Obesity and hypertension

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ARISTOTLE UNIVERSITY THESSALONIKI

GREECE

Obesity: definition

- Measurement of the body mass index

BMI= (weight in kg) / (height in meters)^2 kg/m^2

Table 1

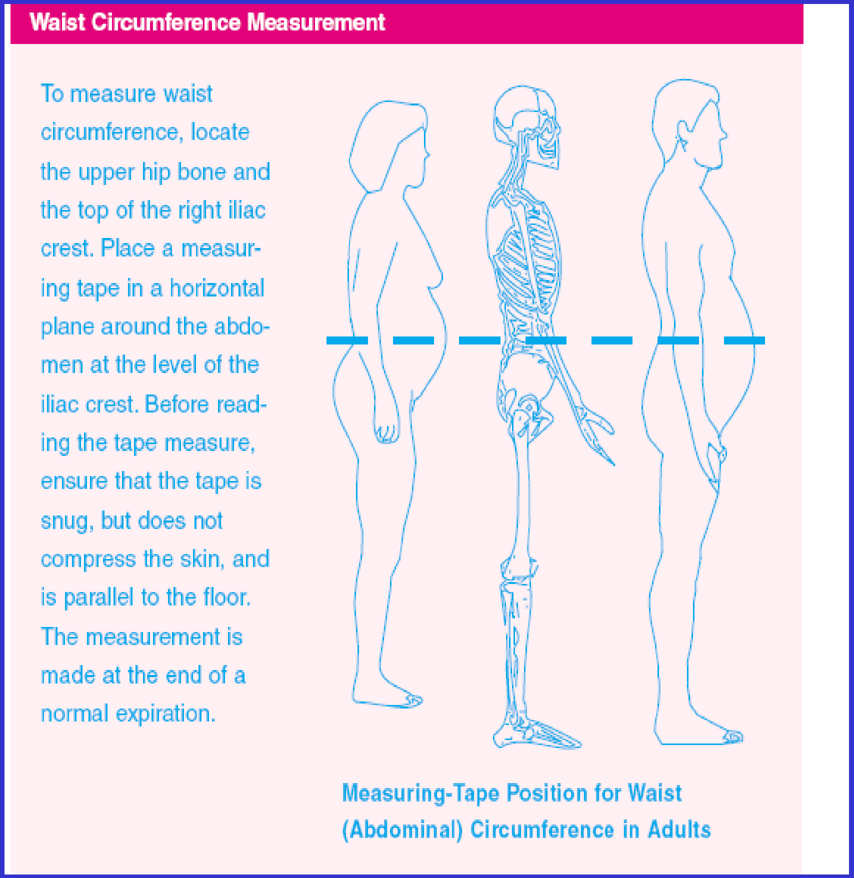
Classifications for BMI	
	BMI
Underweight	<18.5 kg/m^2
Normal weight	18.5–24.9 kg/m^2
Overweight	25–29.9 kg/m^2
Obesity (Class 1)	30–34.9 kg/m^2
Obesity (Class 2)	35–39.9 kg/m^2
Extreme obesity (Class 3)	≥40 kg/m^2

Adapted from the Practical Guide Identification, Evaluation, and Treatment of Overweight and Obesity in Adults , National institute of health, USA

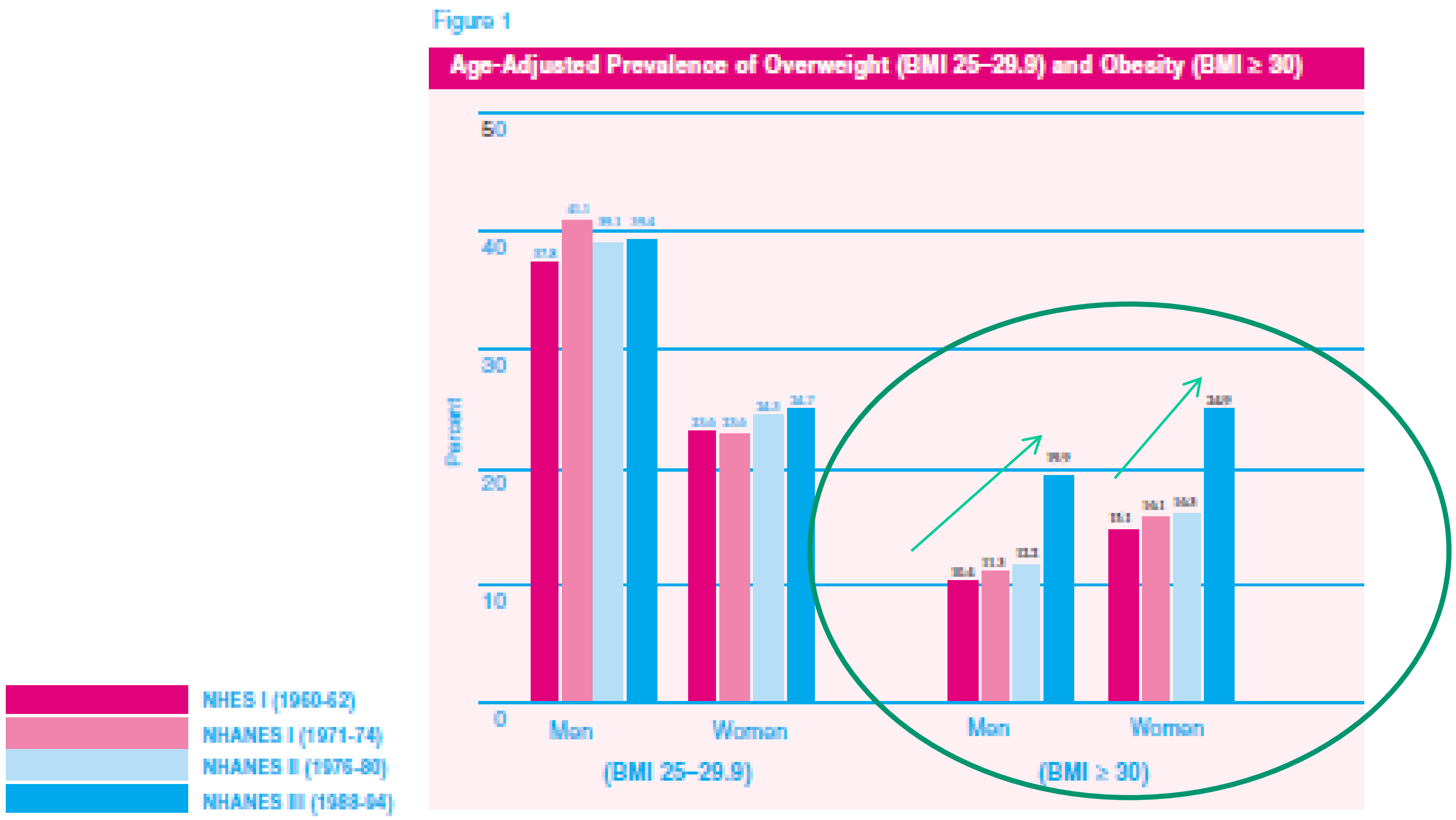
Measurement of waist circumference

- Measurement of waist circumference is a vailable tool for the assessment of the total cardiovascular risk

- Men with waist circumference >102 cm and women with waist circumference > 88 cm are in increased risk for diabetes, dyslipidemia and hypertension due to the increased abdominal fat

