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HYPERTENSION

# Variation in Body Composition Determines Long-Term Blood Pressure Changes in Pre-Hypertension

## The MONICA/KORA (Monitoring Trends and Determinants on Cardiovascular Diseases/Cooperative Research in the Region of Augsburg) Cohort Study

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**Objectives** We studied the relationship between changes in body composition and changes in blood pressure levels.

**Background** The mechanisms underlying the frequently observed progression from pre-hypertension to hypertension are poorly understood.

**Methods** We examined 1,145 subjects from a population-based survey at baseline in 1994/1995 and at follow-up in 2004/2005. First, we studied individuals pre-hypertensive at baseline who, during 10 years of follow-up, either had normalized blood pressure (PreNorm, n = 48), persistently had pre-hypertension (PrePre, n = 134), or showed progression to hypertension (PreHyp, n = 183). In parallel, we studied predictors for changes in blood pressure category in individuals hypertensive at baseline (n = 429).

**Results** After 10 years, the PreHyp group was characterized by a marked increase in body weight (+5.71% [95% confidence interval (CI): 4.60% to 6.83%]) that was largely the result of an increase in fat mass (+17.8% [95% CI: 14.5% to 21.0%]). In the PrePre group, both the increases in body weight (+1.95% [95% CI: 0.68% to 3.22%]) and fat mass (+8.09% [95% CI: 4.42% to 11.7%]) were significantly less pronounced than in the PreHyp group ($p < 0.001$ for both). The PreNorm group showed no significant change in body weight (−1.55% [95% CI: −3.70% to 0.61%]) and fat mass (+0.20% [95% CI: −6.13% to 6.52%], $p < 0.05$ for both, vs. the PrePre group).

**Conclusions** After 10 years of follow-up, hypertension developed in 50.1% of individuals with pre-hypertension and only 6.76% went from hypertensive to pre-hypertensive blood pressure levels. An increase in body weight and fat mass was a risk factor for the development of sustained hypertension, whereas a decrease was predictive of a decrease in blood pressure. (J Am Coll Cardiol 2010;56:65–76) © 2010 by the American College of Cardiology Foundation

The definition of normal blood pressure is difficult because in Western societies, blood pressure tends to increase in most individuals during the aging process. For the gray zone between clearly normal and undoubtedly elevated blood pressure (i.e., the range of 120 to 139 mm Hg systolic or 80 to 89 mm Hg diastolic blood pressure), the term *pre-hypertension* was coined (1). The pathophysiological implications of pre-hypertension are difficult to define, given that

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**Abbreviations and Acronyms**

CI = confidence interval

HypHyp = persistently hypertensive

HypNorm = hypertensive-normotensive

HypPre = hypertensive-pre-hypertensive

OR = odds ratio

PreHyp = pre-hypertensive-hypertensive

PreNorm = pre-hypertensive-normotensive

PrePre = persistently pre-hypertensive

it represents >30% of the overall healthy adult population (2). However, the condition may herald arterial hypertension. Indeed, as many as 49.5% of subjects with pre-hypertension may present with manifest hypertension within 4 years of follow-up (3–5). The mechanisms responsible for such frequently observed progression from pre-hypertension to hypertension are incompletely understood, but pre-hypertension may be considered a starting point in the cardiovascular disease continuum (6).

In cross-sectional samples, blood pressure levels are associated with body composition. In particular, there is a positive relationship between overweight and obesity with the prevalence of hypertension. Specifically, the Framingham Heart Study found that hypertension is about twice as prevalent in obese compared with lean individuals (7). Likewise, the PAMELA (Pressioni Arteriose Monitorate E Loro Associazioni) study showed that total body weight measures predicted new onset of hypertension (8). Moreover, a recent meta-analysis concluded that a 1-kg loss of total body weight was associated with an approximate 1-mm Hg decrease in blood pressure (9). Based on these findings, lifestyle measures have been proposed for individuals to decrease the risk of the manifestation of hypertension.

There are few prospective, population-based studies that examined factors that specifically modify disease progression in pre-hypertensive individuals (2,10). In the present population-based study, we investigated the natural history of pre-hypertension and hypertension over a 10-year period with special emphasis on the impact of dynamic variations in body composition on blood pressure.

## Methods

**Study population.** The MONICA/KORA Augsburg project was part of the international collaborative WHO MONICA project and investigated the cardiovascular risk factor profile of randomly selected subjects of the resident population in cross-sectional surveys. The study design, sampling frame, and data collection were described in detail previously (11). Between October 1994 and June 1995, baseline data were obtained from the third MONICA survey (S3) in the city of Augsburg, Germany. A total of 1,506 participants, age 25 to 74 years at baseline, were invited for a follow-up study (F3) that was conducted between March 2004 and May 2005.

A total of 169 individuals were inaccessible or ineligible for the F3 examination due to death (n = 58), interdiction of recontact (people that refused to be contacted again) (n = 63), having moved (n = 41), and severe illness (n = 7). From the remaining individuals, 1,152 participated in the follow-up study (net response: 76.5%) of whom 7 (0.61%) were excluded because of lack of information about blood pressure levels.

**Interview and medical examination.** On both occasions, all participants underwent an interview related to personal and family medical history, lifestyle and nutrition, health behavior, and psychosocial factors. Body height and total body weight were measured in light clothing. Blood pressure values were corrected for differences of observers and devices between the 2 examinations (see the Statistical analysis section). The mean of the second and third blood pressure measurements was used for the present analyses. The blood pressure categories were defined on the basis of the criteria of the Joint National Committee 7 report (1). Normal blood pressure was defined as a systolic blood pressure <120 mm Hg and a diastolic blood pressure <80 mm Hg. Pre-hypertension was defined as a systolic blood pressure of 120 to 139 mm Hg and/or a diastolic blood pressure of 80 to 89 mm Hg. Arterial hypertension was considered as a systolic blood pressure of ≥140 mm Hg and/or a diastolic blood pressure of ≥90 mm Hg or currently taking antihypertensive medication. If the systolic and diastolic pressure readings belonged to different categories, the higher of the 2 readings was used to assign the blood pressure category. Body mass index was defined as the individual's total body weight divided by the square of its height. Fat mass was calculated as total body weight minus fat-free mass. Fat-free mass was determined by measurement of bioelectrical impedance analysis with the Body Composition Analyzer TVI-10 (Danziger Medical Technology, Heidelberg, Germany), as previously reported in greater detail (12). The percentage of fat-free mass was calculated as absolute fat-free mass multiplied by 100 and divided by total body weight. The percentage of fat mass was calculated as absolute fat mass multiplied by 100 and divided by total body weight. Waist circumference was measured at the level of the navel. Hip circumference was measured at its widest part. The waist-hip ratio was calculated as the waist circumference divided by the hip circumference. In addition, participants underwent standardized medical examinations including collection of nonfasting venous blood samples. Diabetes mellitus was defined as disease known to the patient, as reported by standard questionnaire, the use of antiglycemic oral medications or insulin, or nonfasting glucose blood levels of ≥200 mg/dl. Cardiovascular disease was defined as stroke or myocardial infarction reported by standard questionnaire.

