

# Prevalence and Association of Hypertension with the Different Components of the Metabolic Syndrome

ANTONIO J. PARAGANO<sup>1</sup>, ROGELIO MACHADO<sup>MTSAC, 2</sup>, ANTONIO ABDALA<sup>3</sup>, DIEGO J. CORDERO<sup>1</sup>, ADRIANA ANGEL<sup>1</sup>, JORGE CUROTTO GRASIOSI<sup>1</sup>, CLEMENTE H. MAGALLANES<sup>1</sup>, RICARDO J. ESPER<sup>2,4</sup>

Received: 01/28/2009

Accepted: 05/05/2009

## Address for reprints:

Dr. Antonio J. Paragano  
Francisco Lagorio 1425  
(1682) Martín Coronado  
Pcia. de Buenos Aires  
e-mail:  
antonioparagano@arnet.com.ar

## SUMMARY

### Background

Hypertension coexists with other cardiovascular risk factors, especially obesity and dyslipemia; this association increases the risk particularly in patients with established heart disease. For this reason, the identification and control of these factors is essential for the global management of hypertensive patients.

### Objectives

To assess the prevalence of hypertension and its association with the different components of the metabolic syndrome.

### Material and Methods

We included 975 subjects (37±9 years, 62% were men) without demonstrable heart disease. Metabolic syndrome variables were those defined by the ATP III-IDF according to gender: waist circumference ≥102/88 cm, LDL-cholesterol level ≤40/50 mg/dl, glucose blood level and triglycerides ≥150 mg/dl. Subjects were grouped by gender and classified as hypertensive (JNC 7), with blood pressure ≥140/90 mm Hg, non hypertensive and controls. The frequency of each variable of the metabolic syndrome was established in hypertensive subjects and the prevalence of hypertension was determined for each variable.

### Results

There were 114 hypertensive men that were compared to 495 controls: age: 42±10 versus 36±9 years, waist circumference ≥102 cm: 31% versus 15%, triglycerides ≥150 mg/dl: 33% versus 20%, glycemia ≥100 mg/dl: 30% versus 4%; p<0.001 for all the variables. We found 35 women with hypertension that were compared to 331 non-hypertensive women: age 43±9 versus 35±8 years, and waist circumference ≥88 cm: 49% versus 15%; both, p<0.001. The prevalence of hypertension among all men was 19%; 32% in those with a waist circumference of ≥102; 28% with triglycerides 150; 63% with glycemia of ≥100; p<0.03 for all versus general. Among all women, the prevalence of hypertension was 11%, 25% in those with a waist circumference of ≥88; p<0.0008.

Multivariate analysis showed that age, glucose blood levels ≥100 mg/dl, triglycerides ≥150 mg/dl and a waist circumference ≥102/88 cm are independent predictors of hypertension.

### Conclusions

The components of the metabolic syndrome are more frequent among subjects with hypertension. In addition, they determine a greater prevalence of hypertension, particularly in men.

REV ARGENT CARDIOL 2009;77:274-279.

**Key words** > Hypertension - Risk Factors - Metabolic Syndrome

## Abbreviations >

GL	Glycemia	WC	Waist circumference
HDLc	High-density lipoprotein cholesterol	MS	Metabolic syndrome
Hp	Hypertensive patients	BP	Blood pressure
HT	Hypertension	TG	Triglycerides

Department of Cardiology, Hospital Militar Central

<sup>MTSAC</sup> Full Member of the Argentine Society of Cardiology

<sup>1</sup> University Cardiologist, UBA

<sup>2</sup> Medical Doctor, PhD, UBA

<sup>3</sup> Graduate Teaching Assistant, Chair of Internal Medicine, UBA

<sup>4</sup> Full Professor, Chair of Internal Medicine, UBA

## BACKGROUND

Since the Framingham Heart Study began, continuing research has taught us much about the causes of atherosclerotic cardiovascular disease. At the same time, our knowledge acquisition led us to intervene on these causes, called risk factors, with the intention to reduce the incidence of this disease. (1)

