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Body Mass Index Is Associated with Hypertension in Japanese Young Elderly Individuals: Findings of the New Integrated Suburban Seniority Investigation

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Abstract

Objective This study aimed to investigate the association between BMI at 65 years of age and the development of hypertension during the subsequent five years.

Methods A total of 1,003 participants (65 years of age) who had no history of myocardial infarction and/or hypertension at baseline health check-ups (1996-2005) and participated in a secondary health check-up when the subjects reached 70 years of age were analyzed.

Results Using fully adjusted models, men with a BMI of <18.5 [odds ratio (OR), 4.08; 95% confidence interval (CI), 1.32-1.83], BMI of 23.0-24.9 (OR, 2.00; 95% CI, 1.18-3.40) and BMI of ≥25.0 (OR, 1.98; 95% CI, 1.10-3.56) were found to be at higher risk of developing hypertension than did those with a BMI of 18.5-22.9.

Conclusion Leanness or being overweight/obese at age 65 increases the risk of subsequent hypertension.

Key words: hypertension, overweight, obesity, elderly, body mass index

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Introduction

Hypertension is the strongest and most well established risk factor for stroke (1) and cardiovascular disease (2, 3) and is the leading cause of death worldwide (4). Approximately one-half (51.8%) of all Japanese elderly people have hypertension (5), and 25.8% of individuals with hypertension are overweight/obese, defined as a body mass index (BMI) of ≥25.0 kg/m^2 (5); this proportion continues to increase. Previous studies have indicated that being overweight/obese (6-19) increases the risk of hypertension in general.

Most Japanese employees retire from their jobs between 60 and 65 years of age; this leads to a big change in their lifestyles. In addition, the death rate accelerates after 65 years of age (20), even in Japan, a country with the highest rate of longevity (21). However, few epidemiological studies have focused on younger elderly people.

This study aimed to investigate the association between BMI at 65 years of age and the development of hypertension during the subsequent five years in an age-specified cohort study, the New Integrated Suburban Seniority Investigation (NISSIN).

Materials and Methods

Study population

The protocol for the NISSIN study has been described in detail previously (22). In brief, the participants included 3,073 residents (1,548 men and 1,525 women) from Nisshin city, Japan who were approaching 65 years of age at baseline and attended a health check-up in June during the pe-

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Table 1. Characteristics of the Study Participants at Baseline According to Body Mass Index.

	Body mass index									
	Male					Female				
	<18.5	18.5–22.9	23.0–24.9	≥25.0	p value	<18.5	18.5–22.9	23.0–24.9	≥25.0	p value
Participants who took secondary health check-up	n=18	n=220	n=134	n=88		n=39	n=321	n=110	n=73	
Systolic blood pressure (mmHg)	119.9 ± 11.1	122.6 ± 11.1	124.8 ± 10.3	126.5 ± 9.9	0.008	120.4 ± 11.8	120.7 ± 11.1	125.3 ± 9.3	125.0 ± 10.3	<0.001
Diastolic blood pressure (mmHg)	73.1 ± 9.0	75.2 ± 6.8	76.2 ± 7.4	78.0 ± 6.6	0.003	70.7 ± 8.6	72.0 ± 7.2	74.1 ± 6.9	74.5 ± 6.2	0.001
Current smoker (%)	12 (66.7)	76 (34.6)	35 (26.1)	21 (23.6)	0.001	2 (5.1)	8 (2.5)	3 (2.7)	3 (4.1)	0.74
Current alcohol drinker (%)	13 (72.2)	154 (70.0)	93 (69.4)	59 (66.3)	0.91	6 (15.4)	76 (33.0)	24 (21.8)	11 (15.1)	0.32
Regular exerciser (%)	10 (55.6)	81 (36.8)	35 (26.1)	36 (40.5)	0.02	16 (41.0)	119 (37.0)	48 (43.6)	30 (41.1)	0.63
Lipids (mean ± s.d, mg/dL)										
Total cholesterol	188.1 ± 34.8	202.9 ± 29.9	207.1 ± 28.8	209.8 ± 32.3	0.008	223.6 ± 25.9	226.7 ± 32.2	228.7 ± 33.0	226.2 ± 30.2	0.49
HDL-C	62.8 ± 17.8	53.9 ± 1,305	49.6 ± 11.4	48.7 ± 11.7	<0.001	70.0 ± 17.1	62.7 ± 14.4	57.6 ± 11.0	55.9 ± 12.9	<0.001
Triglycerides	82.9 ± 36.1	110.3 ± 65.6	128.4 ± 65.4	140.4 ± 84.7	<0.001	82.8 ± 28.1	101.4 ± 70.1	118.6 ± 59.2	123.0 ± 56.2	0.001
Fasting blood glucose (mean ± s.d, mg/dL)	103.5 ± 32.5	98.0 ± 18.7	102.3 ± 25.4	105.5 ± 25.9	0.01	92.2 ± 8.4	94.3 ± 14.2	98.9 ± 16.8	101.5 ± 27.8	<0.001
Hemoglobin A1c (mean ± s.d, %)	5.8 ± 1.2	5.4 ± 0.8	5.6 ± 0.9	5.5 ± 0.8	0.18	5.1 ± 0.4	5.3 ± 0.5	5.6 ± 0.8	5.6 ± 0.9	<0.001
Undergoing treatment for hyperlipidemia (%)	1 (5.6)	8 (3.6)	6 (4.5)	6 (6.7)	0.54	1 (2.6)	17 (5.3)	18 (16.4)	4 (5.5)	0.002
Undergoing treatment for hyperglycemia (%)	4 (22.2)	9 (4.1)	8 (6.0)	6 (6.7)	0.04	0 (0)	4 (1.2)	5 (4.6)	2 (2.7)	0.14
Family history of hypertension (%)	2 (11.1)	13 (6.0)	4 (3.0)	5 (5.6)	0.41	3 (7.7)	25 (7.8)	5 (4.6)	7 (9.6)	0.59

