Body Mass Index and Hypertension Hemodynamic Subtypes in the Adult US Population

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Background: Obesity produces various hemodynamic abnormalities that may impact hypertension subtypes. Similarly, the study of hypertension subtypes provides important information regarding the relative importance of hemodynamic abnormalities contributing to obesity-related hypertension.

Methods: Cross-sectional analysis of adults enrolled in the Third National Health and Nutrition Examination Survey (NHANES III) (n = 12,137) and NHANES 1999-2004 (n = 12,137). We examined the relationship between body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared) and the risk of hypertension and hemodynamic subtypes: isolated systolic hypertension (ISH), isolated diastolic hypertension (IDH), and systodiantolic hypertension (SDH).

Results: In NHANES 1999-2004, the odds ratio (OR) for hypertension for every 5-unit increase in BMI was 1.45 (95% confidence interval [CI], 1.39-1.52) (P < .001). However, the magnitude of the relative increase in the odds of hypertension was higher among younger adults. Among patients with hypertension, increasing BMI was a significant predictor of IDH or SDH (OR for IDH or SDH, 1.04; 95% CI, 1.02-1.06) (P < .001), as opposed to ISH. Isolated systolic hypertension represented a minority of hypertension cases in obese men (38.9%; 95% CI, 30.9-47.6) but remained the most prevalent type in obese women (62.1%; 95% CI, 52.4%-71.0%) (P < .001), despite a significant relative decrease in the frequency of ISH with increasing BMI in both sexes. Findings in NHANES III were very similar.

Conclusions: Isolated diastolic hypertension and SDH account for most cases of obesity-related hypertension, suggesting that determinants of mean arterial pressure account for the major burden of obesity-related hypertension in US adult men. These findings should be considered in the design of clinical trials and therapeutic strategies for obesity-related hypertension. Further studies should assess determinants of mean arterial pressure in obesity and the role of sex in the pathogenesis of obesity-related hypertension.

increase in the relative frequency of ISH and a relative decrease in IDH and SDH with aging.\textsuperscript{8,24} Although multiple studies have documented the association between obesity and HTN, data regarding the relative prevalence of HTN subtypes in the obese are needed. In the present study, we analyzed representative samples of the noninstitutionalized US adult population and aimed to (1) examine the prevalence of HTN and pre-HTN across BMI, sex, and age strata and (2) examine the changes in the relative frequency of different HTN subtypes (ISH, IDH, and SDH) according to BMI.

### METHODS

**STUDY POPULATION AND SAMPLING DESIGN**

We analyzed data from the Third National Health and Nutrition Examination Survey (NHANES III) (1988-1994) and NHANES 1999-2004, which included nationally representative samples of the US population.\textsuperscript{23-25} For both surveys, the sample was weighted to the US adult population corresponding to the respective time periods during which the surveys were performed. We analyzed data from nonpregnant adults 20 years or older. We selected 16,545 adults (8,646 women and 7,899 men) with valid anthropometric and blood pressure data enrolled in NHANES III and 12,137 adults (5,929 women and 6,208 men) enrolled in NHANES 1999-2004. These subjects were included in analyses related to the prevalence of pre-HTN and HTN in different BMI, sex, and age strata. Since antihypertensive medications may have differing effects on systolic vs diastolic blood pressure, analyses that included only individuals with HTN, which were performed to investigate the relative proportions of different HTN subtypes (ISH, SDH, or IDH) included only those subjects who were not receiving antihypertensive medications at the time of the survey. The resulting sample size was 2552 subjects from NHANES III (1154 women and 1398 men) and 1687 subjects from NHANES 1999-2004 (890 men and 797 women).

Blood pressure was measured using a mercury sphygmomanometer, with the participant in the sitting position after 5 minutes of rest. Pre-HTN and HTN were defined according to the seventh report of the Joint National Committee for the diagnosis, evaluation, and treatment of high blood pressure (JNC-7).\textsuperscript{26} Isolated systolic HTN was defined as systolic blood pressure of 140 mm Hg or higher and diastolic blood pressure lower than 90 mm Hg. Isolated diastolic HTN was defined as diastolic blood pressure lower than 140 mm Hg and systolic blood pressure of 90 mm Hg or higher. Systolic-diastolic HTN was defined as systolic blood pressure of 140 mm Hg or higher and a diastolic blood pressure of 90 mm Hg or higher.\textsuperscript{7,8} Obesity was defined as BMI of 30 or higher. The NHANES surveys were approved by the Centers for Disease Control and Prevention institutional review board, and all participants provided written informed consent.