**Study groups.** From the 1,145 subjects for whom blood pressure was measured in both examinations 10 years apart, we extracted 2 baseline groups that were then subdivided into 3 subgroups each. The first group consisted of participants who presented with pre-hypertensive blood pressure levels (120 to 139 mm Hg systolic or 80 to 89 mm Hg diastolic blood pressure, without medication: 365 individuals) and the second group consisted of participants who presented with hypertensive blood pressure levels (>139 mm Hg systolic or >89 mm Hg diastolic or taking antihypertensive medication: 429 individuals) in the baseline examination. The baseline pre-hypertensive group was then subdivided. The first subgroup consisted of participants who presented with pre-hypertensive blood pressure levels in the baseline and with normal blood pressure levels (<120 mm Hg systolic blood pressure and <80 mm Hg diastolic blood pressure, no medication) in the follow-up examination (n = 48), which we called the pre-hypertensive-normotensive (PreNorm) group. The second subgroup consisted of individuals who presented with pre-hypertensive blood pressure levels in the baseline study and again with pre-hypertensive blood pressure levels in the follow-up study (n = 134), which we called the persistently pre-hypertensive (PrePre) group. The third group consisted of individuals who presented with pre-hypertensive blood pressure levels in the baseline study and with hypertensive blood pressure levels (>139 mm Hg systolic or >89 mm Hg diastolic or taking antihypertensive medication) at the follow-up examination (n = 183), which we called the pre-hypertensive-hypertensive (PreHyp) group. The baseline hypertensive group had also 3 subgroups. The first subgroup consisted of participants who presented with hypertensive blood pressure levels in the baseline study and with normal blood pressure levels at the follow-up examination (n = 8), which we called the hypertensive-normotensive (HypNorm) group. The second subgroup consisted of individuals who presented with hypertensive blood pressure levels in the baseline study and with pre-hypertensive blood pressure levels in the follow-up study (n = 29), which we called the hypertensive-pre-hypertensive (HypPre) group. Finally, the third subgroup consisted of individuals who presented with hypertensive blood pressure levels in the baseline and again with hypertensive blood pressure levels at the follow-up examination (n = 392), which we called the persistently hypertensive (HypHyp) group. The HypNorm subgroup was excluded from further analyses because of the small number of individuals in this group (n = 8).

**Statistical analysis.** Blood pressure measurements were performed with different measurement devices in S3 and F3, reflecting technological progress. Systematic differences between surveys due to different measurement methods were assessed by using data from a sample of 1,005 individuals examined on both occasions using a mixed regression model, as described in more detail previously (13).

The groups were compared with regard to their crude characteristics at baseline and follow-up using frequencies, mean values, and SDs. Statistical significances were tested with *t* tests for the mean values for continuous variables and chi-square tests for categorical variables. Adjusted mean values and the 95% confidence interval (CI) in the cross-sectional analysis of baseline and follow-up measurements were calculated with multivariate linear regression models that included age, sex, body mass index, and systolic blood pressure at the baseline study. For prospective analyses, the adjusted relative changes in the variables of interest, that is, [(value F3 − value S3)/value S3], were calculated in each group and expressed as percentages. To account for regression to the mean effects in the variable for which the cross-sectional analysis of the follow-up and the relative changes were studied, we additionally adjusted for the overall baseline mean of the variable of interest. Odds ratios (ORs) for the cumulative risk of incident hypertension and the possibility of incident normalization of blood pressure levels, comparing quartiles and a 5% increase and decrease of relative changes in variables of total body weight and composition, were calculated with a logistic regression model that included age, sex, body mass index, and systolic blood pressure at baseline and the overall baseline mean of the variable of interest. All analyses were performed using SPSS version 15.0.0 for Windows (SPSS Inc., Chicago, Illinois).

## Results

**Clinical and laboratory characteristics.** BASELINE Pre-Hyp GROUP. The prevalence of pre-hypertension at the baseline study was 31.9% (365 of 1,145 study subjects with 10-year follow-up). We identified 204 (55.9%) men and 161 (44.1%) women with pre-hypertension. After 10 years of follow-up, blood pressure values normalized in 48 (13.2%) individuals, 134 (36.7%) had persistent pre-hypertension, and hypertension developed in 183 (50.1%). One individual (2.08%) in the PreNorm group, 3 (2.27%) in the PrePre group, and 17 (9.29%) in the PreHyp group developed cardiovascular disease (stroke or myocardial infarction, p for trend = 0.016). The PreNorm group included 1 (2.13%), the PrePre 6 (4.51%) and the PreHyp 19 (10.4%) individuals with incident or prevalent diabetes mellitus at the follow-up study (p for trend = 0.049). Finally, 17 (35.4%) individuals in the PreNorm group, 34 (25.6%) in the PrePre group, and 27 (14.8%) in the PreHyp group were smokers (p for trend = 0.018).

The anthropometric characteristics of the baseline pre-hypertensive group are contained in Table 1. Almost two-thirds of subjects in the PreNorm group were women. Other differences, at baseline, between the 3 groups were found with respect to age, blood pressure, and glycosylated hemoglobin.

In pre-hypertensive individuals in whom hypertension subsequently developed, baseline nonadjusted body mass index, fat mass, percentage of fat mass, waist circumference, and waist-hip ratio were already higher, whereas the percentage fat-free mass was lower than in those who remained pre-hypertensive. No statistical difference was seen for total body weight and absolute fat-free mass (Table 1).

BASELINE HYPERTENSIVE GROUP. The prevalence of hypertension at the baseline study was 37.5% (429 of 1,145 study

**Table 1** **Crude Anthropometric and Laboratory Characteristics of the PreNorm, PrePre, and PreHyp Individuals at Baseline (1994/1995) and at the Follow-Up Examination (2004/2005) of the MONICA/KORA Cohort Study**