p values were calculated by the analysis of variance, χ^2 test, or Fisher's exact test.
Values are expressed as mean ± standard deviation or numbers (percentage).

riod of 1996 through 2005 (response rate, 43.9%). Patients with myocardial infarction and/or hypertension at baseline were excluded.

Data collection

The health check-up included measurements of height and weight, systolic blood pressure (SBP) and diastolic blood pressure (DBP) and laboratory blood testing, such as assessments of serum lipids and glucose. All clinical tests were performed at a single laboratory. Blood pressure was measured using a standard mercury sphygmomanometer on the right arm in the sitting position. BMI was calculated as weight (kg) divided by height (m) squared. Four categories of BMI (<18.5, 18.5-22.9, 23.0-24.9 and ≥25.0) were created (23). Hyperlipidemia was defined as a total cholesterol level of ≥240 mg/dL or the self-reported use of medications for hyperlipidemia, and hyperglycemia was defined as a fasting blood glucose level of ≥126 mg/dL, hemoglobin A1c (HbA1c) level of ≥6.5% or the self-reported use of medications for hyperglycemia. The HbA1c levels were converted from the format of the Japan Diabetes Society (JDS) to the National Glycohemoglobin Standardization Program [NGSP: NGSP (%) =1.02× JDS (%) + 0.25 (%)]. Demographic and lifestyle characteristics, such as smoking, alcohol consumption, medication use and family history of hypertension, were also collected using a baseline self-administered questionnaire.

All participants provided their informed consent to participate in the current study at the site of the health check-up. Oral consent for the questionnaire survey and use of test results from the health check-up was obtained using an opt-out approach until 2001, and written consent was obtained via an opt-in approach thereafter (24). The study protocol was approved by the Ethics Committee of Nagoya University Graduate School of Medicine, National Center for Geriatrics and Gerontology of Japan, Aichi Medical University School of Medicine and Hokkaido University Graduate School of Medicine.

Follow-up

The prevalence of hypertension was ascertained at the secondary health check-up at the same site of the June check-up when the participants reached 70 years of age. Hypertension was defined as SBP ≥140 mmHg and/or DBP ≥90 mmHg and/or self-reported medication treatment for hypertension.

Statistical analysis

Of the 3,073 original cohort members, 1,406 participants with a history of myocardial infarction and/or hypertension at baseline and 116 and 75 participants who died or moved from the study area, respectively, were excluded. Another 473 participants who did not undergo the secondary health check-up were also excluded. Finally, data for 1,003 participants (460 men and 543 women) were analyzed in the present study (Table 1). An analysis of variance or the χ^2 test was used to analyze the associations of BMI with the participant characteristics. Multivariate odds ratios (ORs) and 95% confidence intervals (95% CIs) of the BMI at baseline for the development of hypertension at 70 years of age were calculated using logistic regression models and adjusted for potential confounders, such as the survey year, baseline SBP (continuous), current smoking (yes, no/unknown), current alcohol drinking (yes, no/unknown), regular exercise (yes, no/unknown), hyperlipidemia (yes, no/unknown), hyperglycemia (yes, no/unknown) and family history of hypertension (yes, no/unknown). In the additional analyses, participants who developed isolated systolic hypertension (ISH: SBP ≥140 mmHg, DBP <90 mmHg and no use of antihypertensive medications) (25) were compared with the normotensive (SBP <140 mmHg, DBP <90 mmHg and no antihypertensive medications) participants. An alpha level of 0.05 was considered to be statistically significant. All statistical analyses were performed using the SAS version 9.4 software pro-