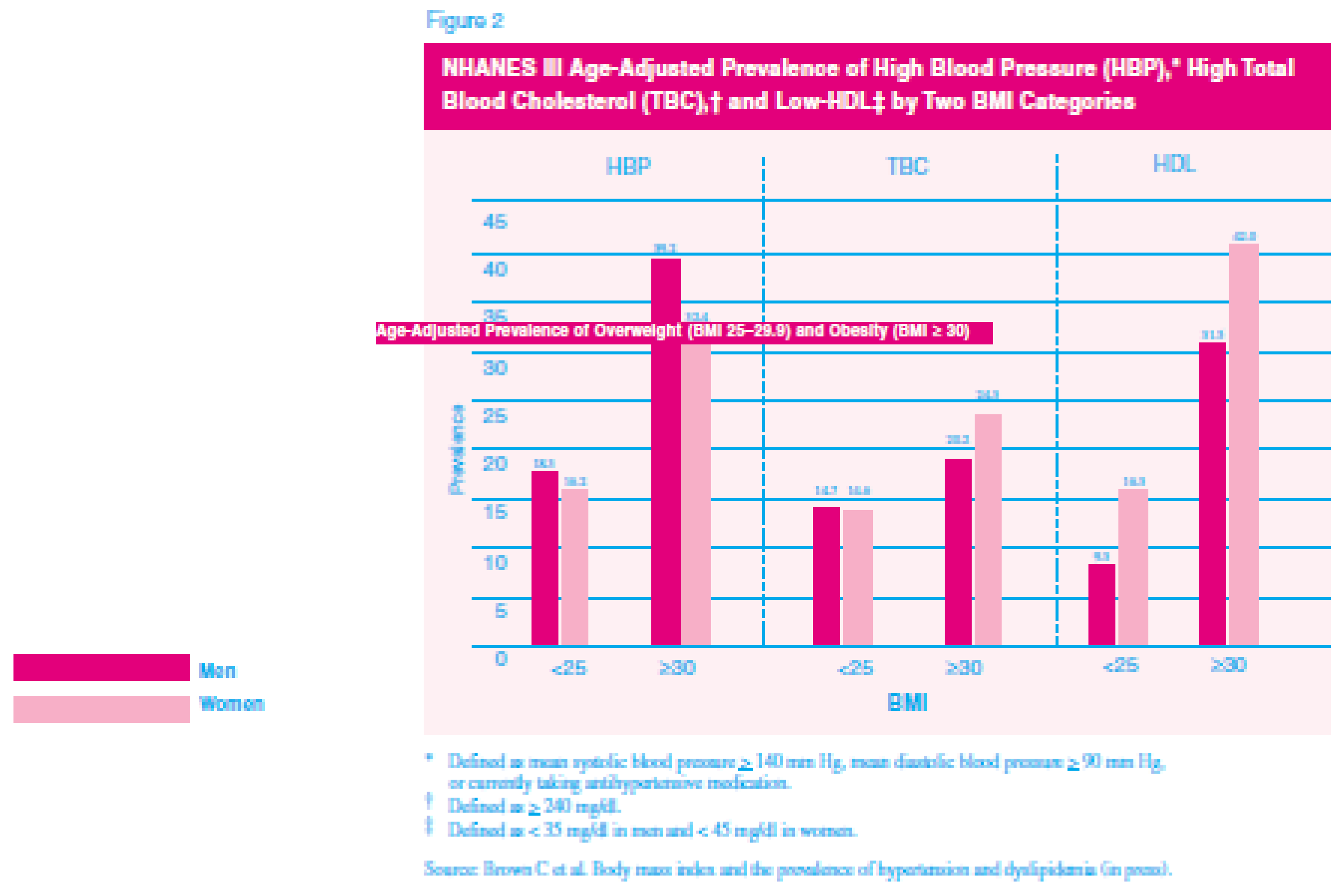


Increased trends for obesity in USA between 1960 -2004



Source: CDC/NCHS. United States. 1960-94, Ages 20-74 years. For comparison across surveys, data for subjects ages 20 to 74 years were age-adjusted by the direct method to the total U.S. population for 1980, using the age-adjusted categories 20-29y, 30-39y, 40-49y, 50-59y, 60-69y, and 70-79y.

Age-adjusted prevalence of risk factors in obese patients



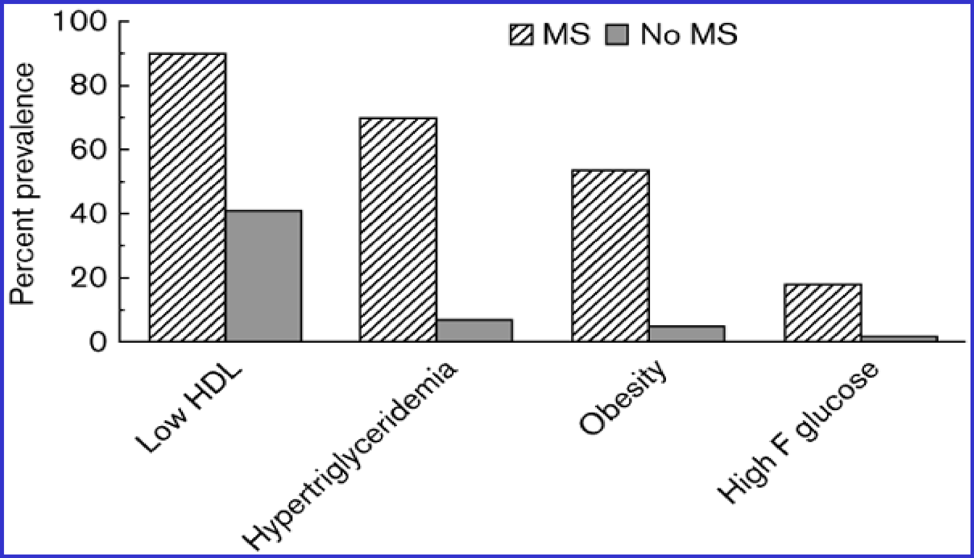
Adapted from the Practical Guide Identification, Evaluation, and Treatment of Overweight and Obesity in Adults , National institute of health, USA

Diagnosis of the metabolic syndrome (ATP III)

- Central obesity
  (waist circumference):
  - — Men >102 cm (40 in)
  - — Women >88 cm (35 in)
- Triglycerides: >150 mg/dL
- HDL cholesterol:
  - — Men <40 mg/dL
  - — Women <50 mg/dL
- Hypertension
- Fasting Glucose : >110 mg/dL

* Diagnosis is based of at least 3 from the above factors

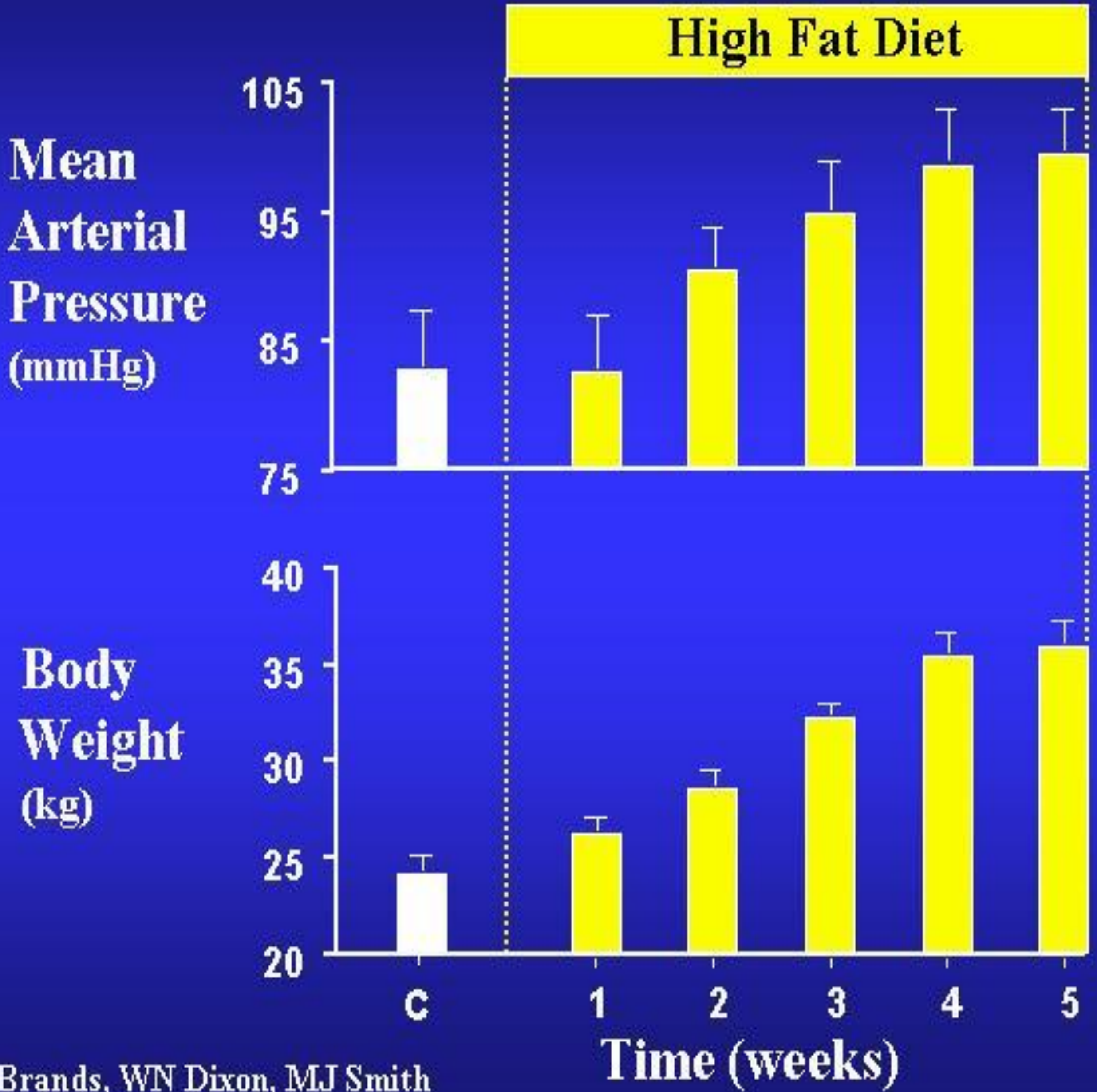
Metabolic Syndrome = High total cardiovascular risk due to the coexistence of multiple risk factors