| Characteristic | PreNorm | PrePre | PreHyp | p Value |
|---|---|---|---|---|
| Men (%) | 19 (39.6) | 85 (63.4) | 100 (54.6) | |
| Women (%) | 29 (60.4) | 49 (36.6) | 83 (45.4) | 0.015 |
| Age at baseline (yrs) | 40.5 ± 13.3 | 43.8 ± 11.9 | 52.7 ± 11.2 | <0.001 |
| Height at baseline (cm) | 169.1 ± 8.10 | 171.5 ± 9.36 | 168.4 ± 9.17 | 0.012 |
| BMI (kg/m$^2$) | | | | |
| 1994/1995 | 25.3 ± 3.59 | 25.9 ± 3.66 | 26.9 ± 3.47 | 0.004 |
| 2004/2005 | 25.4 ± 3.64 | 26.6 ± 3.64 | 28.1 ± 3.87 | <0.001 |
| TBW (kg) | | | | |
| 1994/1995 | 72.4 ± 11.1 | 76.2 ± 12.5 | 76.6 ± 12.6 | NS |
| 2004/2005 | 72.7 ± 11.8 | 78.2 ± 12.7 | 79.8 ± 13.6 | 0.004 |
| FFM (kg) | | | | |
| 1994/1995 | 51.0 ± 8.17 | 54.5 ± 9.25 | 52.5 ± 9.65 | NS |
| 2004/2005 | 50.9 ± 8.48 | 54.9 ± 9.70 | 53.1 ± 10.0 | 0.042 |
| FFM (%) | | | | |
| 1994/1995 | 71.0 ± 8.03 | 71.9 ± 7.91 | 68.6 ± 6.98 | <0.001 |
| 2004/2005 | 69.9 ± 8.15 | 70.4 ± 7.68 | 66.4 ± 7.24 | <0.001 |
| Fat mass (kg) | | | | |
| 1994/1995 | 21.3 ± 7.74 | 21.6 ± 8.08 | 24.2 ± 6.87 | 0.004 |
| 2004/2005 | 22.3 ± 8.02 | 23.4 ± 7.78 | 27.0 ± 7.74 | <0.001 |
| Fat mass (%) | | | | |
| 1994/1995 | 29.0 ± 8.03 | 28.1 ± 7.91 | 31.4 ± 6.98 | <0.001 |
| 2004/2005 | 30.1 ± 8.15 | 29.6 ± 7.68 | 33.6 ± 7.24 | <0.001 |
| WC (cm) | | | | |
| 1994/1995 | 81.8 ± 10.4 | 87.9 ± 10.9 | 89.9 ± 10.8 | <0.001 |
| 2004/2005 | 87.1 ± 11.4 | 94.0 ± 11.1 | 97.4 ± 11.4 | <0.001 |
| WHR | | | | |
| 1994/1995 | 0.81 ± 0.08 | 0.86 ± 0.08 | 0.87 ± 0.08 | <0.001 |
| 2004/2005 | 0.84 ± 0.08 | 0.89 ± 0.07 | 0.91 ± 0.08 | <0.001 |
| SBP (mm Hg) | | | | |
| 1994/1995 | 119.8 ± 8.33 | 123.1 ± 8.36 | 126.1 ± 7.29 | <0.001 |
| 2004/2005 | 109.6 ± 7.07 | 128.2 ± 6.60 | 142.7 ± 19.8 | <0.001 |
| DBP (mm Hg) | | | | |
| 1994/1995 | 80.2 ± 6.36 | 80.0 ± 6.52 | 81.7 ± 5.64 | 0.033 |
| 2004/2005 | 72.9 ± 4.00 | 80.8 ± 5.53 | 86.8 ± 10.4 | <0.001 |
| Total cholesterol (mg/dl) | | | | |
| 1994/1995 | 226.0 ± 38.3 | 227.9 ± 41.5 | 236.6 ± 43.6 | NS |
| 2004/2005 | 214.3 ± 40.9 | 220.3 ± 35.2 | 220.6 ± 42.5 | NS |
| LDL cholesterol (mg/dl) | | | | |
| 1994/1995 | 134.2 ± 41.9 | 139.0 ± 42.3 | 146.3 ± 42.0 | NS |
| 2004/2005 | 128.4 ± 37.7 | 130.4 ± 30.0 | 127.3 ± 33.9 | NS |
| HDL cholesterol (mg/dl) | | | | |
| 1994/1995 | 60.4 ± 20.5 | 53.9 ± 16.0 | 54.3 ± 15.6 | 0.049 |
| 2004/2005 | 57.6 ± 15.4 | 57.6 ± 15.4 | 57.3 ± 16.2 | NS |
| HbA1c (%) | | | | |
| 1994/1995 | 5.14 ± 0.42 | 5.03 ± 0.45 | 5.26 ± 0.92 | 0.030 |
| 2004/2005 | 5.18 ± 0.22 | 5.19 ± 0.30 | 5.36 ± 0.46 | <0.001 |
| Total (%) | 48 (13.2) | 134 (36.7) | 183 (50.1) | |

Values are presented as mean ± SD. p values are given for the comparison among the pre-hypertensive-normotensive (PreNorm), persistently pre-hypertensive (PrePre), and pre-hypertensive-hypertensive (PreHyp) individuals at the baseline (1994/1995) and the follow-up examination (2004/2005) of the MONICA-KORA cohort study.

BMI = body mass index; DBP = diastolic blood pressure; FFM = fat-free mass; HbA1c = glycosylated hemoglobin; SBP = systolic blood pressure; TBW = total body weight; WC = waist circumference; WHR = waist-hip ratio.

subjects with 10-year follow-up). We identified 236 (55.0%) men and 193 (45.0%) women with hypertension. After 10 years of follow-up, 8 (1.86%) individuals had normalized blood pressure values, 29 (6.76%) had pre-hypertension, and 392 (91.4%) individuals had persistent hypertension. The individuals from the HypNorm group were, from this point, excluded from further analyses because of their small number. Cardiovascular disease developed in none of the individuals in the HypPre group, but did in 34 (8.81%) in the HypHyp group (stroke or myocardial infarction, p = NS). The HypPre group included 1 (3.57%) and the HypHyp 58 (14.9%) individuals with incident or prevalent diabetes mellitus at the follow-up study (p = NS). Finally, 3 (10.3%) individuals in the HypPre group and 48 (12.2%) in the HypHyp group were smokers (p = NS).

The characteristics of the hypertensive group at baseline are shown in Table 2. More than two thirds of subjects in whom blood pressure levels decreased to pre-hypertension were men. Again, there were other differences at baseline such as age and blood pressure between subjects who remained hypertensive and those who became pre-hypertensive. In hypertensive individuals who subsequently remained hypertensive, the baseline nonadjusted absolute fat mass value and the percentage of fat mass were already higher, whereas the absolute fat-free mass value and percentage of fat-free mass were lower compared with the HypPre group. No statistical difference was seen for body mass index, total body weight, waist circumference, and waist-hip ratio (Table 2).

**Dynamic changes in body measures and composition.** BASELINE PRE-HYPERTENSIVE GROUP. At follow-up, pre-hypertensive subjects who became hypertensive (i.e., the PreHyp group) presented a more pronounced increase in total body weight, waist circumference, and waist-hip ratio compared with the other 2 pre-hypertensive groups (Fig. 1A). The increase in these parameters in individuals in the PrePre group was moderate and significantly less pronounced than in the PreHyp group. The PreNorm group had the lowest values in each category. Likewise, when the alterations in body measures were expressed as a percentage of change from baseline values, the PreHyp group showed the most prominent dynamic changes in total body weight and the other variables (Fig. 1A).

The most prominent change in body composition was observed in terms of a marked increase in fat mass in subjects in the PreHyp group (Fig. 1B). By contrast, changes in absolute fat-free mass were less prominent, and there was even a marked decrease in the percentage of fat-free mass. The group with normalized blood pressure levels had only a small increase in the absolute and percentage of fat mass and a decrease in the absolute and percentage of fat-free mass. Consequently, there were significant differences in dynamic changes in body composition overtime between the PreNorm and the PreHyp groups, whereas the PrePre group was at an intermediary level (Fig. 1B).