Table 2. Odds Ratios for Newly Hypertension at Age of 70 Years According to Baseline Body Mass Index.

	Body mass index(kg/m^2)			
	<18.5	18.5–23.0	23.0–24.9	≥25.0
Male				
No. of participants	18	220	134	88
No. of cases (No. of medication for hypertension)	8(3)	49(16)	45(22)	33(17)
Model 1 OR (95%CI)	3.48 (1.23–9.84)*	ref	1.96 (1.19–3.23)*	2.11 (1.20–3.68)*
Model 2 OR (95%CI)	4.08 (1.32–12.4)*	ref	2.00 (1.18–3.40)*	1.98 (1.10–3.56)*
Female				
No. of participants	39	321	110	73
No. of cases (No. of medication for hypertension)	8(1)	78(35)	36(14)	26(12)
Model 1 OR (95%CI)	0.73 (0.32–1.71)	ref	1.46 (0.90–2.36)	1.74 (0.99–3.05)
Model 2 OR (95%CI)	0.75 (0.31–1.83)	ref	0.93 (0.55–1.59)	1.39 (0.76–2.54)
Isolated systolic hypertension				
Male				
No. of participants	13	182	108	66
No. of cases	5	38	26	23
Model 1 OR (95%CI)	2.47 (0.78–7.81)	ref	1.27 (0.72–2.23)	1.77 (0.96–3.27)
Model 2 OR (95%CI)	2.98 (0.87–10.2)	ref	1.27 (0.70–2.32)	1.73 (0.90–3.31)
Female				
No. of participants	32	271	83	55
No. of cases	7	51	27	18
Model 1 OR (95%CI)	1.02 (0.40–2.55)	ref	1.73 (0.99–3.01)	1.78 (0.94–3.40)
Model 2 OR (95%CI)	1.05 (0.41–2.74)	ref	1.22 (0.67–2.23)	1.49 (0.76–2.94)

OR: odds ratio, CI: confidence interval. $p < 0.05$.
[a]ORs for developing isolated systolic hypertension (systolic blood pressure ≥140 mmHg, diastolic blood pressure <90, and no antihypertensive medication) compared with normal blood pressure (systolic blood pressure <140 mmHg, diastolic blood pressure <90 mmHg, and no antihypertensive medication).
Model 1: adjusted for survey year.
Model 2: adjusted for survey year, systolic blood pressure (as continuous), current smoking (yes/no), current alcohol drinking (yes, no/unknown), regular exercising (yes, no/unknown), hyperlipidemia (yes, no/unknown), hyperglycemia(yes, no/unknown), and family history of hypertension (yes, no/unknown).
Hyperlipidemia was defined as total cholesterol ≥240 mg/dL or self-reported medication for hyperlipidemia, and hyperglycemia was defined as fasting blood glucose ≥126 mg/dL or hemoglobin A1c ≥6.5% or self-reported medication for hyperglycemia.

gram (SAS Institute, Cary, USA).

Results

At 70 years of age, 283 participants (135 men and 148 women) had developed hypertension. Of these subjects, 195 (92 men and 103 women) had isolated systolic hypertension.

Table 1 shows the characteristics of the study participants at baseline according to BMI. Among the male participants, the group with a higher BMI demonstrated higher SBP, DBP, total cholesterol, triglyceride and fasting blood glucose levels and lower HDL-C levels and included fewer current smokers and regular exercisers than did the group with a lower BMI. Among the female participants, those with a higher BMI showed higher triglyceride, fasting blood glucose and HbA1c levels and lower HDL-C levels than did the group with lower BMIs.