The prevalence of hypertension (HT) is high, and 26% of the adult population in 2000 had hypertension. Blood pressure tends to increase with age; thus, a greater prevalence of hypertension would be expected as a consequence of the growth of the elderly population. (1, 2) Hypertension is one of the risk factors undoubtedly linked to the development of cardiovascular disease and stroke. In consequence, blood pressure control is essential, given the great morbidity and mortality associated with HT. (3, 4) Although there are several effective treatments, blood pressure control is low (5-8); for this reason it is extremely important to analyze the potential factors related to poor blood pressure control. The metabolic syndrome (MS) has emerged as a novel marker of risk of type 2 diabetes and cardiovascular disease. (9) Approximately 38% to 62% of hypertensive patients have MS, characterized by the association of at least two additional cardiometabolic risk factors. (10-13) These factors include central obesity, elevated fasting glucose (GL), elevated triglycerides (TG) and reduced high-density lipoprotein cholesterol (HDLc), (11-13); all these components are probably correlated with insulin resistance. The identification of MS determined the development of guidelines promoting lifestyle modifications in all hypertensive patients and appropriate drug therapy in the presence of other cardiovascular risk factors. (5, 14, 15) For most persons with hypertension the blood pressure goal is to achieve a systolic and/or diastolic blood pressure < 140/90 mmHg. Yet, in patients with diabetes or multiple risk factors, the BP goal should be < 130/80 mmHg. The intervention should start before significant damage develops; nevertheless, blood pressure goals are difficult to achieve in the elder and in diabetics.

The association between HT and metabolic abnormalities increases cardiovascular risk, especially in patients with established cardiovascular disease. For this reason, identification and control of these abnormalities are key elements for the global management of hypertensive patients. Considering that HT usually coexists with other metabolic risk factors, (5, 16) the goal of our study was to investigate the prevalence and association of hypertension with the different components of the metabolic syndrome.

## MATERIAL AND METHODS

We conducted a descriptive, cross-sectional study from data collected in three centers from January 2006 to December 2007. The researchers were randomly selected among gen-

eral practitioners and cardiologists, and they all received instructions regarding how to collect and enter patients' information into the medical record. All patients who sought medical care for a routine examination and accepted to participate in the study were consecutively included.

*Inclusion criteria:* outpatients of both genders > 18 years old who were apparently healthy and actively working.

*Exclusion criteria:* patients under treatment or with medical conditions that might affect the patient registry data were excluded from the study.

*Blood pressure measurement:* blood pressure was measured with the patient in the sitting position, using a recently calibrated aneroid sphygmomanometer with a cuff with an appropriate bladder size matched to the size of the arm. If the blood pressure was elevated above 140/90 mm Hg, a second reading was taken after an interval of 5 minutes; the average value was recorded.

*Anthropometric measurements:* weight and height were estimated with a mechanical scale. Waist circumference (WC) was measured with a non-stretchable measuring tape, with the patient in the standing position at the end of expiration. The waist circumference was determined twice at the midpoint between the lower rib margin and the iliac crest, and the average of both observations was recorded.

Blood samples for measurement of HDLc, TG and GL were obtained after a 12-hour fast and were analyzed in the same day with an autoanalyzer using the corresponding reagents.

Metabolic syndrome was defined according to the ATP III (Adult Treatment Panel III) criteria (men/women): WC (cm)  $\geq$  102/88, HDLc (mg/dl)  $\leq$  40/50 and TG (mg/dl)  $\geq$  150. We considered the value of GL  $\geq$  100 proposed by the IDF (International Diabetes Federation). (17, 18)

A total of 975 subjects were eligible for inclusion, and were considered hypertensive patients (Hp) when blood pressure was 140/90 mm Hg or greater, or non-hypertensive controls if BP was < 140/90, as recommended by the JNC 7 (Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure). (14)

## Statistical Analysis

Data were recorded in a Microsoft Excel spreadsheet and were analyzed using Minitab 15 statistical software. Univariate analysis was performed using Student's *t* test, chi square test of Fisher's exact test according to the variable analyzed. We used binomial logistic regression for multivariate analysis.

## RESULTS

The general characteristics of the population were as follows: men, 609; age  $37 \pm 9$  years; WC  $89 \pm 13$  cm; TG  $107 \pm 76$  mg/dl; GL  $82 \pm 16$  mg/dl; HDLc  $49 \pm 13$  mg/dl; systolic blood pressure  $125 \pm 14$  mm Hg; diastolic blood pressure  $78 \pm 9$  mm Hg. The prevalence of HT was 149/975 (15%).