**Table 2** Crude Anthropometric and Laboratory Characteristics of the HypPre and HypHyp Individuals at the Baseline (1994/1995) and the Follow-Up Examination (2004/2005) of the MONICA/KORA Cohort Study

| Characteristic | HypPre | HypHyp | p Value |
|---|---|---|---|
| Men (%) | 21 (72.4) | 211 (53.8) | |
| Women (%) | 8 (27.6) | 181 (46.2) | NS |
| Age at baseline (yrs) | 45.8 ± 14.2 | 56.1 ± 10.8 | <0.001 |
| Height at baseline (cm) | 172.1 ± 8.69 | 167.2 ± 9.08 | 0.004 |
| BMI (kg/m$^2$) | | | |
| 1994/1995 | 27.1 ± 3.60 | 28.4 ± 3.87 | NS |
| 2004/2005 | 26.7 ± 3.55 | 28.8 ± 4.34 | 0.011 |
| TBW (kg) | | | |
| 1994/1995 | 80.3 ± 11.5 | 79.3 ± 12.8 | NS |
| 2004/2005 | 79.2 ± 12.2 | 80.7 ± 14.5 | NS |
| FFM (kg) | | | |
| 1994/1995 | 56.5 ± 8.71 | 52.4 ± 9.48 | 0.026 |
| 2004/2005 | 56.3 ± 9.14 | 52.4 ± 10.1 | 0.049 |
| FFM (%) | | | |
| 1994/1995 | 70.7 ± 7.50 | 66.2 ± 7.05 | 0.001 |
| 2004/2005 | 71.5 ± 7.70 | 65.1 ± 7.21 | <0.001 |
| Fat mass (kg) | | | |
| 1994/1995 | 23.8 ± 7.50 | 27.0 ± 7.73 | 0.029 |
| 2004/2005 | 22.8 ± 7.47 | 28.4 ± 8.61 | 0.001 |
| Fat mass (%) | | | |
| 1994/1995 | 29.3 ± 7.50 | 33.8 ± 7.05 | 0.001 |
| 2004/2005 | 28.5 ± 7.70 | 34.9 ± 7.21 | <0.001 |
| WC (cm) | | | |
| 1994/1995 | 91.2 ± 9.03 | 93.7 ± 10.9 | NS |
| 2004/2005 | 94.7 ± 10.2 | 100.0 ± 11.7 | 0.017 |
| WHR | | | |
| 1994/1995 | 0.88 ± 0.07 | 0.89 ± 0.08 | NS |
| 2004/2005 | 0.90 ± 0.08 | 0.92 ± 0.08 | NS |
| SBP (mm Hg) | | | |
| 1994/1995 | 132.5 ± 10.2 | 144.1 ± 17.1 | <0.001 |
| 2004/2005 | 128.7 ± 6.31 | 144.4 ± 21.5 | <0.001 |
| DBP (mm Hg) | | | |
| 1994/1995 | 90.3 ± 5.22 | 90.3 ± 11.3 | NS |
| 2004/2005 | 83.2 ± 4.61 | 86.5 ± 12.8 | NS |
| Total cholesterol (mg/dl) | | | |
| 1994/1995 | 238.7 ± 47.7 | 240.3 ± 39.4 | NS |
| 2004/2005 | 227.3 ± 47.0 | 220.6 ± 40.5 | NS |
| LDL cholesterol (mg/dl) | | | |
| 1994/1995 | 143.8 ± 48.0 | 151.5 ± 40.2 | NS |
| 2004/2005 | 134.5 ± 37.9 | 128.9 ± 32.8 | NS |
| HDL cholesterol (mg/dl) | | | |
| 1994/1995 | 55.4 ± 19.5 | 51.7 ± 14.3 | NS |
| 2004/2005 | 58.9 ± 19.1 | 54.2 ± 15.3 | NS |
| HbA1c (%) | | | |
| 1994/1995 | 5.07 ± 0.43 | 5.37 ± 0.88 | NS |
| 2004/2005 | 5.26 ± 0.27 | 5.48 ± 0.55 | 0.035 |
| Total (%) | 29 (6.89) | 392 (93.1) | |

Values are presented as mean ± SD. p values are given for the comparison of the hypertensive-pre-hypertensive (HypPre) and hypertensive-hypertensive (HypHyp) individuals at the baseline (1994/1995) and the follow-up examination (2004/2005) of the MONICA-KORA cohort study. Abbreviations as in Table 1.