Incidence of other risk factors in patients with or without the metabolic syndrome
HDL, high-density lipoprotein; F, fasting.

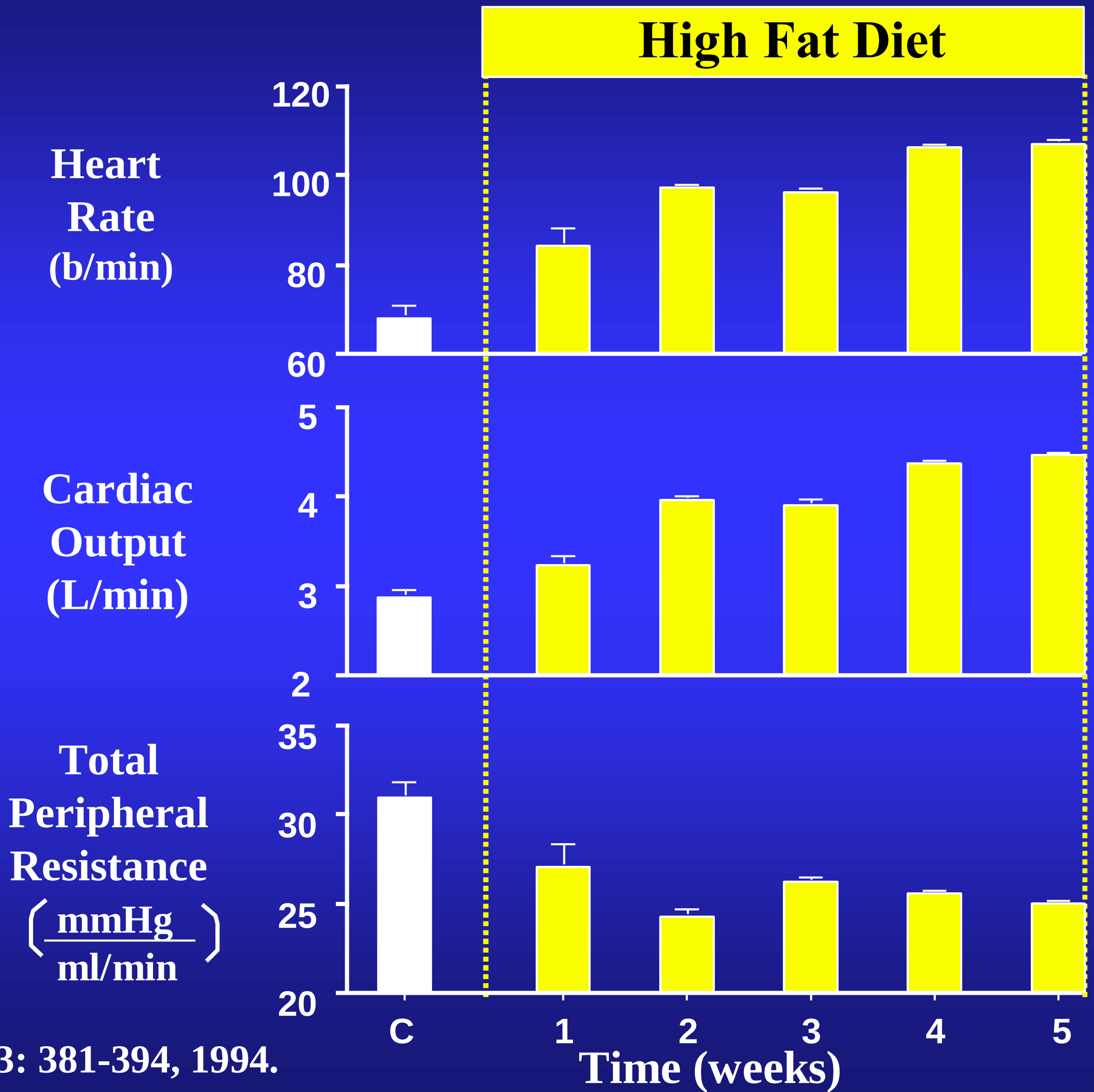
Cuspidi C et al. Journal of Hypertension 2004, 22:1991–1998

High Fat Diet Increases Arterial Pressure



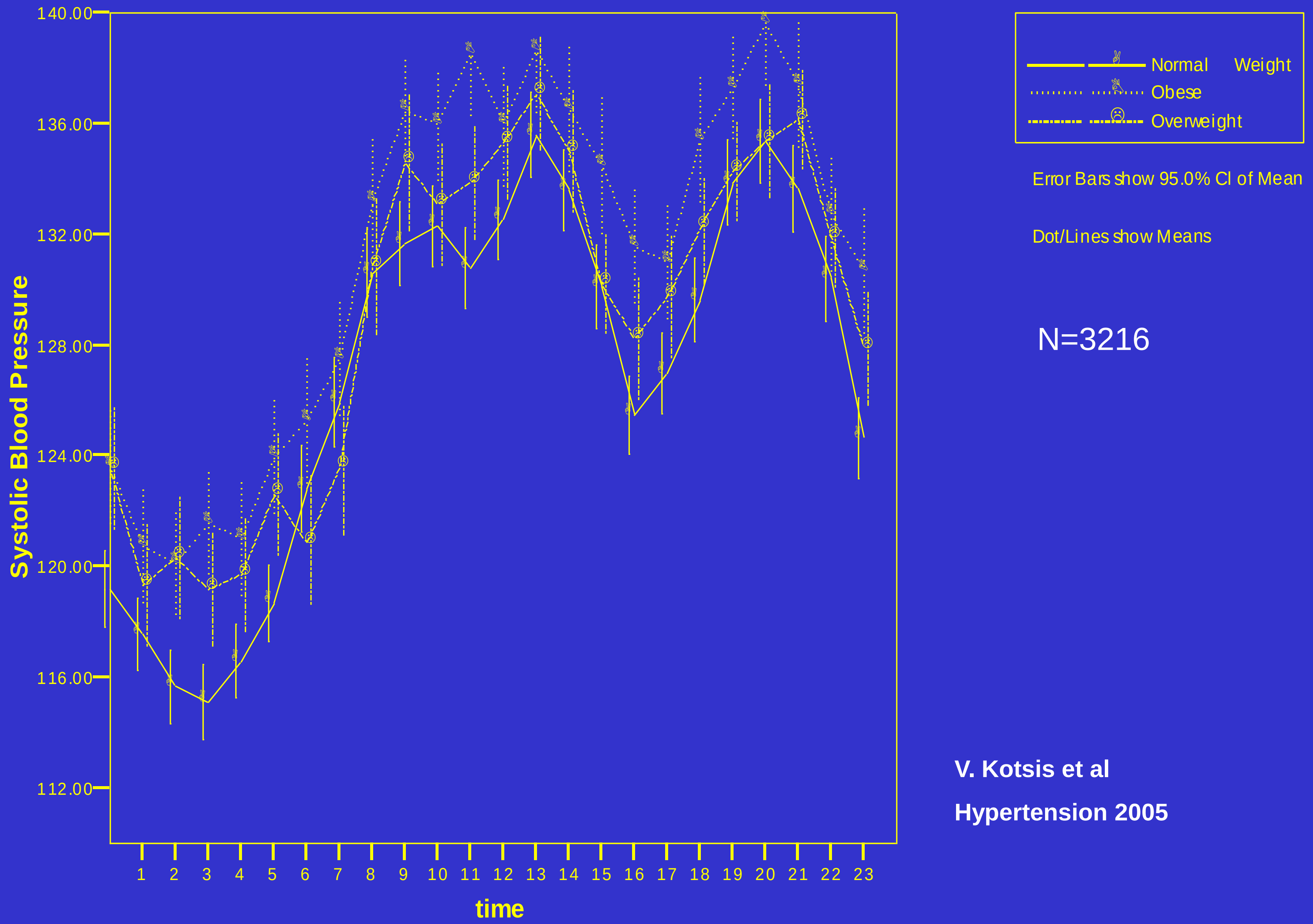
JE Hall, MW Brands, WN Dixon, MJ Smith
Hypertension 22: 292-299, 1993.