Table 2 shows the ORs for new hypertension at 70 years of age according to the baseline BMI. After adjusting for possible confounding factors, the ORs for the male participants with a BMI of <18.5, 23.0-24.9 and ≥25.0 were 4.08 (95% CI, 1.32-12.4), 2.00 (95% CI, 1.18-3.40) and 1.98 (95% CI, 1.10-3.56), respectively, while those for women with a BMI of 23.0-24.9 and ≥25.0 were 0.93 (95% CI, 0.55-1.59) and 1.39 (95% CI, 0.76-2.54), respectively, when compared to the participants with a BMI of 18.5-22.9. Similar associations were found for newly-developed isolated systolic hypertension, although they did not reach statistical significance.

Because the ratio of current smokers among lean men was high (66.7%), these subjects might have given up smoking, and the subsequent body weight gain might have led to an elevated blood pressure. Therefore we conducted an additional analysis using the change in weight during the five-year study period. The following categories for weight changes were evaluated (≤-1 kg/m^2, >-1 to ≤1 kg/m^2, >1 to ≤2.9 kg/m^2, ≥2.9 kg/m^2) (26); however, there were no significant associations between the change in weight and the new onset of hypertension. In addition, there were no significant associations between the categories of BMI at baseline and the change in weight (data not shown).

Discussion

The current findings showed that both being underweight and overweight/obese increased the risk of developing hypertension among younger elderly men.

Several interventional studies have reported that treating patients with hypertension using antihypertensive drugs reduces the risk of developing stroke, coronary heart disease and heart failure (27-29). However, the use of these antihypertensive treatments has a great burden on the Japanese health insurance system, as the annual medical cost of treating hypertension in Japan is ¥1,830 billion (30) and contin-

ues to increase. Because 51.8% of Japanese elderly people are treated for hypertension (5), preventing hypertension is therefore a matter of social importance.

Our findings are compatible with those of many previous studies across various cohorts reporting that being overweight/obese increases the risk of developing hypertension (6-19). The biological mechanisms involved in the development of hypertension associated with hyperadiposity have not been fully elucidated. However, previous studies have found associations of obesity with insulin resistance (31), hyperinsulinemia (32), enhanced sympathetic nervous system activity (33) and activation of the renin-angiotensin-aldosterone system (34), all of which are involved in the development of hypertension. In addition, enhanced salt sensitivity, which increases the blood volume, has been found among obese subjects (35).

ISH is characterized by increased SBP without an increase in DBP (36). The prevalence of ISH rises rapidly after 60 years of age in the Japanese population (37), and ISH reportedly increases the risk of stroke (38) and cardiovascular disease (39, 40) in elderly people, even in older elderly patients, among whom the mean age of ISH onset is around 70 years (37). The results of the present study showed that a BMI of >25 nonsignificantly increases the likelihood of developing ISH. Therefore, maintaining a normal BMI may be one of the most important issues for preventing hypertension and subsequent stroke and cardiovascular disease.

The present study also demonstrated that a low body weight (i.e., BMI <18) markedly increases the risk of developing hypertension among men. The mechanisms of this association are unclear. However, previous studies have reported that an increased BMI and latent adiposity, such as that associated with a relatively increased fat mass and decreased fat-free mass, are associated with mortality (41). Additionally, persons with a low BMI and elevated waist circumference have an increased risk of mortality (42). For these reasons, the presence of abdominal adiposity, which was not measured in the current study, may have influenced our results. Overt or latent hyperthyroidism associated with a low body weight might also increase blood pressure. Further epidemiological investigations are thus needed.

The strengths of this study include its prospective cohort design and the collection of information on potential confounders for hypertension at baseline and adjusted for in the analysis to the extent possible. In addition, previous studies have suggested that BP, especially SBP, increases with increasing age (43). However, we completely eliminated this age-derived bias because of the nature of the age-specific cohort.

This study is associated with several limitations. First, we did not evaluate information regarding the amount of daily sodium intake associated with hypertension (44, 45), which might have caused residual confounding. Although we controlled for major lifestyle issues, family history of hypertension and clinical risk factors for hypertension, our inferences may include overestimation of physique-blood pressure associations. Second, of the 1,667 eligible participants, 664 (39.8%) were lost to follow-up due to death, relocation or missing the secondary health check-up. This could result in some selection bias. However, the BMI, SBP and DBP values at baseline did not differ between the repeat visitors and non-repeat visitors. Therefore, such bias is expected to be minimal in this study.

Conclusion

This age-specific cohort study demonstrated that leanness or being overweight/obese at age 65 increases the risk of subsequent hypertension.

The authors state that they have no Conflict of Interest (COI).