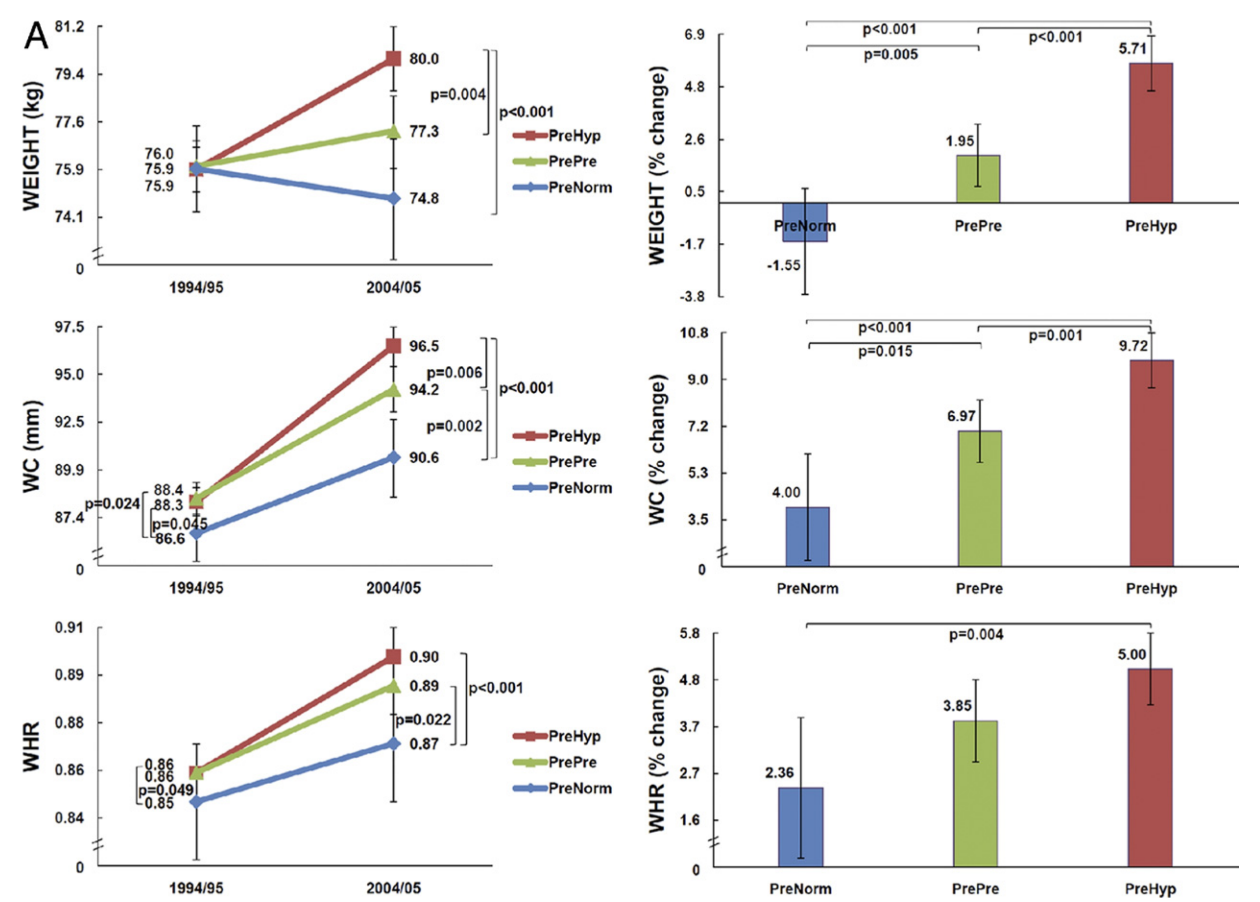


**Figure 1** **Baseline Pre-Hypertensive Group Body Measures and Body Composition**

**(Left)** The mean values and the 95% confidence interval (adjusted for sex, age, body mass index, and systolic blood pressure, all at baseline) for body measures **(A)** of body weight, waist circumference (WC), waist-hip ratio (WHR), and for body composition **(B)** including fat mass (FAT), percentage of fat mass (PFAT), fat-free mass (FFM), and percentage of fat-free mass (PFFM) of the pre-hypertensive-normotensive (PreNorm), persistently pre-hypertensive (PrePre), and pre-hypertensive-hypertensive (PreHyp) groups at the baseline (1994 to 1995) and at follow-up examination (2004 to 2005). **(Right)** The relative changes and the 95% confidence interval (adjusted for sex, baseline age, body mass index, and systolic blood pressure plus overall baseline mean of the variable under analysis) of the same variables of the PreNorm, PrePre, and PreHyp groups over the 10-year period.

BASELINE HYPERTENSIVE GROUP. At follow-up, subjects in the HypHyp group had significantly higher values in total body weight, waist circumference, and waist-hip ratio compared with the HypPre group (Fig. 2A). Importantly, over the 10-year period, the HypPre group was characterized by a marked decrease in total body weight and smaller increases in waist circumference and waist-hip ratio (Fig. 2A).

Dynamic changes in body composition were significantly different in the subjects in the HypPre group compared with the HypHyp group (Fig. 2B). Over the 10-year period, the HypPre group was characterized by a marked decrease in the absolute and percentage of fat mass and the absolute fat-free mass, but not in the percentage of fat-free mass, which increased markedly. By contrast, the absolute and percentage of fat mass increased in the group who remained maintained hypertensive with small decreases in the absolute and percentage of fat-free mass (Fig. 2B).

**Factors associated with blood pressure category.** In pre-hypertensive subjects, sex had no influence on the incident OR of hypertension (data not shown), but women had greater chance than men (adjusted for baseline age, body mass index, and systolic blood pressure) to have normalized blood pressure levels (OR: 2.18; 95% CI: 1.09 to 4.36). After adjustment (for sex, baseline body mass index, and systolic blood pressure), age had a strong effect on the probability of the development of hypertension but no influence on the probability of blood pressure normalization. The OR for incident hypertension in the group with ages between 65 and 74 years was 7.36 (95% CI: 2.66 to 20.3) compared with the group of ages between 25 and 34 years.

Figure 3 represents parameters of body composition, divided in quartiles, that influenced the OR (adjusted for sex and baseline age, body mass index, and systolic blood pressure plus overall baseline mean of the variable of

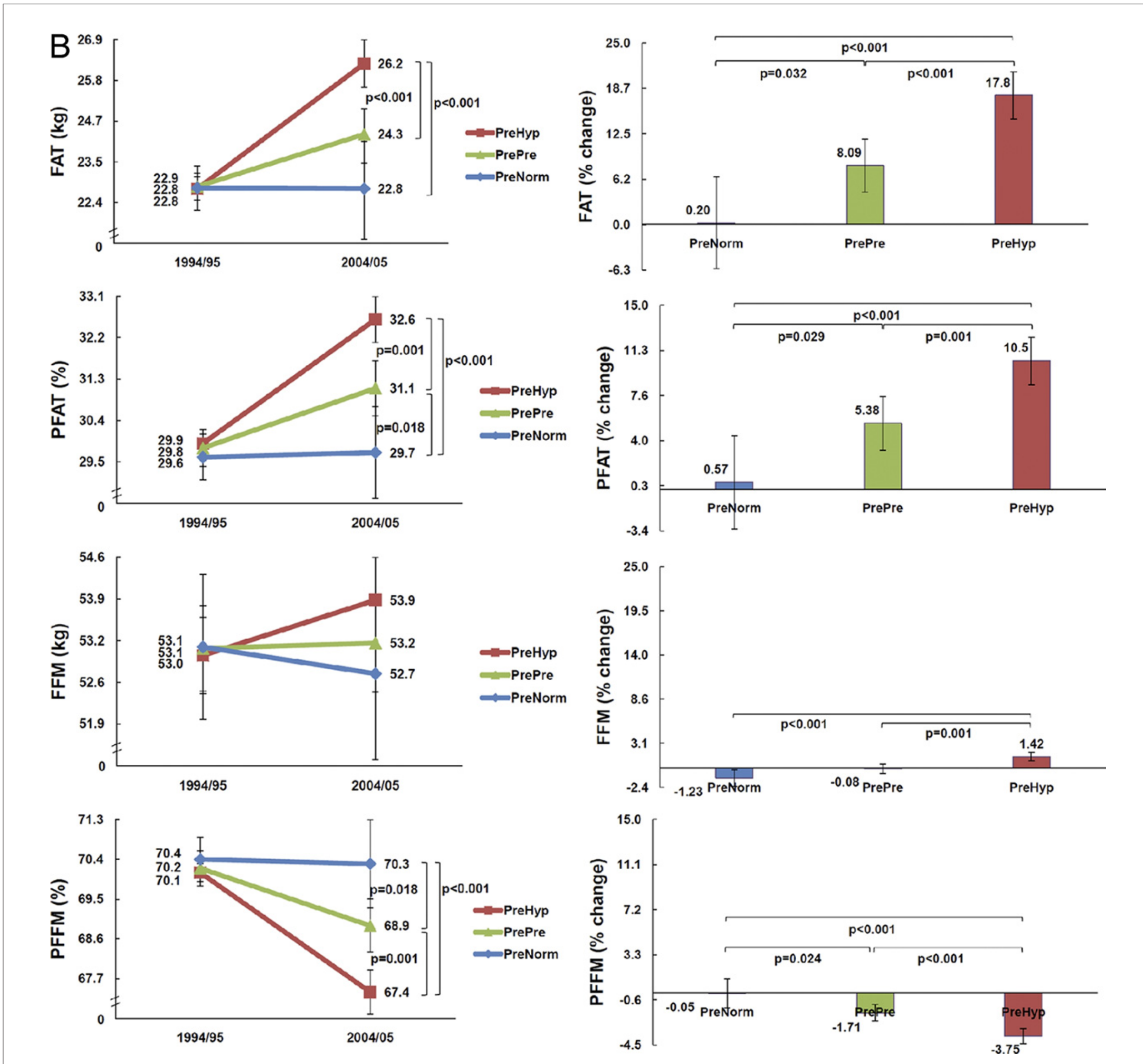


**Figure 1** Continued

interest) for the cumulative risk of incident hypertension (Fig. 3A) and normalization of blood pressure levels (Fig. 3B) over the 10-year period. Again, dynamic changes in the absolute and percentage of fat mass showed strong effects on these developments.