### RESULTS

**PREVALENCE OF HTN AND PRE-HTN IN DIFFERENT BMI, AGE, AND SEX STRATA**

Figure 1 shows the weighted prevalence estimates of HTN, pre-HTN, and normal blood pressure among women and men in predefined age groups in NHANES III and NHANES 1999-2004. It can be seen that increasing BMI increases the risk of pre-HTN and HTN at any age, so that the prevalence of normal blood pressure, as defined by JNC-7, markedly decreases as BMI increases.

**BMI AND CROSS-SECTIONAL RISK ESTIMATES OF HTN**

Increasing BMI was associated with a significantly increased risk of HTN in both NHANES III and NHANES 1999-2004. The OR for HTN for every 5-unit increase in BMI was 1.58 (95% CI, 1.52-1.65) (P < .001) in NHANES III and 1.45 (95% CI, 1.39-1.52) (P < .001) in NHANES 1999-2004. However, in both surveys, the magnitude of the relative increase in the risk of HTN varied according to age in men and women. In NHANES III, the OR for HTN associated with a 5-point increase in BMI was 1.92 (95% CI, 1.76-2.10) among subjects aged 40 years or younger, 1.73 (95% CI, 1.59-1.87) among subjects aged 40 to 60 years, and 1.29 (95% CI, 1.18-1.41) among subjects older than 60 years. In NHANES 1999-2004, the OR for HTN associated with a 5-point increase in BMI was 1.65 (95% CI, 1.51-1.80) among subjects younger than 40 years, 1.60 (95% CI, 1.48-1.73) among subjects aged 40 to 60 years, and 1.30 (95% CI, 1.19-1.42) among subjects older than 60 years. These differences in the magnitude of the OR between age groups were not affected by adjustments for ethnicity in either survey and were present in both men and women.

Differences in prevalence ratios were even more pronounced. Figure 2 shows the prevalence ratios associated with obesity (BMI $\geq$30) using lean individuals (BMI <25) as the reference group in men and women in both...
surveys. It can be seen that the prevalence ratios for HTN associated with obesity were much higher among younger individuals (compared with older individuals) in both men and women in both surveys. These differences were not significantly affected by adjustments for race/ethnicity.

In agreement with these results, younger subjects with HTN were more likely to be obese compared with older subjects with HTN. In NHANES III, 46.9% (95% CI, 39.0%-55.0%) of all subjects with HTN younger than 40 years were obese compared with 46.5% (95% CI, 41.5%-51.6%) of those aged 40 to 59 years and only 27.5% (95% CI, 25.1%-30.0%) of those aged 60 years or older. Among men with HTN, the respective proportions of obese subjects in these age groups were 41.7% (95% CI, 32.8-51.2), 41.3% (95% CI, 36.0-46.8), and 24.5% (95% CI, 21.1-28.2), whereas among women with HTN, the respective proportions were 59.1% (95% CI, 47.1-70.1), 52.9% (95% CI, 46.0-59.6), and 29.4% (95% CI, 26.6-32.4). Similarly, in NHANES 1999-2004, 55.0% (95% CI, 48.9-60.9) of all subjects with HTN aged 40 years or younger were obese compared with 49.8% (95% CI, 46.9-52.8) of those aged 40 to 59 years and 35.6% (95% CI, 33.2-38.0) of those aged 60 years or older. The respective proportions were 52.9% (95% CI, 45.2-60.5), 44.8% (95% CI, 41.0-48.8), and 33.1% (95% CI, 29.9-36.5) among men with HTN and 59.9% (95% CI, 49.1-69.8), 54.9% (95% CI, 50.5-59.2), and 37.2% (95% CI, 34.4-40.1) among women with HTN.