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References

1. Shekelle RB, Ostfeld AM, Klawans HL Jr. Hypertension and risk of stroke in an elderly population. Stroke **5**: 71-75, 1974.
2. Siegel D, Kuller L, Lazarus NB, et al. Predictors of cardiovascular events and mortality in the Systolic Hypertension in the Elderly Program pilot project. Am J Epidemiol **126**: 385-399, 1987.
3. Psaty BM, Furberg CD, Kuller LH, et al. Isolated systolic hypertension and subclinical cardiovascular disease in the elderly. Initial findings from the Cardiovascular Health Study. JAMA **268**: 1287-1291, 1992.
4. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. Lancet **365**: 217-223, 2005.
5. Ministry of Health, Labour and Welfare. National Health and Nutrition Examination Survey, 2011 [Internet]. [cited 2014 Apr 5]. Available from: http://www.mhlw.go.jp/bunya/kenkou/eiyou/h23-houkoku.html (in Japanese).
6. Huang Z, Willett WC, Manson JE, et al. Body weight, weight change, and risk for hypertension in women. Ann Intern Med **128**: 81-88, 1998.
7. Wilsgaard T, Schirmer H, Arnesen E. Impact of body weight on blood pressure with a focus on sex differences: the Tromso Study, 1986-1995. Arch Intern Med **160**: 2847-2853, 2000.
8. Hu FB, Wang B, Chen C, et al. Body mass index and cardiovascular risk factors in a rural Chinese population. Am J Epidemiol **151**: 88-97, 2000.
9. Zhu S, Wang Z, Heshka S, Heo M, Faith MS, Heymsfield SB. Waist circumference and obesity-associated risk factors among whites in the third National Health and Nutrition Examination Survey: clinical action thresholds. Am J Clin Nutr **76**: 743-749, 2002.

10. Foucan L, Hanley J, Deloumeaux J, Suissa S. Body mass index (BMI) and waist circumference (WC) as screening tools for cardiovascular risk factors in Guadeloupean women. J Clin Epidemiol **55**: 990-996, 2002.

11. Kawada T. Body mass index is a good predictor of hypertension and hyperlipidemia in a rural Japanese population. Int J Obes Relat Metab Disord **26**: 725-729, 2002.

12. Hu G, Barengo NC, Tuomilehto J, Lakka TA, Nissinen A, Jousilahti P. Relationship of physical activity and body mass index to the risk of hypertension: a prospective study in Finland. Hypertension **43**: 25-30, 2004.

13. Sharabi Y, Grotto I, Huerta M, Grossman E. Susceptibility of the influence of weight on blood pressure in men versus women: lessons from a large-scale study of young adults. Am J Hypertens **17**: 404-408, 2004.

14. Chen PC, Sung FC, Su TC, Chien KL, Hsu HC, Lee YT. Two-year change in body mass index and subsequent risk of hypertension among men and women in a Taiwan community. J Hypertens **27**: 1370-1376, 2009.

15. Gelber RP, Gaziano JM, Manson JE, Buring JE, Sesso HD. A prospective study of body mass index and the risk of developing hypertension in men. Am J Hypertens **20**: 370-377, 2007.

16. Stevens J, Truesdale KP, Katz EG, Cai J. Impact of body mass index on incident hypertension and diabetes in Chinese Asians, American Whites, and American Blacks: the People's Republic of China Study and the Atherosclerosis Risk in Communities Study. Am J Epidemiol **167**: 1365-1374, 2008.

17. Shuger SL, Sui X, Church TS, Meriwether RA, Blair SN. Body mass index as a predictor of hypertension incidence among initially healthy normotensive women. Am J Hypertens **21**: 613-619, 2008.

18. Oda E, Kawai R. Body mass index is more strongly associated with hypertension than waist circumference in apparently healthy Japanese men and women. Acta Diabetol **47**: 309-313, 2010.

19. Shihab HM, Meoni LA, Chu AY, et al. Body mass index and risk of incident hypertension over the life course: the Johns Hopkins Precursors Study. Circulation **126**: 2983-2989, 2012.

20. Ministry of Health, Labour and Welfare. Abridged Life Tables, 2012 [Internet]. [cited 2014 Feb 5]. Available from: http://www.mhlw.go.jp/toukei/saikin/hw/life/21th/ (in Japanese).

21. Organisation for Economic Co-operation and Development. Society at a Glance 2014 [Internet]. [cited 2014 Feb 5]. Available from: http://www.oecd-ilibrary.org/social-issues-migration-health/society-at-a-glance-2014_soc_glance-2014-en

22. Kitamura T, Kawamura T, Tamakoshi A, Wakai K, Ando M, Ohno Y. Rationale, design, and profiles of the New Integrated Suburban Seniority Investigation (NISSIN) Project: a study of an age-specific, community-based cohort of Japanese elderly. J Epidemiol **19**: 237-243, 2009.