Statistical analysis was performed by grouping the participants according to gender in order to avoid sex-specific differences. The frequency of the different components of the MS among hypertensive men and women was then established. Patients with HT were compared to non-hypertensive controls to evaluate the presence of a significant association between each component of the MS and HT (Tables 1 and 2).

The prevalence of HT in men was 19% (114 patients). Hypertensive men were older and the frequency of the different components of the MS was greater than in controls, except for HDLc ≤ 40 (see Table 1). In women, the prevalence of HT was 10%; women with HT were older had a WC ≥ 88 cm compared to controls (see Table 2).

The prevalence of HT and its association with the different components of the MS by gender was compared with the results for the general population. The prevalence of HT in men with GL ≥ 100 mg/dl was three times greater than that of the general population (63% versus 19%). A similar pattern was observed for the other components of the MS, except for HDLc ≤ 40 (Table 3).

Among women, the prevalence of HT was higher when the WC was above 88 cm (25% versus 10%). Yet, the other components of the MS do not seem to have any influence on BP (Table 4).

The study concluded with multivariate analysis. Each component of the MS was considered a predictor and a dichotomic variable; HT was the dependent factor. Multivariate analysis revealed that age, GL ≥ 100, TG ≥ 150 and WC ≥ 102/88 were independent predictors with statistical significance. Conversely, the odds ratio for gender and HDLc ≤ 40/50 was not statistically significant (Table 5).

DISCUSSION

The metabolic syndrome is a cluster of risk factors for cardiovascular disease. (9, 10) In general, the components of the MS are synergistic in their effect and interact in a way that worsens the prognosis. Obesity and insulin resistance contribute to increase blood pressure levels and are associated with the development of HT. (11) Hypertension also coexists with other risk factors; hypertensive patients with no evidence of cardiovascular disease frequently present obesity, diabetes or dyslipemia. (19) In these patients, risk ratio is four times greater than expected, suggesting that HT may depend on these factors which are the key components of the MS.

Different clinical trials have established that metabolic syndrome exaggerates the risk for coronary artery disease (17, 20) and have demonstrated its value to predict global mortality, cardiovascular disease and cardiovascular mortality among all age groups. (20-25)

Obesity is a particularly important component of the MS due to its high prevalence. According to the NHANES report, 30% of the adult population in the USA is obese. (26) Obesity is a risk factor for HT, cardiovascular disease and chronic kidney disease. (11, 20-25) Obesity also correlates with 24-hour ambulatory blood pressure. (27) The activity of the renin-

	Number (%)	Age	WC ≥ 102	TG ≥ 150	GL ≥ 100	HDLc ≤ 40
Hp	114 (19%)	42 ± 10	35 (31%)	38 (33%)	34 (30%)	44 (39%)
Non-Hp	495 (81%)	36 ± 9	74 (15%)	100 (20%)	20 (4%)	198 (40%)
p <		0.001	0.005	0.0004	0.0001	ns

Table 1. Frequency of the different components of the metabolic syndrome in men

	Number (%)	Age	WC ≥ 88	TG ≥ 150	GL ≥ 100	HDLc ≤ 50
Hp	35 (10%)	43 ± 9	17 (49%)	3 (9%)	2 (6%)	21 (60%)
Non-Hp	331 (90%)	35 ± 8	51 (15%)	21 (6%)	6 (2%)	153 (46%)
p <		0.001	0.0001	ns	ns	ns

Table 2. Frequency of the different components of the metabolic syndrome in women

	Number (%)	WC ≥ 102 (109)	TG ≥ 150 (138)	GL ≥ 100 (54)	HDLc ≤ 40 (242)
Hp	114/609 (19%)	35 (32%)	38 (28%)	34 (63%)	44 (18%)
p <		0.003	0.03	0.0001	ns

Table 3. Prevalence of HT according to the different components of the metabolic syndrome in men

	Number (%)	WC ≥ 88 (68)	TG ≥ 150 (24)	GL ≥ 100 (8)	HDLc ≤ 50 (174)
Hp	35/366 (10%)	17 (25%)	3 (13%)	2 (25%)	21 (12%)
p <		0.0008	ns	ns	ns

Table 4. Prevalence of HT according to the different components of the metabolic syndrome in women

ns: non significant. WC: Waist circumference. TG: Triglycerides. GL: Glycemia. HDLc: High-density lipoprotein cholesterol. Hp: Hypertensive patients.