HTN SUBTYPES ACCORDING TO BMI

Figure 3 shows the relative proportions of ISH, IDH, and SDH according to predefined BMI strata among men and women with untreated HTN in both NHANES III and NHANES 1999-2004. Significant relative increases in IDH and SDH with a relative decrease in ISH were observed with increasing BMI in both men and women in both surveys. In NHANES III, the proportions of obese subjects with HTN with IDH, SDH, and ISH were 23.6% (95% CI, 18.8-29.2), 27.6% (95% CI, 22.4-33.6), and 48.7% (95% CI, 42.5-55.0) among men with HTN and 59.9% (95% CI, 49.1-69.8), 54.9% (95% CI, 50.5-59.2), and 37.2% (95% CI, 34.4-40.1) among women with HTN.
CI-44.0-53.5), respectively. In NHANES 1999-2004, the proportions of obese subjects with HTN with IDH, SDH, and ISH were 28.54%, 21.51%, and 49.96%, respectively. Sex-stratified analyses showed that most obese men with HTN demonstrate either IDH or SDH rather than ISH (Figure 3A and C). Isolated systolic HTN represented only 36.6% of cases of HTN among obese men in NHANES III (95% CI, 30.7-43.0) and 38.9% of cases of HTN among obese men in NHANES 1999-2004 (95% CI, 30.9-47.6). Furthermore, ISH represented only a small minority of cases of HTN in morbidly obese men in both surveys (30%). In contrast, ISH remained the most prevalent HTN subtype in obese women in NHANES III (63.5%; 95% CI, 54.5-71.7) and NHANES 1999-2004 (62.1%; 95% CI, 52.4%-71.0%) (P < .001 for sex difference in both surveys), despite a relative decrease in the frequency of ISH with increasing BMI in both sexes (Figure 3).

Mean age was significantly different between subjects with untreated HTN in these BMI strata; age decreased progressively as BMI increased. In NHANES III, the mean ages for subjects with BMIs lower than 20, from 20.0 through 24.9, 25.0 through 29.9, 30.0 through 34.9, and 35.0 or higher were 69.6, 62.9, 58.8, 54.7, and 47.3 years, respectively (P < .001). In NHANES 1999-2004, the mean age for subjects in these BMI strata was 59.0, 60.7, 56.7, 52.6, and 47.4 years, respectively (P < .001).

In unadjusted analyses involving the entire study sample, a unit increase in BMI was associated with a 0.1% increased odds of systolic HTN (95% CI, 5.2%-7.1%) (P < .001) and an 8.6% increased odds of diastolic HTN (95% CI, 7.2%-10.0%) (P < .001) in NHANES III. In NHANES 1999-2004, a unit increase in BMI was associated with a 3.6% increased odds of systolic HTN (95% CI, 2.6%-4.5%) (P < .001) and a 6.0% increased odds of diastolic HTN (95% CI, 4.9%-7.2%) (P < .001). Age and BMI were independent (positive) predictors of the odds of systolic HTN in both surveys. Furthermore, a significant negative interaction was found between age and BMI as predictors of the odds of systolic HTN in both surveys (P = .001 for interaction in each survey). Similarly, a negative interaction was found between BMI and age as predictors of the odds of diastolic HTN (P = .001 for interaction in each survey). These interactions indicated a significantly less pronounced effect of BMI in the odds of HTN (both systolic and diastolic) with increasing age, consistent with the observed differences in the magnitude of the increase in the prevalence of HTN according to BMI, between different age strata in men and women (Figure 1).

When only subjects with untreated HTN were included in regression models, increasing BMI was a significant predictor of the odds of IDH or SDH (as opposed to ISH). The OR for IDH or SDH per unit increase in BMI was 1.068 (95% CI, 1.046-1.09) (P < .001) in NHANES III and 1.042 (95% CI, 1.023-1.062) (P < .001) in NHANES 1999-2004. Adjustment for sex, ethnicity, and poverty index did not affect this relationship, and BMI remained an independent predictor of IDH or SDH (as opposed to ISH). After adjustment for age, this relationship disappeared, and BMI was no longer a predictor of SDH or IDH in NHANES III (OR, 1.00) (P = .95) or NHANES 1999-2004 (OR, 1.00) (P = .97). Similarly, after adjustment for age, sex, race and/or ethnicity, and poverty index, BMI was not a significant predictor of the odds of SDH or IDH. There were no significant interactions between age and BMI as predictors of SDH or IDH in these models.

