 45% among participants with a normal BMI, 56% in those who were overweight, and 66% in subjects with class I obesity. After adjustment for numerous demographic factors as

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well as alcohol and tobacco use, physical activity, and glomerular filtration rate, a marginally increased waist circumference—that is, 80-88 cm in women and 94-102 cm in men—was independently associated with a 58% higher hypertension prevalence in normal-weight individuals and a 31% higher hypertension prevalence in those who were overweight, compared with participants with comparable BMI values but normal waist circumference.

An elevated waist circumference was associated with a 2.1-fold increased hypertension prevalence in normal-weight subjects, a 1.6-fold increase in those who were overweight, and a 48% increase in REGARDS participants who were obese class I.

ACE Inhibitor/ARB Combination Does More Harm Than Good

CHICAGO — Telmisartan is as effective as ramipril in reducing vascular events in high-risk patients, but combining the two drugs provides no incremental benefit and increases side effects.

That was the key message of ONTARGET (the Ongoing Telmisartan Alone and in Combination With Ramipril Global End Point Trial), a 25,620-patient megatrial presented by Dr. Salim Yusuf at the annual meeting of the American College of Cardiology.

ONTARGET was designed to answer two clinically relevant questions: Is the angiotensin-receptor blocker (ARB) telmisartan an effective alternative to ramipril in the 20%-30% of patients who can't tolerate an angiotensin-converting enzyme (ACE) inhibitor because of cough, angioedema, or other side effects? And does combining two blockers of the renin-angiotensin system provide additional risk reduction?

"We found that combining the two led to some harm. This is important because there are a significant number of people out there who use combination therapy, either to have greater blood pressure lowering or to protect the kidney," said Dr. Yusuf, lead investigator in ONTARGET and director of the Population Health Research Institute at McMaster University, Hamilton, Ont.

ONTARGET participants had vascular disease or high-risk diabetes at entry, but no heart failure. They were randomly assigned in double-blind fashion to receive 10 mg/day of ramipril, 80 mg/day of telmisartan, or both.

The primary composite end point in ONTARGET was cardiovascular death, stroke, MI, or hospitalization for heart failure. At a median



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follow-up of 56 months, this end point had occurred in 16.5% of the ramipril group, 16.7% in the telmisartan arm, and—to the investigators' surprise—16.3% on combination therapy. They had expected combined therapy to perform best.

Moreover, the combined therapy group had significantly higher rates of renal dysfunction, hypotensive symptoms, and diarrhea—and a 20% greater relative risk of treatment discontinuation.

Telmisartan was slightly better tolerated than ramipril, but patients known to be intolerant of ACE inhibitors were excluded from the study. They were assigned instead to TRANSCEND (the Telmisartan Randomized Assessment Study in Ace-Intolerant Subjects With Cardiovascular Disease), a placebo-controlled trial to be presented later this year at the European Society of Cardiology meeting. Dr. Yusuf reported receiving consulting fees from Boehringer Ingelheim, the ONTARGET sponsor.

Sodium, Potassium Intake Ratio Predicts Cardiac Risks

COLORADO SPRINGS — The intake ratio of sodium to potassium bears a much stronger association with subsequent development of cardiovascular disease than does consumption of either alone, according to new findings from the Trials of Hypertension Followup (TOPH) Study.

"We found that sodium and potassium may have a joint effect on the development of cardiovascular disease, in keeping with a proposed biologic symmetry. In our data the ratio was the most important predictor," Nancy R. Cook, Sc.D., reported at a conference of the American Heart Association.

She presented a 10- to 15-year follow-up of 2,275 participants in TOPH-I and -II, a pair of National Institutes of Health-sponsored randomized clinical trials of sodium reduction and other interventions aimed at preventing hypertension in individuals who were prehypertensive at baseline. There were 193 cardiovascular events—acute MI, stroke, revascularization procedures, or cardiovascular death—during follow-up.

A key feature of both studies was the periodic collection of 24-hour urine sodium and potassium excretions over several years.

In the TOPH follow-up analysis,

there was a significant, linear relationship with cardiovascular risk from lowest to highest quartile of the sodium to potassium excretion ratio.

After full statistical adjustment for numerous variables, including demographics, alcohol intake, body weight, physical activity, smoking status, and changes in those variables over the course of the study, individuals in the highest quartile of sodium to potassium ratio had a highly significant 50% increased risk of a cardiovascular event during follow-up, compared with those in the lowest quartile. For each unit increase in sodium to potassium ratio, future cardiovascular risk rose by 24%, added Dr. Cook of Brigham and Women's Hospital, Boston, and the Harvard School of Public Health.

The mean ratio was 2.9 in both men and women in the study population as a whole. But it differed modestly by age and more profoundly by race. Black participants had lower potassium excretion levels than whites, leading to a much higher sodium to potassium ratio of 3.4. Considered separately, neither sodium nor potassium excretion alone was significantly related to cardiovascular risk across quartiles.