23. Consultation WE. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet **363**: 157-163, 2004.

24. Tamakoshi A, Kawamura T, Wakai K, Ando M. Written informed consent for participation in a study and reduction in consent rate. J Epidemiol **18**: 291-294, 2008.

25. Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA **289**: 2560-2572, 2003.

26. Grootveld LR, Van Valkengoed IG, Peters RJ, et al. The role of body weight, fat distribution and weight change in ethnic differences in the 9-year incidence of hypertension. J Hypertens **32**: 990-996; discussion 6-7, 2014.

27. SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). JAMA **265**: 3255-3264, 1991.

28. Staessen JA, Fagard R, Thijs L, et al. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. Lancet **350**: 757-764, 1997.

29. Franse LV, Pahor M, Di Bari M, et al. Serum uric acid, diuretic treatment and risk of cardiovascular events in the Systolic Hypertension in the Elderly Program (SHEP). J Hypertens **18**: 1149-1154, 2000.

30. Ministry of Health, Labour and Welfare. Estimates of National Medical Care Expenditure, 2011 [Internet]. [cited 2014 Apr 5]. Available from: http://www.mhlw.go.jp/toukei/saikin/hw/k-iryohi/11/index.html (in Japanese).

31. Ikeda T, Gomi T, Hirawa N, Sakurai J, Yoshikawa N. Improvement of insulin sensitivity contributes to blood pressure reduction after weight loss in hypertensive subjects with obesity. Hypertension **27**: 1180-1186, 1996.

32. Kaplan NM. The deadly quartet. Upper-body obesity, glucose intolerance, hypertriglyceridemia, and hypertension. Arch Intern Med **149**: 1514-1520, 1989.

33. Raison J, Achimastos A, Asmar R, Simon A, Safar M. Extracellular and interstitial fluid volume in obesity with and without associated systemic hypertension. Am J Cardiol **57**: 223-226, 1986.

34. Tuck ML, Sowers J, Dornfeld L, Kledzik G, Maxwell M. The effect of weight reduction on blood pressure, plasma renin activity, and plasma aldosterone levels in obese patients. N Engl J Med **304**: 930-933, 1981.

35. Reisin E, Cook ME. Obesity, hypertension, and the heart. In: The Heart and Lung in Obesity. Alpert MA, Alexander JK, Eds. NY: Futura Publishing Co., New York, 1998: 95-108.

36. Staessen JA, Gasowski J, Wang JG, et al. Risks of untreated and treated isolated systolic hypertension in the elderly: meta-analysis of outcome trials. Lancet **355**: 865-872, 2000.

37. Seto S, Soda M, Nakashima E, Yano K, Akahoshi M. Longitudinal analysis of blood pressure trends and prognosis in isolated systolic hypertension in elderly individuals. Am J Hypertens **20**: 134-139, 2007.

38. Kannel WB, Gordan T. Evaluation of cardiovascular risk in the elderly: the Framingham study. Bull NY Acad Med **54**: 573-591, 1978.

39. Sutton-Tyrrell K, Wildman R, Newman A, Kuller LH. Extent of cardiovascular risk reduction associated with treatment of isolated systolic hypertension. Arch Intern Med **163**: 2728-2731, 2003.

40. Franklin SS. Systolic blood pressure: it's time to take control. Am J Hypertens **17**: 49s-54s, 2004.

41. Allison DB, Faith MS, Heo M, Kotler DP. Hypothesis concerning the U-shaped relation between body mass index and mortality. Am J Epidemiol **146**: 339-349, 1997.

42. Pischon T, Boeing H, Hoffmann K, et al. General and abdominal adiposity and risk of death in Europe. N Engl J Med **359**: 2105-2120, 2008.

43. Antikainen R, Jousilahti P, Tuomilehto J. Systolic blood pressure, isolated systolic hypertension and risk of coronary heart disease, strokes, cardiovascular disease and all-cause mortality in the middle-aged population. J Hypertens **16**: 577-583, 1998.

44. Staessen J, Fagard R, Lijnen P, Amery A. Body weight, sodium intake and blood pressure. J Hypertens Suppl **7**: S19-S23, 1989.

45. He J, Whelton PK. What is the role of dietary sodium and potassium in hypertension and target organ injury? Am J Med Sci **317**: 152-159, 1999.