We report on the prevalence of HTN and the relative frequency of HTN subtypes associated with overweight and obesity in the general US adult population. We present analyses regarding the prevalence of pre-HTN and HTN in different age and BMI strata using NHANES III data and more recent data from NHANES 1999-2004.25-27 Obesity was associated with HTN in all age groups and both sexes. However, the odds for HTN associated with obesity were relatively higher in younger people. Therefore, younger subjects with HTN were more likely to be obese compared with older subjects with HTN; and conversely, obese subjects with HTN were younger than lean subjects with HTN. This phenomenon resulted in important differences in the proportions of HTN subtypes with increasing BMI: proportions of IDH and SDH increased with obesity, and important sex differences came to light as well. Our findings indicate that IDH and SDH account for most cases of obesity-related HTN in US adult men, a phenomenon that was seen in both representative samples of the US adult population from 1994-1998 and 1999-2004. These findings indicate that, in addition to determinants of large-artery stiffness, determinants of mean arterial pressure account for an important magnitude of the public burden of obesity-related HTN in the United States. Our study provides novel findings regarding (1) age differences in the relationship between BMI and the prevalence of HTN and (2) clear differences in the relative frequency of HTN subtypes according to the level of BMI. The reported differences in HTN subtypes, in turn, provide important clues to the relative importance of specific hemodynamic abnormalities underlying HTN in obese individuals, which have implications for pathophysiology, prognosis, and possibly therapeutic approaches for HTN in the obese.
From a hemodynamic standpoint, blood pressure is determined by a steady component (mean pressure) and pulsatile phenomena during each cardiac cycle. Large-artery stiffness is a key determinant of pulsatility and is thought to be the main underlying arterial abnormality of older individuals with ISH, whereas both large-artery stiffness and stroke volume play a role in ISH in young adults. In contrast, diastolic HTN is more closely correlated with increases in mean arterial pressure. With these considerations in mind, the observation of a shift in the relative frequencies of HTN subtypes with a progressive increase in IDH and a progressive decrease in ISH with increasing BMI is important because it suggests that underlying abnormalities in the determinants of mean arterial pressure are common in (and, indeed, underlie most cases of) obesity-related HTN in the general US population. Hemodynamic determinants of mean arterial pressure include cardiac output and systemic vascular resistance. Previous studies have demonstrated that cardiac output is increased in obese adults with and without HTN, whereas systemic vascular resistance tends to be inappropriately normal in obese adults without HTN but increased among obese adults with HTN. However, there is wide interindividual variability in these parameters, suggesting the need for a more direct hemodynamic assessment when evaluating individual subjects.

Separating HTN into systolic and diastolic subtypes not only provides clues to hemodynamic mechanisms but carries important prognostic implications. Using data from the Framingham Heart Study, Franklin et al demonstrated that diastolic blood pressure is superior to systolic blood pressure as an indicator of coronary heart disease risk in young adults, and therefore, IDH should not be regarded as a benign condition in younger and middle-aged individuals. Both baseline BMI and subsequent weight gain have been shown to be strong predictors of the future onset of IDH and SDH, whereas BMI at baseline was not a predictor of ISH. It should be noted that although BMI is a useful marker of obesity, fat distribution is an important determinant of metabolic abnormalities and the risk of HTN.

As shown in Figure 3, the relative proportions of isolated systolic hypertension (ISH), isolated diastolic hypertension (IDH), and systodiastolic hypertension (SDH) in predefined BMI strata among men (A and C) and women (B and D) with untreated hypertension in the Third National Health and Nutrition Examination Survey (NHANES III) (A and B) and NHANES 1999-2004 (C and D). BMI indicates body mass index (calculated as weight in kilograms divided by height in meters squared).
greatest likelihood of metabolic syndrome, and it was diagnosed based on the presence of increased waist circumference and associated metabolic abnormalities. Collectively, these data suggest that obesity and the metabolic syndrome are more closely associated with IDH and SDH than with ISH. Our study adds to the information of previous studies because it demonstrates that in the general US adult population, most cases of obesity-related HTN are either IDH or SDH, as opposed to ISH, which is otherwise rare in the most prevalent HTN subtype. Therefore, a large burden of HTN in obese subjects is due to elevated mean arterial pressure.