Table 3 shows the OR for an increase of 5% (risk of hypertension) or a decrease of 5% (normalization of blood pressure levels) for each parameter of body composition over the 10-year interval in subjects who were pre-hypertensive at baseline.

## Discussion

The prevalence of pre-hypertension in this population-based sample was 31.9% at the baseline study, which is similar to previous studies of other populations (14,15). Another important finding in the present study and previous studies (16,17) is the high rate of progression from pre-hypertension to hypertension (i.e., 50% over a 10-year period). In the PAMELA study (18), in which the risks of white-coat or masked hypertension for the development of sustained hypertension were evaluated; in 60% of patients, true hypertension developed from normotension. In the accompanying editorial about that study (19), it was emphasized that identifying clues to discover patients who are prone to progress would be a seminal issue. In addition to aging, nearly all parameters of body composition analyzed, namely fat mass, fat-free mass, body weight, waist circumference, and waist-hip ratio were profoundly related to the subsequent

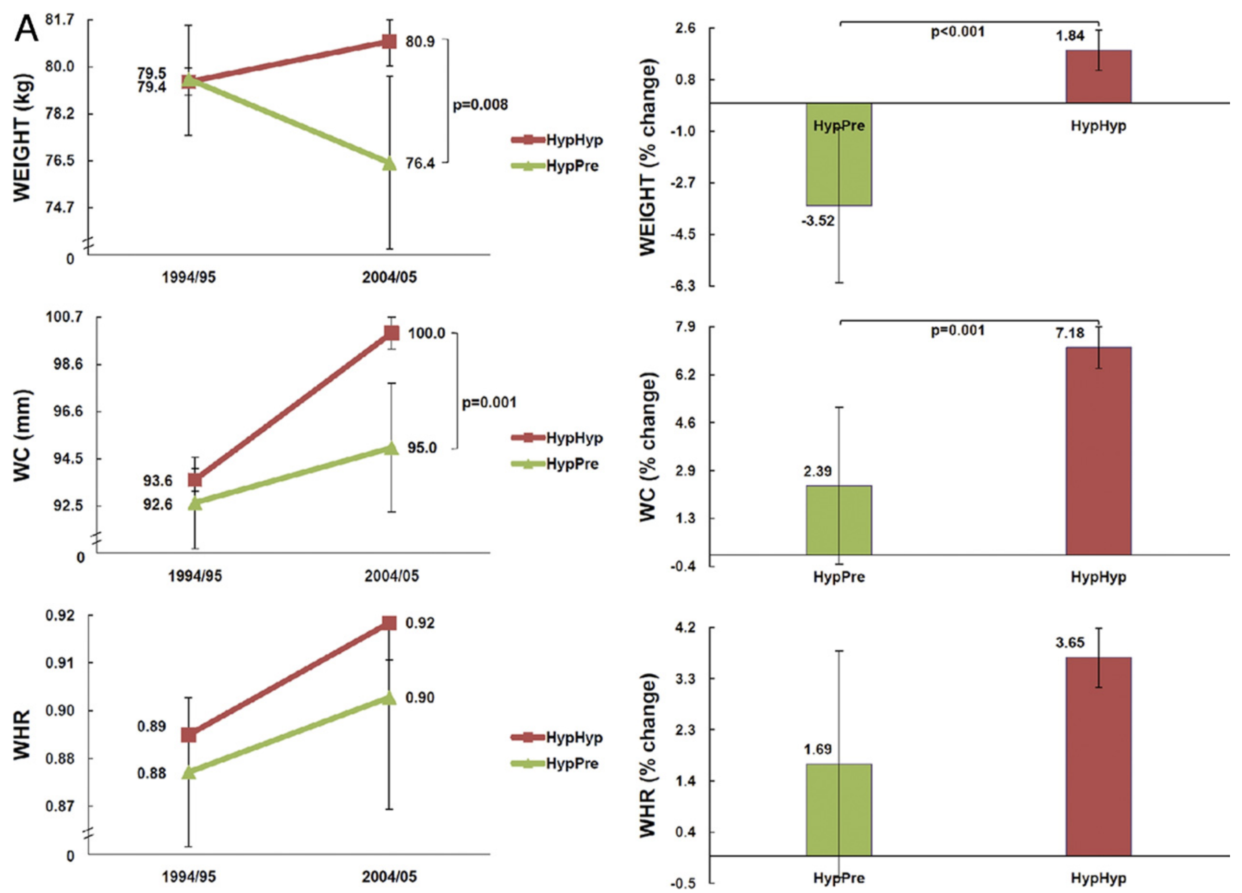


**Figure 2** **Baseline Hypertensive Group Body Measures and Body Composition**

**(Left)** The mean values and the 95% confidence interval (adjusted for sex, age, body mass index, and systolic blood pressure, all at baseline) for body measures **(A)** of body weight, WC, and WHR and for body composition **(B)** including FAT, PFAT, FFM, and PFFM of the hypertensive-pre-hypertensive (HypPre) and hypertensive-hypertensive (HypHyp) groups at the baseline (1994 to 1995) and follow-up examination (2004 to 2005). **(Right)** The relative changes and the 95% confidence interval (adjusted for sex, baseline age, body mass index, and systolic blood pressure plus overall baseline mean of the variable under analysis) of the same variables of the HypPre and HypHyp groups over the 10-year period. Abbreviations as in Figure 1.

progression from pre-hypertension to hypertension; consequently, the MONICA/KORA Augsburg cohort study provides such a clue, showing that weight gain is a powerful risk factor for the development of sustained hypertension.

The prevalence of hypertension at the baseline study was 37.5%. As expected, after 10 years of follow-up, 91.4% of these individuals persistently had hypertension. Similarly, in the PAMELA study (18), just 8% of the subjects reverted from true hypertension to normotension. Although the probability of moving into a lower blood pressure category was small, any change was again strongly affected by dynamic changes in body composition.

Beyond age, the most important contributors to the evolution from pre-hypertension to hypertension were dynamic weight changes. The effect of obesity on the progression of hypertension was also reported in the study by Vasan et al. (3), who assessed in nonhypertensive subjects the frequency of progression to hypertension. In agreement with this study, which analyzed the effects of dynamic changes on total body weight, we observed, in addition, that dynamic changes in body composition are important determinants of incident hypertension. These findings add to the substantial data linking obesity and weight gain to the future risk of hypertension (20,21).