High Fat Diet Increases Heart Rate and Cardiac Output



Hall et al.
Hypertension 23: 381-394, 1994.

Obese subjects exhibit higher 24h SBP levels

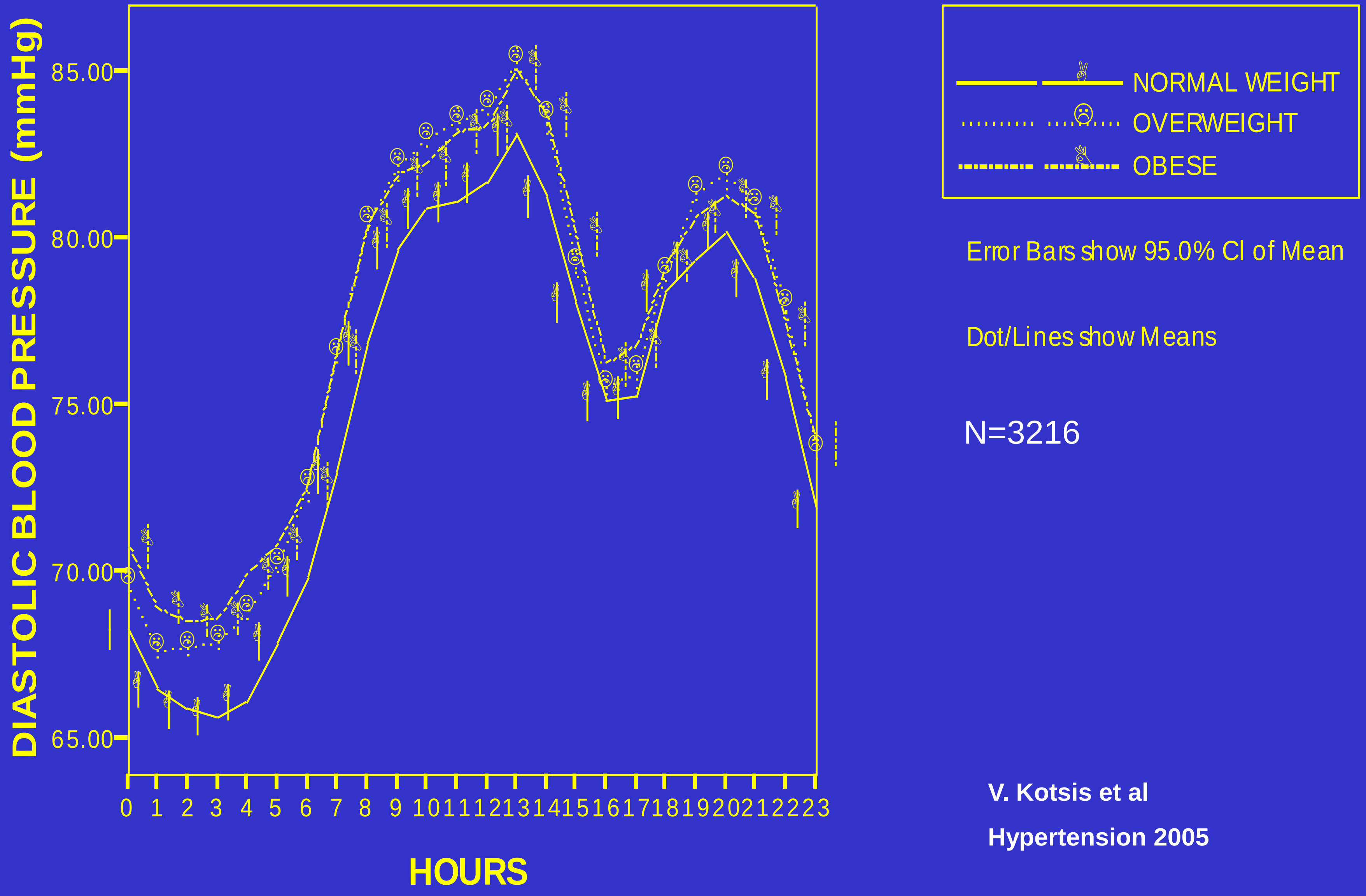


N=3216

V. Kotsis et al

Hypertension 2005

Obese subjects exhibit higher 24h DBP levels



Error Bars show 95.0% CI of Mean

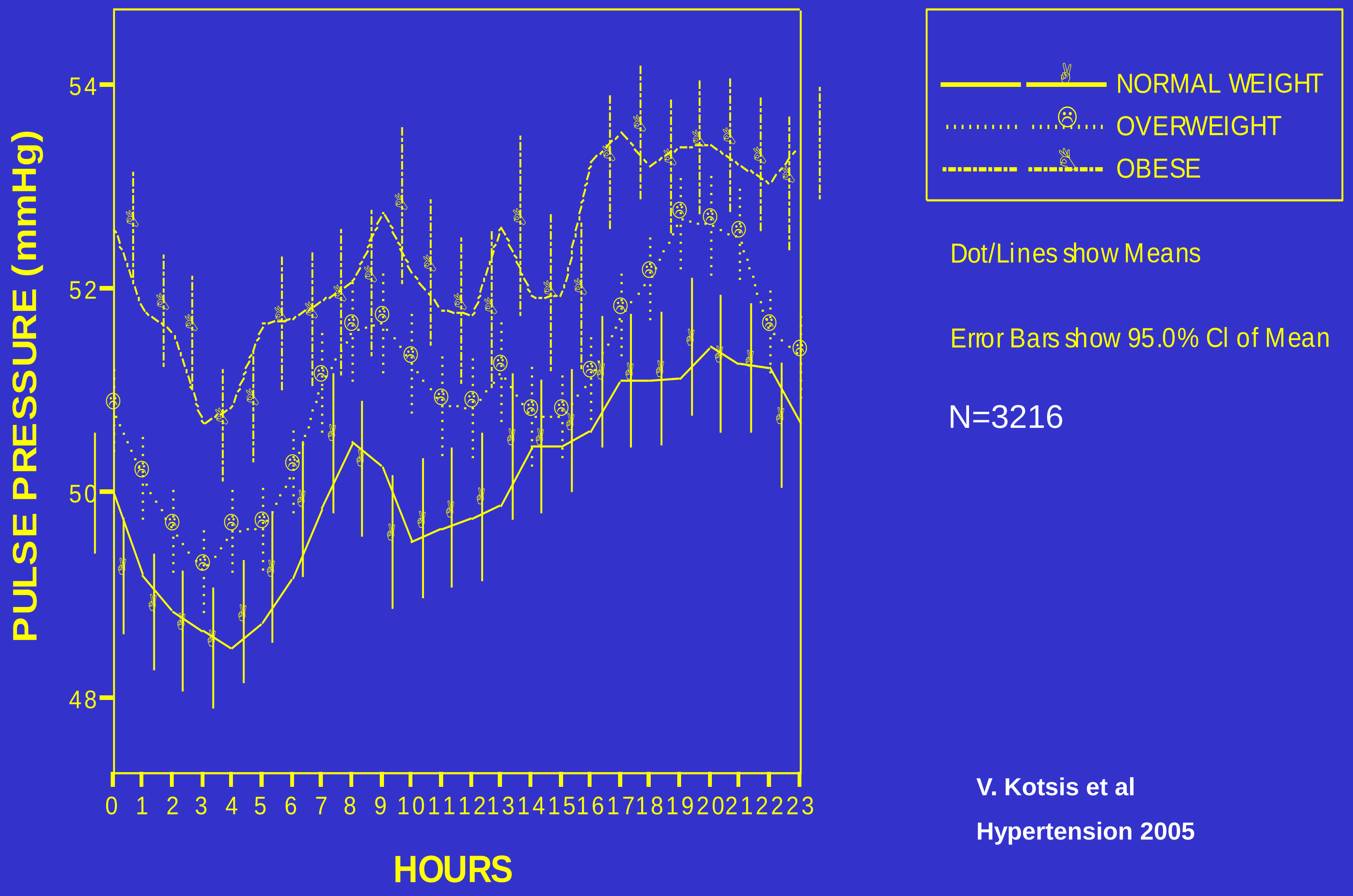