The differences in HTN subtypes with increasing BMI were largely related to the differences in the mean age of obese vs lean subjects with HTN, since among untreated subjects with HTN, BMI no longer predicted IDH or SDH (vs ISH) after adjustment for age, without significant BMI-age interactions in these models. However, the younger age of obese subjects with HTN was due to an increased prevalence ratio for HTN associated with obesity among younger adults, which was reflected by the significant interaction between sex and BMI as predictors of the odds of HTN in the entire population. We speculate that this may occur for at least 2 reasons: (1) competing causes of HTN (ie, unrelated to obesity) become more prevalent in older individuals (which is demonstrated by the absolute age-related increase in the prevalence of HTN in nonobese individuals); (2) obese subjects without HTN but with stiff large arteries may die prematurely (before the onset of systolic HTN), being underrepresented in older age groups.

Large-artery stiffness is increased in obese individuals at any given age, and increases in large-artery stiffness independently predict an increased cardiovascular risk in various populations. Since age is the most powerful single determinant of large-artery stiffness, increases in large-artery stiffness relative to normal age-specific values may be present early in life in the absence (and before the onset) of systolic HTN. It is likely that more directly assessing large-artery stiffness to detect deviations from age-specific normative values may provide superior (and earlier) prognostic information than simply assessing for the presence of systolic HTN in younger obese individuals. It is also possible that the integration of measurements of large-artery stiffness, pressure wave reflections, and the determinants of mean arterial pressure may provide better risk stratification and understanding of hemodynamic mechanisms involved in HTN. These hypotheses should be investigated in large prospective studies. In addition, more research is needed to determine whether age directly modulates the effect of obesity on the risk of HTN.

Finally, the sex difference in the relative proportions of HTN subtypes deserves mention. It is possible that gender differences in the pathogenesis and/or mediators of obesity-related HTN exist between men and women, leading to differences in hypertensive hemodynamic phenotypes. Such differences have been supported by experimental models and observational studies in humans. An additional important finding of our study is that ISH is a more common subtype among US adult women than men at any given BMI.

Our study is limited by its cross-sectional nature and because our classification of HTN was based on the measurement of brachial pressures. Decreased amplification of the pressure pulse from the aorta to brachial artery occurs with increased central pressure augmentation; however, higher values of central augmentation have not been observed in association with obesity. making it unlikely that the overall prevalence of systolic HTN was systematically underestimated in obese individuals with the use of brachial (vs aortic) pressures. However, it should be emphasized that central pressure measurements are still likely to be relevant in individual obese subjects, who are at increased risk of cardiovascular disease. In addition, while treated subjects with HTN were excluded, treatment patterns in NHANES may vary by region, race, sex, socioeconomic status, and other unidentified variables. Although BMI is a useful index of adiposity, it is well known that BMI is an imperfect marker of obesity and is affected by variables independent of obesity, such as increased muscle mass. Finally, our observational study cannot establish mechanistic roles for biologic pathways that may affect blood pressure in the obese.

Our results have immediate implications regarding the level of awareness of diastolic HTN (which is particularly prevalent in the obese) among epidemiologists, clinicians, and the general public. These findings should also be considered in the design of clinical trials that assess therapies for HTN among individuals across different ranges of BMI or that specifically address obesity-related HTN. Further studies should be performed to assess the specific hemodynamic abnormalities leading to increased mean arterial pressure in obese individuals, assess the mechanistic determinants of these abnormalities, and investigate the role of sex in the pathogenesis of obesity-related HTN. These studies may open the path for therapeutic strategies that target specific hemodynamic abnormalities in obese individuals with HTN.

Accepted for Publication: July 30, 2008.

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Author Contributions: Dr Chirinos had full access to all the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis. Study concept and design: Chirinos and Raij. Analysis and interpretation of data: Chirinos, Franklin, Townsend, and Raij. Drafting of the manuscript: Chirinos and Raij. Critical revision of the manuscript for important intellectual content: Franklin, Townsend, and Raij. Statistical analysis: Chirinos. Administrative, technical, and material support: Chirinos and Townsend. Study supervision: Franklin and Raij.

Financial Disclosure: Dr Chirinos has received minor research support from Cardiodynamics Inc and Atcor Medical Inc, companies that manufacture devices for noninvasive hemodynamic measurements.

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