In addition to changes in absolute weight, we observed that maintenance (rather than increase) of fat mass was associated with a lower likelihood of the progression from pre-hypertension to hypertension. In the group that was pre-hypertensive at baseline and whose blood pressure levels decreased (i.e., PreNorm group), we observed even a decrease in body weight, which resulted mainly from a decrease in fat-free mass. Moreover, individuals hypertensive at baseline whose blood pressure levels decreased (i.e., HypPre group) presented a similar pattern, but with a more pronounced decrease in fat mass that even resulted in an increase in the relative percentage of fat-free mass despite a decrease in absolute fat-free mass. Interestingly, obese subjects who underwent gastric surgery showed that in

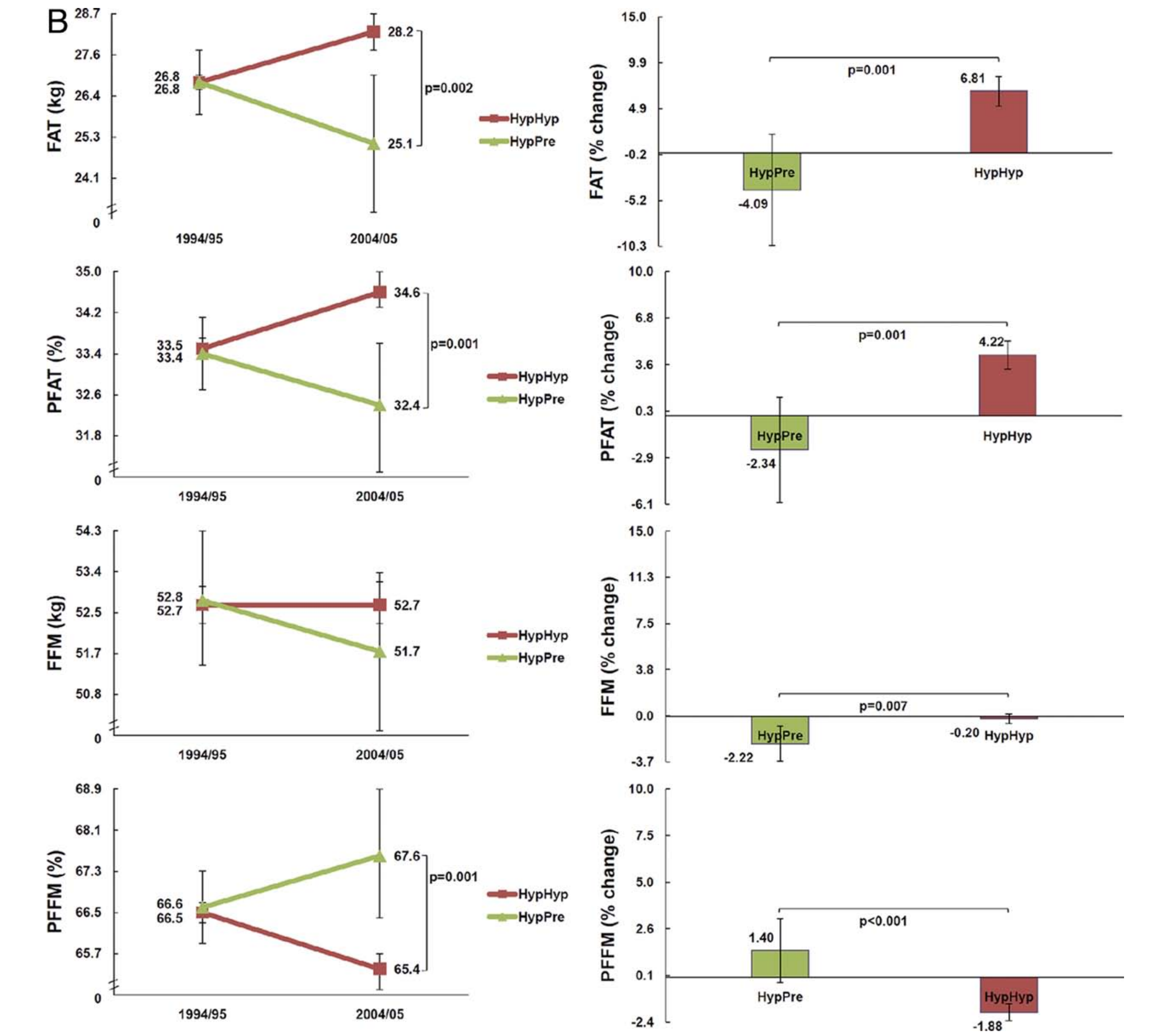


**Figure 2** Continued

parallel with a significant and persistent weight loss after bariatric surgery, blood pressure levels return to pre-surgical levels after a follow-up of 10 years (22). Thus, although it has been well established that an increase in weight is a risk for the development of hypertension, it is not clear what, over a prolonged period of time, the effect of a decrease in weight will have on blood pressure, but drastic changes in body composition may be mandatory to reestablish pre-hypertension once hypertension has been diagnosed, as was the case in our study.

The majority of subjects in this population-based sample gained weight over the 10-year period. This dynamic change was almost exclusively driven by an increase in fat mass and linked to progression from pre-hypertension to hypertension. Thus, during aging, fat mass accounts for an increasing proportion of total body weight. If this generally observed process is being slowed down or even stopped, there are increased chances that pre-hypertensive individuals remain in this blood pressure category or even have normalized blood pressure.

Although the effects of chronic weight changes in pre-hypertensive individuals are incompletely understood (23), several trials assessed the effect of weight loss on hypertension. On predominantly hypertensive individuals, a recent meta-analysis of 25 randomized, controlled trials showed that a weight loss of 1 kg (by means of energy restriction, increased physical activity, or both) was associated with a decrease of 1.05 mm Hg in