Dot/Lines show Means

N=3216

V. Kotsis et al

Hypertension 2005

Obese subjects exhibit higher 24h Pulse Pressure



Dot/Lines show Means

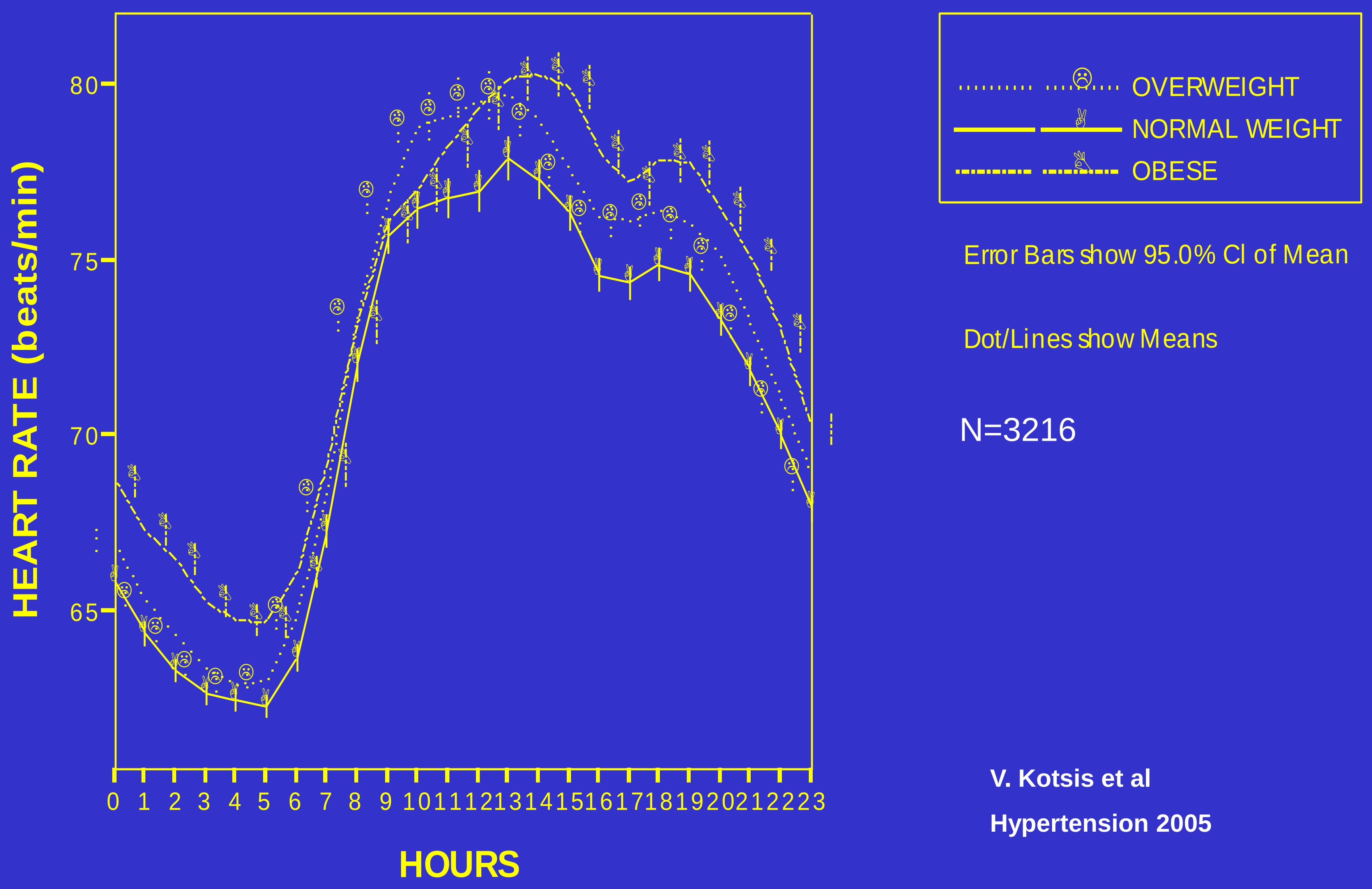
Error Bars show 95.0% CI of Mean

N=3216

V. Kotsis et al

Hypertension 2005

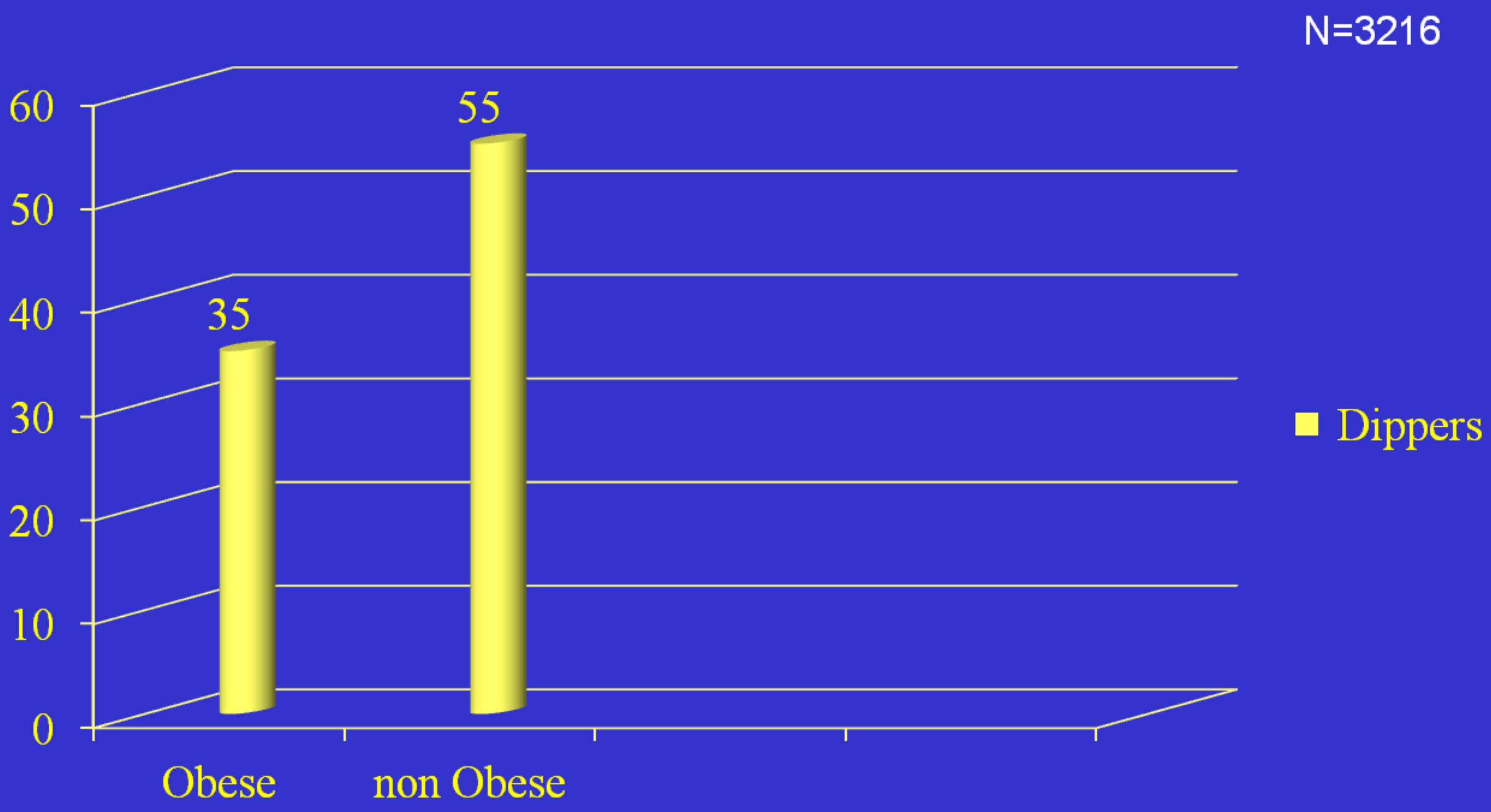
Obese subjects exhibit higher 24h heart rate