**Table 5.** Binary logistic regression

Variable	Code	Total
HT	1	149
no HT	0	826
Total		975

  

Predictor	p	Odds ratio	95% CI	
			Lower limit	Upper limit
Gender	0.060	1.53	0.98	2.40
Age (per)	0.000	1.06	1.03	1.08
GL $\geq$ 100	0.000	6.43	3.56	11.64
TG $\geq$ 150	0.018	1.76	1.10	2.81
HDLc $\leq$ 40/500.314	0.81	0.55	1.21	
WC $\geq$ 102/880.000	2.20	1.43	3.39	

HT: Hypertension GL: Glycemia TG: Triglycerides. HDLc: High-density lipoprotein cholesterol. WC: Waist circumference

angiotensin-aldosterone system and autonomous nervous system is increased in obese subjects. (17, 28-30) In addition, the presence of metabolic abnormalities, as diabetes and dyslipemia, may explain the effect of obesity on cardiovascular risk.

Between 24% and 35% of the adult hypertensive population also have dyslipemia (19, 31); however, this prevalence varies among the different studies according to the definition of dyslipemia used. The combination of HT and dyslipemia increases cardiovascular disease risk. (32) A 10% reduction in blood cholesterol and blood pressure could reduce major cardiovascular events by 45%. (33)

The association between abnormal glucose metabolism and HT is frequent and about 15% of hypertensive patients are diabetics. (19) Conversely, HT has a frequency twice as high among diabetics. (5, 34) This strong association determines a greater risk of renal damage and cardiovascular disease; for this reason, strict blood pressure control is necessary in diabetic patients. (5, 17)

We have demonstrated the contrasts in the metabolic profile of Hp compared to controls. The presence of any of the components of the MS is lower among normotensive patients. On the contrary, overweight and obesity, accompanied by increased WC, abnormal GL metabolism and dyslipemia are more frequent in Hp. The prevalence of HT among men was higher when fasting glycemia was greater than 100 mg/dl, and when WC and TG were above the normal limits.

Which are the difference between normotensive patients with MS and Hp with MS?

In normotensive patients, environmental and dietary factors might modify the sympathetic tone, the

renin-angiotensin-aldosterone system activity, or induce insulin resistance. In this way, the development of hypertension might reveal the existence of a complex cluster of previous metabolic changes.

Briefly, we find that the components of the MS increase the prevalence of hypertension. In addition, each of these components is more frequent in Hp. These observations might partially explain the high prevalence of cardiovascular disease and the poor response to treatment in subjects with hypertension. Once we had identified concomitant risk factors, we might perform appropriate interventions to reduce the incidence of cardiovascular events.

### Study limitations

Initially, our conclusions were based on data obtained from patients who sought medical care for a routine examination. The characteristics of the study population indicate that these results may not be extrapolated to patients under antihypertensive treatment or to the general population. The lack of follow-up is another study limitation; thus, we do not know the rate of events in this group of subjects.

### CONCLUSIONS

The components defining MS increase the prevalence of hypertension, especially in men. At the same time, each of these components is more frequent among hypertensive subjects. The correlation between metabolic syndrome components and hypertension indicate the necessity to evaluate the metabolic profile of all hypertensive patients. In addition, we should have an active intervention to prevent the direct impact on the incidence of cardiovascular disease.

### RESUMEN

#### Prevalence and Association of Hypertension with the Different Components of the Metabolic Syndrome

#### Introducción

La hipertensión arterial con frecuencia coexiste con otros factores de riesgo cardiovascular, principalmente obesidad y dislipidemia; ésta es una conexión que eleva el riesgo, especialmente en los pacientes que ya tienen enfermedad cardiovascular, y por ello su identificación y control son esenciales para el manejo global de los pacientes hipertensos.