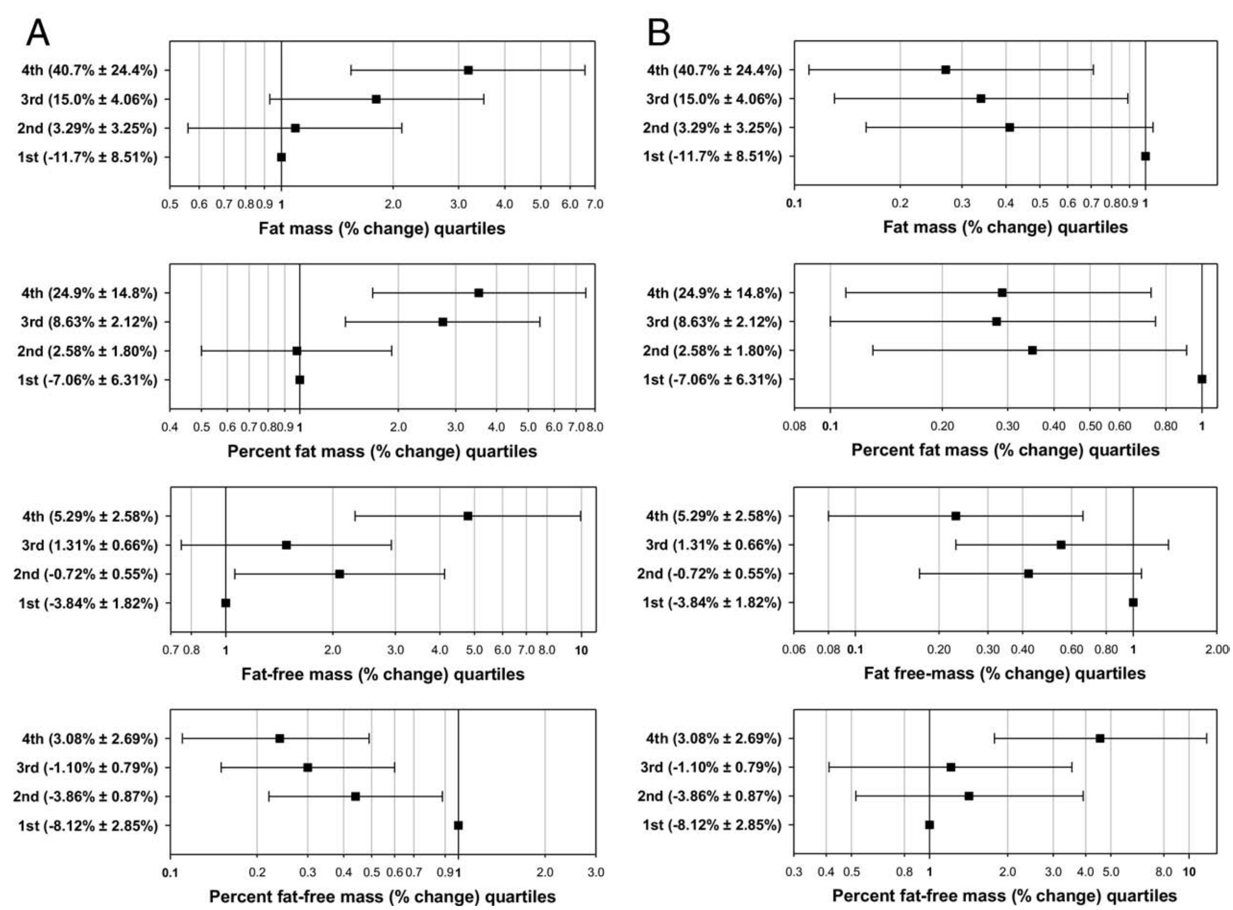


**Figure 3** **Incident Hypertension and Incident Normalization of Blood Pressure Levels**

**(A)** The mean values and the 95% confidence interval of adjusted (for sex, baseline age, body mass index, and systolic blood pressure plus overall baseline mean of the variable under analysis) odds ratio for 10-year cumulative risk of incident hypertension in individuals with baseline pre-hypertension, by quartiles (mean ± SD) of relative changes in FAT, PFAT, FFM, and PFFM. **(B)** The same values of adjusted odds ratio for 10-year cumulative probability of incident normalization of blood pressure levels in individuals with baseline pre-hypertension. Abbreviations as in Figure 1.

**Table 3** **Adjusted Odds Ratios for 10-Year Cumulative Probability of Incident Hypertension or Incident Normalization of Blood Pressure Levels in Individuals With Pre-Hypertension at Baseline**

| | Odds Ratio (95% Confidence Interval) | |
|---|---|---|
| Characteristics* | Risk of Hypertension | Normalization |
| TBW | 1.55 (1.31–1.84) | 1.60 (1.26–2.05) |
| WC | 1.43 (1.21–1.70) | 1.51 (1.19–1.92) |
| WHR | 1.32 (1.0–1.66) | 1.40 (1.04–1.90) |
| FAT | 1.15 (1.08–1.22) | 1.15 (1.05–1.25) |
| PFM | 1.23 (1.11–1.36) | 1.23 (1.07–1.40) |
| FFM | 2.13 (1.49–3.04) | 2.19 (1.30–3.68) |
| PFFM | 0.49 (0.36–0.66) | 0.53 (0.37–0.78) |

Odds ratios are shown for an increase of 5% (risk of hypertension) or a decrease of 5% (normalization of blood pressure levels) for each parameter of body composition over the 10-year interval of follow-up. *Adjusted for sex, baseline age, body mass index, and systolic blood pressure plus overall baseline mean of the variable of interest.

Abbreviations as in Table 1.

systolic blood pressure and 0.92 mm Hg in diastolic blood pressure (9). This blood pressure reduction was accomplished without the necessity of also attaining normal total weight (9,23). The present study extends these data to the situation in a population-based sample with pre-hypertension and long-term follow-up. Particularly, the data suggest that weight maintenance in pre-hypertensive subjects is important and effective to decrease the probability of the development of hypertension. In individuals with already established hypertension, the loss in total body weight increases the probability of a normalization of blood pressure levels. This finding adds to data from randomized studies that demonstrated the effect of lifestyle modification on blood pressure and supports the intentions of primary prevention as derived from the Framingham Heart Study (24).

Although changes in fat mass most accurately predicted changes in the blood pressure category, we were surprised by the increase in waist circumference and waist-hip ratio in the individuals who actually lost weight during 10 years of follow-up. As fat mass occupies more space than the same weight of fat-free mass, the increase in fat mass observed in the pre-hypertensive group could be the explanation for this observation. Thus, it appears that during aging, body composition is redistributed, even when the overall weight stays the same, toward an increase in fat mass and expansion of the abdominal cavity. This is noteworthy because few previous observational longitudinal studies analyzed the effects of aging and the changes in total body weight and body composition on blood pressure levels and waist circumference.

**Study limitations.** This study was conducted in white subjects, so the results cannot be extended to other ethnic groups. The necessary adjustment by sex may carry some limitations, but it was not possible to present the data for men and women separately because of the small sample size in some subgroups. The study sample was derived from a population-based sampling frame but loss to follow-up or comorbid conditions may have introduced some imbalances in our participants. Blood pressure measurements were performed by different methods in the baseline and follow-up studies. Systematic differences were estimated from specified models and used to derive adequate correction values. We cannot conceive of any methodological imbalances arising from these corrections that would lead to systematically biased cardiac results among the groups in this study.

## Conclusions

We observed in a population-based sample that changes in body composition are highly predictive of the risk of progression from pre-hypertension to hypertension. Most notably, increases in fat mass resulting in an increase in waist circumference predicted the onset of hypertension.

Our findings serve to emphasize the importance of controlling the gain in fat mass and thereby central obesity in the primary prevention of hypertension at the level of the overall population. There is an urgent need to increase the awareness among both health professionals and the general public about the health hazards of central or abdominal obesity. This notion is emphasized by the close correlation of incident hypertension with dynamic changes in fat mass and waist circumference. Because the progression rates from pre-hypertension to hypertension increase with age, it appears important to introduce lifestyle modifications (as suggested by the Joint National Committee 7 Report [1]) as early in adult life as possible. According to Hu (25), "Although maintaining a healthy weight should continue to be a cornerstone in the prevention of chronic diseases and premature death, maintaining a healthy waist size should also be an important goal."

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**Key Words:** body composition ▪ hypertension ▪ population-based study ▪ pre-hypertension ▪ risk factors.