V. Kotsis et al

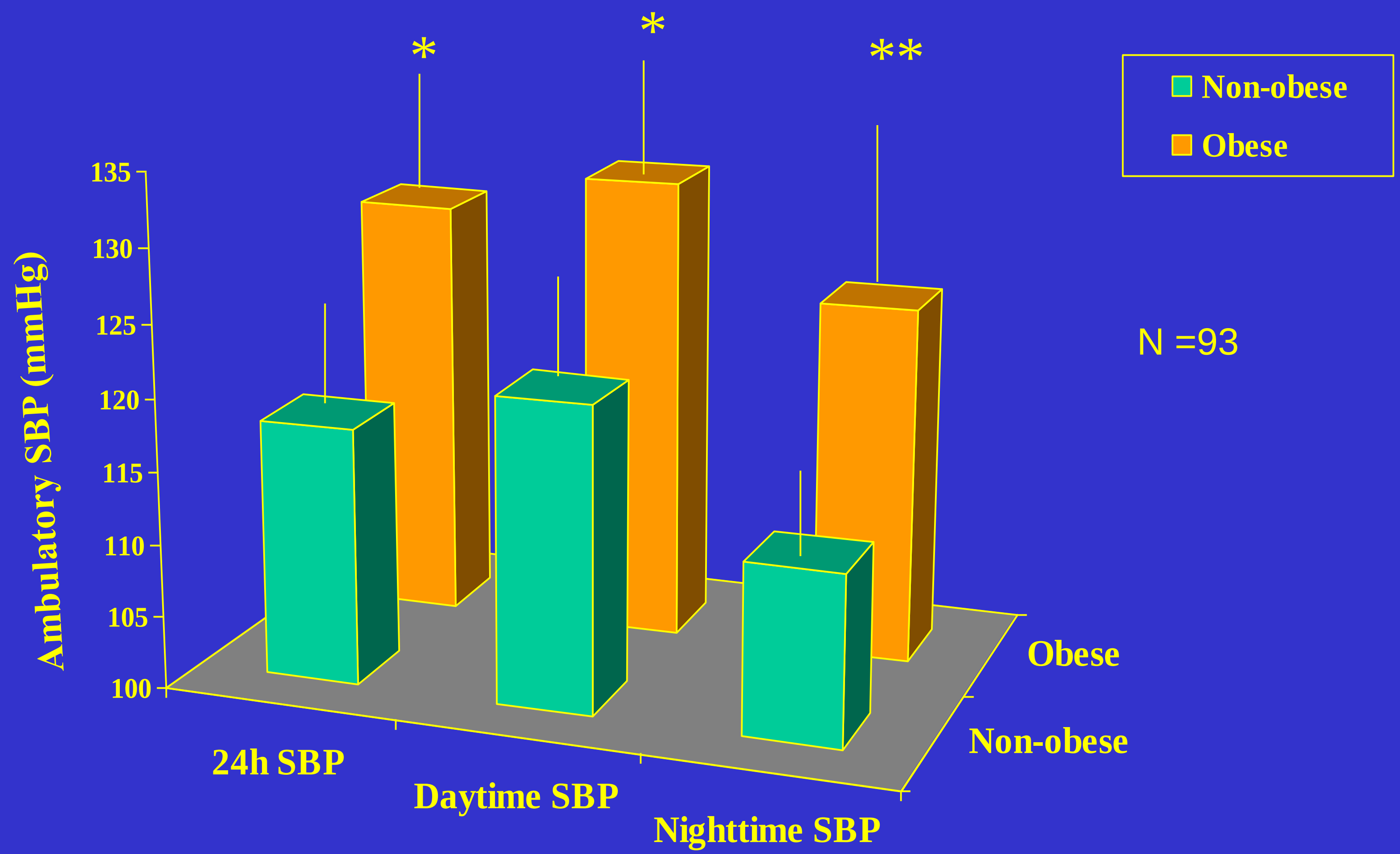
Hypertension 2005

Dipping status in obesity



V. Kotsis et al Hypertension 2005

Obese adolescents exhibit higher 24h, daytime and nighttime SBP levels



N =93

* P < 0.002, ** P< 0.004

Stabouli et al. The Journal of Pediatrics 2005;147:651-6

Logistic regression analysis

Obese children had 3.46 times more likelihood to be hypertensive for 24h systolic BP values

Dependent variable: Ambulatory Hypertension (yes-no)	B	S.E.	Wald	*P*	Exp. B
Obesity (yes-no)	**1.24**	**0.72**	**2.96**	**0.05**	**3.46**
Age	-0.03	0.07	0.18	0.67	0.97
Sex (boys.-girls)	0.13	0.6	0.05	0.83	1.14
Glucose	0.008	0.01	0.61	0.43	1.0
Total Cholesterol	-0.09	0.009	0.95	0.39	0.99
Triglycerides	0.005	0.07	0.64	0.42	1.0

Stabouli et al. The Journal of Pediatrics 2005;147:651-6

Mechanisms of obesity-induced hypertension.

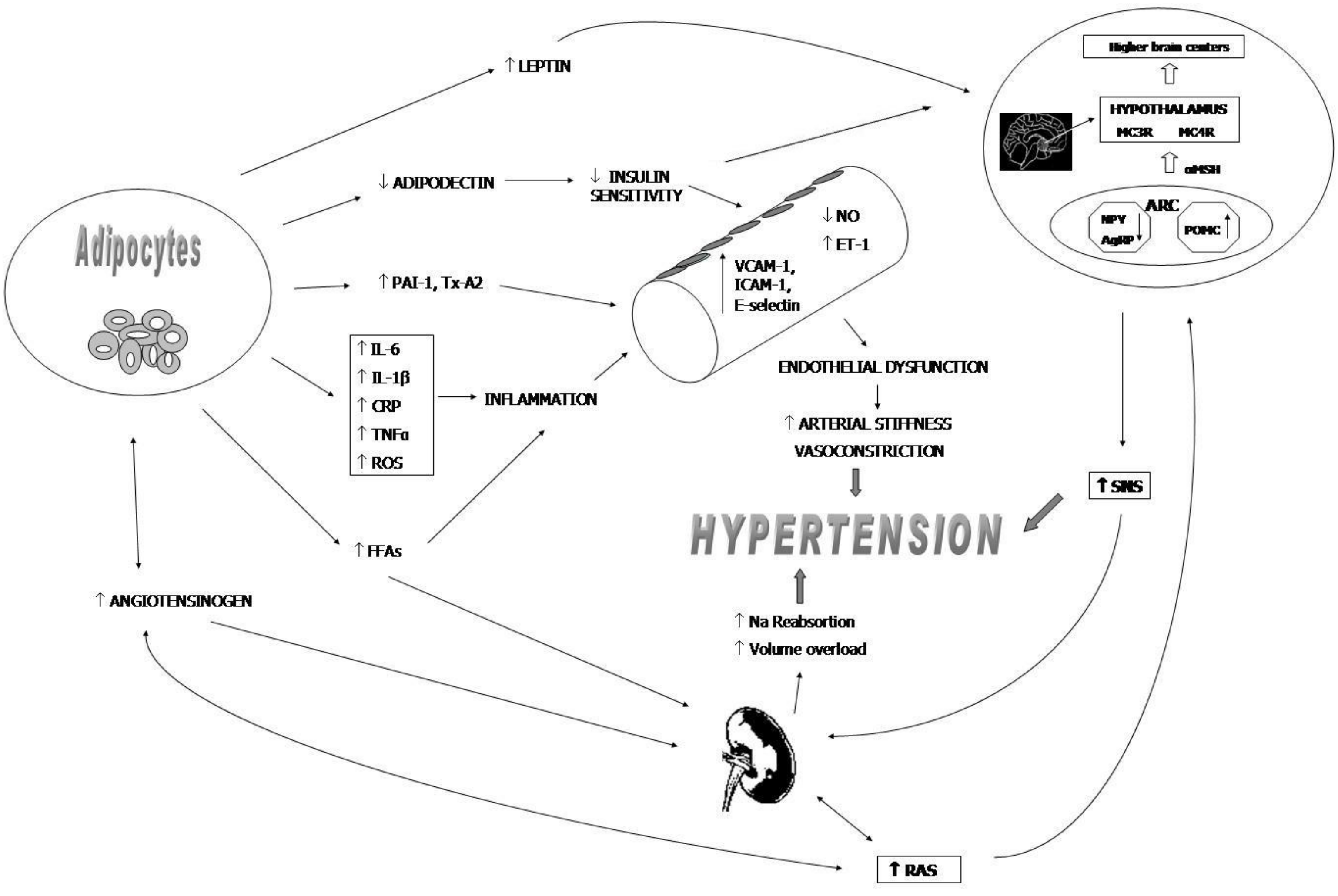
- **Hypertens Res. 2010 May;33(5):386-93.**
- Kotsis V, Stabouli S, Papakatsika S, Rizos Z, Parati G.