#### Objetivos

Evaluar la prevalencia de hipertensión arterial según los distintos componentes del síndrome metabólico y establecer su vínculo con ellos.

#### Material y métodos

Se incluyeron 975 individuos ( $37 \pm 9$  años, 62% hombres) sin enfermedad demostrable. Se registraron las variables que conforme al sexo definen el síndrome metabólico (ATPIII-IDF): perímetro de cintura  $\geq$  102/88 cm, lipoproteínas de alta densidad  $\leq$  40/50 mg/dl, glucemia  $\geq$  100 mg/dl

y triglicéridos  $\geq 150$  mg/dl. Se agruparon a los participantes por sexo y se clasificaron en hipertensos (JNC 7), con tensión arterial  $\geq 140/90$  mm Hg, y en no hipertensos o controles. Se estableció la frecuencia de cada elemento del síndrome metabólico entre hipertensos y se determinó la prevalencia de hipertensión según cada componente.

### Resultados

Entre los hombres de la población en estudio se hallaron 114 hipertensos que se compararon con 495 controles: edad:  $42 \pm 10$  versus  $36 \pm 9$  años, perímetro de cintura  $\geq 102$  cm: 31% versus 15%, triglicéridos  $\geq 150$  mg/dl: 33% versus 20%, glucemia  $\geq 100$  mg/dl: 30% versus 4%; todas  $p < 0,001$ . Entre las mujeres hubo 35 hipertensas que se confrontaron con 331 no hipertensas: edad  $43 \pm 9$  versus  $35 \pm 8$  años y perímetro de cintura  $\geq 88$  cm: 49% versus 15%; ambas,  $p < 0,001$ . La prevalencia de hipertensión entre hombres fue: del 19% general, del 32% con perímetro de cintura  $\geq 102$ , del 28% con triglicéridos  $\geq 150$ , del 63% con glucemia  $\geq 100$ ; todas  $p < 0,03$  versus general. En las mujeres, la prevalencia de hipertensión fue: del 11% general, del 25% con perímetro de cintura  $\geq 88$ ;  $p < 0,0008$ .

El análisis multivariado demostró que la edad, la glucemia  $\geq 100$  mg/dl, los triglicéridos  $\geq 150$  mg/dl y el perímetro de cintura  $\geq 102/88$  cm son predictores independientes de hipertensión arterial.

### Conclusiones

Los componentes del síndrome metabólico son más frecuentes entre los hipertensos. Además, particularmente en los hombres, determinan una prevalencia mayor de hipertensión arterial.

**Palabras clave >** Hipertensión · Factores de riesgo · Síndrome metabólico

### BIBLIOGRAPHY

- Levenson JW, Skerrett PJ, Gaziano JM. Reducing the global burden of cardiovascular disease: the role of risk factors. *Prev Cardiol* 2002;5:188-99.
- Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet* 2005;365:217-23.
- Lawes CM, Vander Hoorn S, Law MR, Elliott P, MacMahon S, Rodgers A. Blood pressure and the global burden of disease 2000. Part II: estimates of attributable burden. *J Hypertens* 2006;24:423-30.
- Franco OH, Peeters A, Bonneux L, de Laet C. Blood pressure in adulthood and life expectancy with cardiovascular disease in men and women: life course analysis. *Hypertension* 2005;46:280-6.
- Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, et al. 2007 Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 2007;25:1105-87.
- Volpe M, Tocci G, Trimarco B, Rosei EA, Borghi C, Ambrosioni E, et al. Blood pressure control in Italy: results of recent surveys on hypertension. *J Hypertens* 2007;25:1491-8.
- Wang YR, Alexander GC, Stafford RS. Outpatient hypertension treatment, intensification, and control in Western Europe and the United States. *Arch Intern Med* 2007;167:141-7.
- Wolf-Maier K, Cooper RS, Kramer H, Banegas JR, Giampaoli S, Joffres MR, et al. Hypertension treatment and control in five Euro-

pean countries, Canada, and the United States. *Hypertension* 2004;43:10-7.