3rd Department of Medicine, Hypertension Center, Papageorgiou Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece.

Abstract

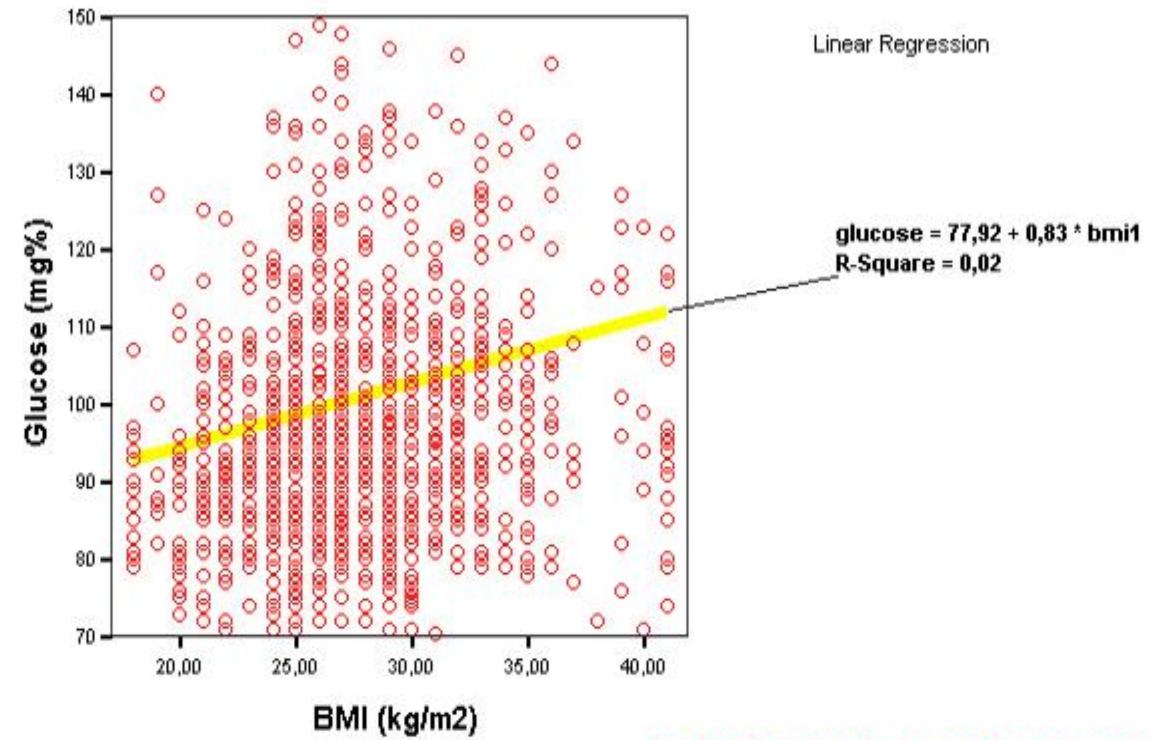
The relationship between obesity and hypertension is well established both in children and adults. The mechanisms through which obesity directly causes hypertension are still an area of research. Activation of the sympathetic nervous system has been considered to have an important function in the pathogenesis of obesity-related hypertension. The arterial-pressure control mechanism of diuresis and natriuresis, according to the principle of infinite feedback gain, seems to be shifted toward higher blood-pressure levels in obese individuals. During the early phases of obesity, primary sodium retention exists as a result of increase in renal tubular reabsorption. Extracellular-fluid volume is expanded and the kidney-fluid apparatus is resetted to a hypertensive level, consistent with a model of hypertension because of volume overload. Plasma renin activity, angiotensinogen, angiotensin II and aldosterone values display significant increase during obesity. Insulin resistance and inflammation may promote an altered profile of vascular function and consequently hypertension. Leptin and other neuropeptides are possible links between obesity and the development of hypertension. Obesity should be considered as a chronic medical condition, which is likely to require long-term treatment. Understanding of the mechanisms associated with obesity-related hypertension is essential for successful treatment strategies.

Mechanisms involved in the pathogenesis of hypertension in obesity and metabolic syndrome



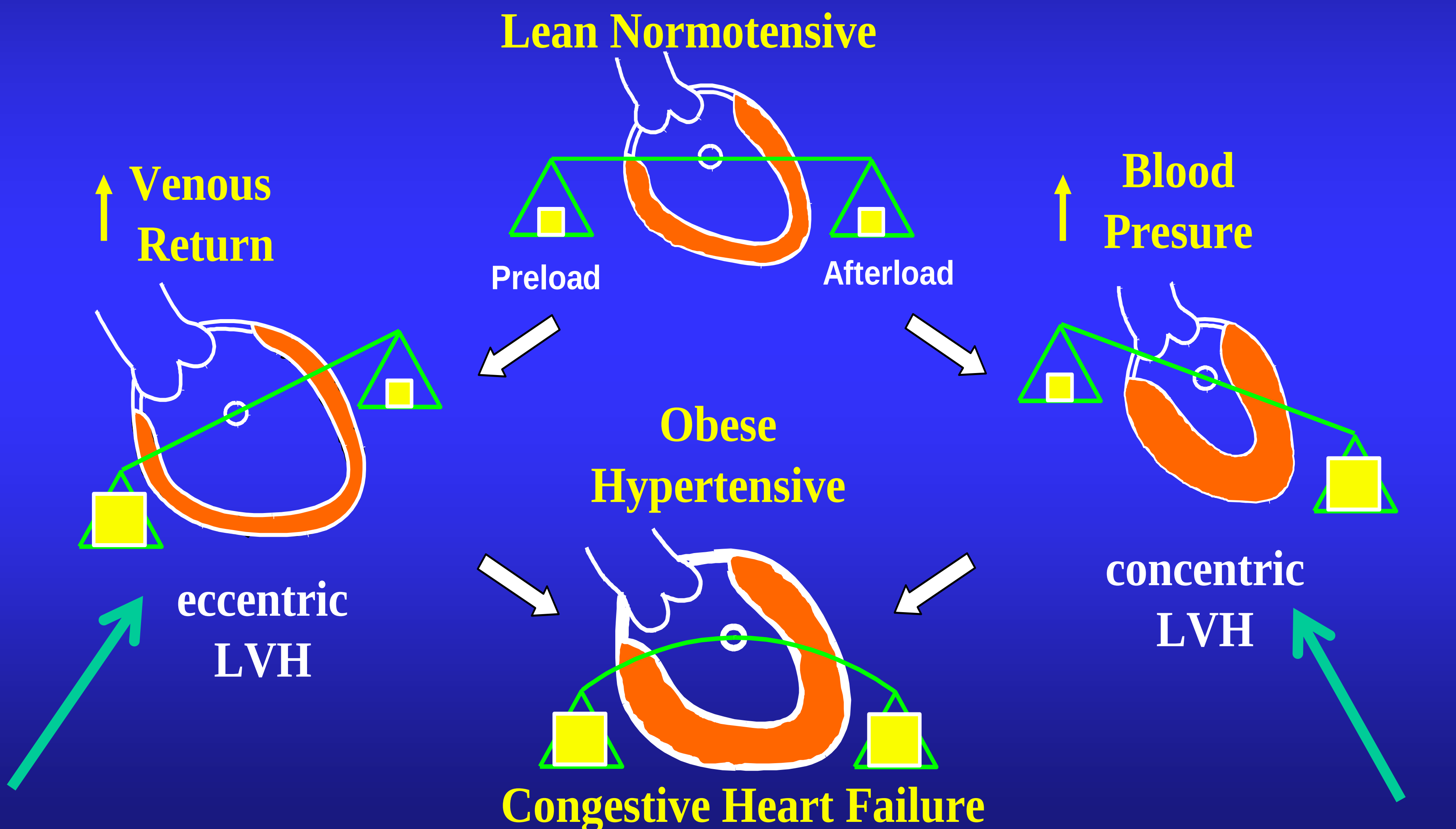
Kotsis et al, Hypertens. Res. 2010;33:386-93