- Alberti KG, Zimmet P, Shaw J, for the IDF Epidemiology Task Force consensus Group. The metabolic syndrome- a new worldwide definition. *Lancet* 2005;366:1059-62.
- Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation* 2005;112:2735-52.
- Vazquez Vigoa A, Vazquez Cruz A, Calderin RO, Buchaca EF, Cruz Alvarez NM, Jimenez Paneque R, et al. Metabolic syndrome in patients with essential hypertension. *Nefrología* 2003;23:423-31.
- Egan BM, Papademetriou V, Wofford M, Calhoun D, Fernandes J, Riehle JE, et al. Metabolic syndrome and insulin resistance in the TROPHY substudy: contrasting views in patients with high-normal blood pressure. *Am J Hypertens* 2005;18:3-12.
- Schillaci G, Pirro M, Vaudo G, Gemelli F, Marchesi S, Porcellati C, et al. Prognostic value of the metabolic syndrome in essential hypertension. *J Am Coll Cardiol* 2004;43:1817-22.
- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, 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* 2003;289:2560-72.
- European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. *J Hypertens* 2003;21:1011-53.
- Macdonald TM, Morant SV, Mozaffari E. Treatment patterns of hypertension and dyslipidaemia in hypertensive patients at higher and lower risk of cardiovascular disease in primary care in the United Kingdom. *J Hum Hypertens* 2007;21:925-33.
- The Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001;285:2486-97.
- International Diabetes Federation. The IDF consensus worldwide definition of the metabolic syndrome [article online] 2005. [http://www.idf.org/webdata/docs/metac\\_syndrome\\_def.pdf](http://www.idf.org/webdata/docs/metac_syndrome_def.pdf).
- Weycker D, Nichols GA, O'Keefe-Rosetti M, Edelsberg J, Khan ZM, Kaura S, et al. Risk-factor clustering and cardiovascular disease risk in hypertensive patients. *Am J Hypertens* 2007;20:599-607.
- Sattar N, Gaw A, Scherbakova O, Ford I, O'Reilly DS, Haffner SM, et al. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. *Circulation* 2003;108:414-9.
- Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. *N Engl J Med* 1999;341:1097-105.
- Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, et al. In middle-aged men. *JAMA* 2002;288:2709-16.
- Ridker PM, Buring JE, Cook NR, Rifai N. C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: an 8-year follow-up of 14 719 initially healthy American women. *Circulation* 2003;107:391-7.
- Han TS, Williams K, Sattar N, Hunt KJ, Lean ME, Haffner SM. Analysis of obesity and hyperinsulinemia in the development of metabolic syndrome: San Antonio Heart Study. *Obes Res* 2002;10:923-31.
- Isomaa B, Almgren P, Tuomi T, Forsén B, Lahti K, Nissén M, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care* 2001;24:683-9.
- Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999-2004. *JAMA* 2006;295:1549-55.

27. Kotsis V, Stabouli S, Bouldin M, Low A, Toumanidis S, Zakopoulos N. Impact of obesity on 24-hour ambulatory blood pressure and hypertension. *Hypertension* 2005;45:602-7.
28. Hall JE. The kidney, hypertension, and obesity. *Hypertension* 2003;41:625-33.
29. Schmieder RE, Messerli FH. Does obesity influence early target organ damage in hypertensive patients? *Circulation* 1993;87:1482-8.
30. Goodfriend TL, Calhoun DA. Resistant hypertension obesity, sleep apnea and aldosterone: theory and therapy. *Hypertension* 2004;43:518-24.
31. Cowie MR. Simultaneous treatment of hypertension and dyslipidemia may help to reduce overall cardiovascular risk: focus on amlodipine/atorvastatin single-pill therapy. *Int J Clin Pract* 2005;59:839-46.
32. Thomas F, Bean K, Guize L, Quentzel S, Argyriadis P, Benetos A. Combined effects of systolic blood pressure and serum cholesterol on cardiovascular mortality in young (< 55 years) men and women. *Eur Heart J* 2002;23:528-35.
33. Emberson J, Whincup P, Morris R, Walker M, Ebrahim S. Evaluating the impact of population and high-risk strategies for the primary prevention of cardiovascular disease. *Eur Heart J* 2004;25:484-91.
34. Sowers JR, Epstein M, Frohlich ED. Diabetes, hypertension, and cardiovascular disease: an update. *Hypertension* 2001;37:1053-9.