Linear relationship between fasting glucose and BMI

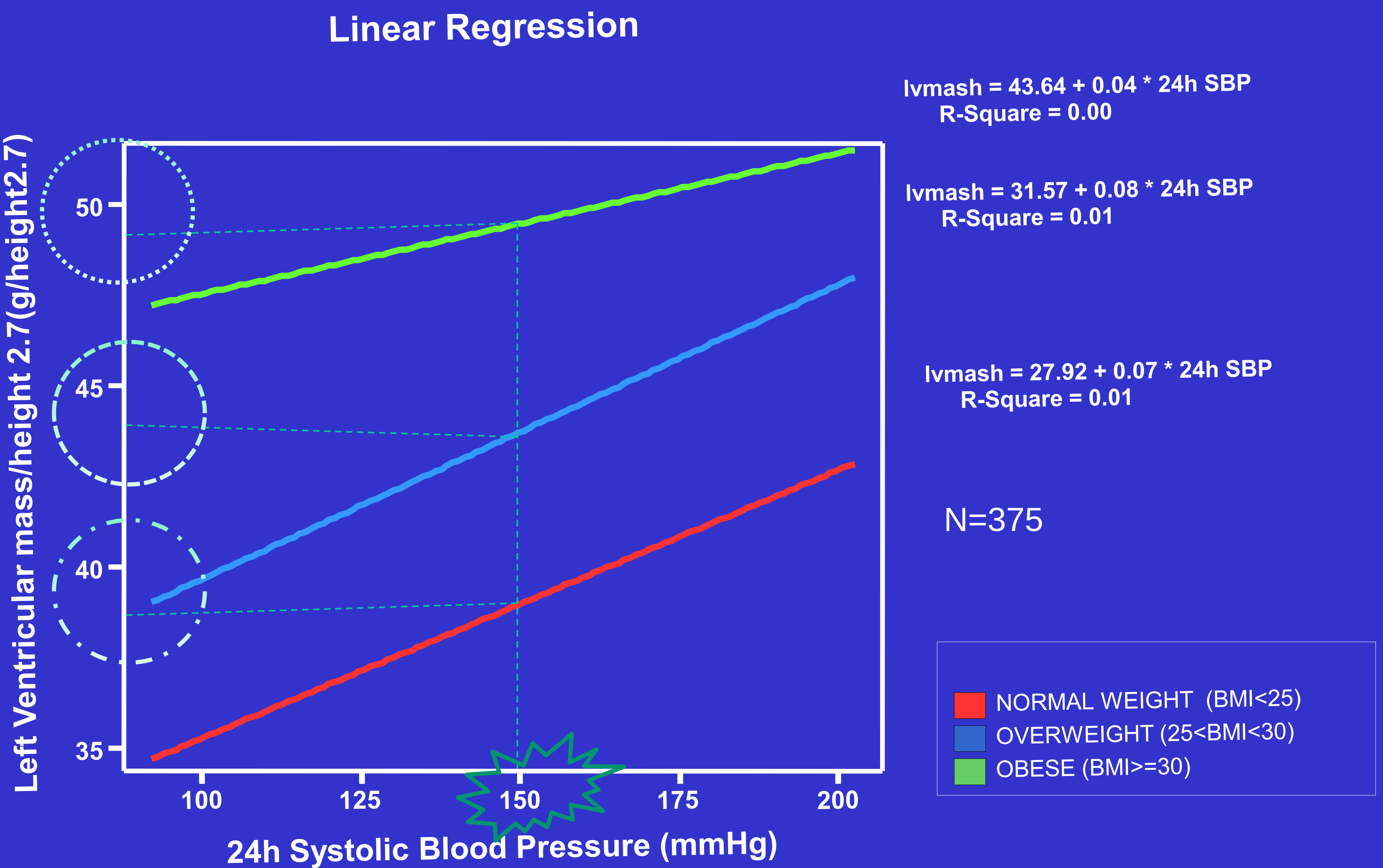


V. Kotsis et al, Hypertension 2005

Obesity causes concentric and eccentric cardiac hypertrophy and increases risk for congestive heart failure



Obesity, mean 24h Systolic Blood Pressure and Left Ventricular Mass



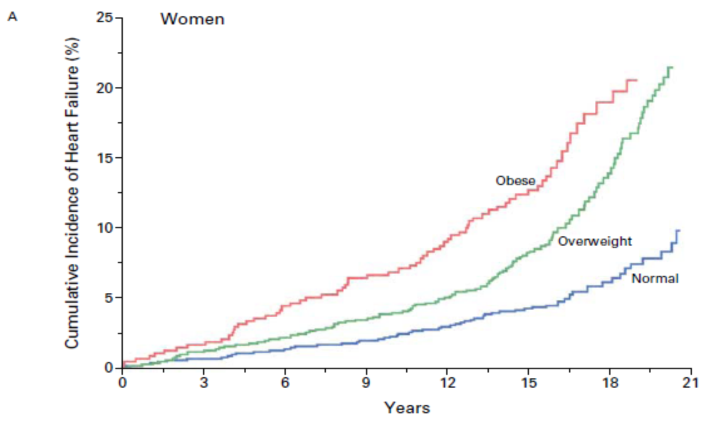
V Kotsis et al. Journal of Hypertension 2002, Vol 20, Suppl 4

Obesity and the risk of heart failure

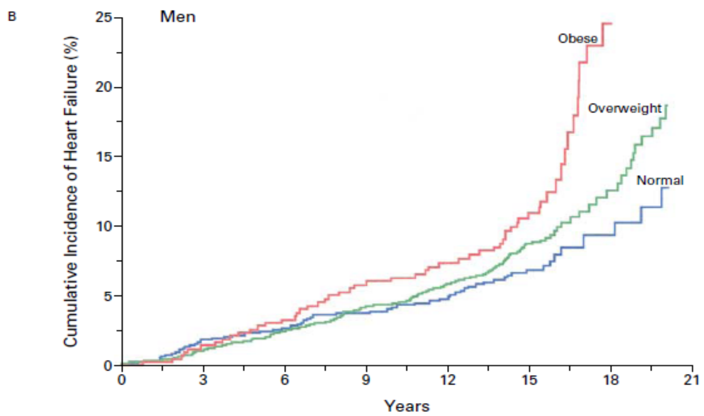
S. Kenchaiah, JC Evans, D Levy, PW Wilson, EJ Benjamin, MG Larson, WB Kannel, RS Vasan
New England J. Medicine 347: 305-313, 2002

Results: **In the Framingham cohort (5881 participants), a graded increase in risk of heart failure was observed with increasing BMI.** ***Obese subjects had a 2x greater risk for heart failure*** **even after adjustment for established risk factors such as hypertension, diabetes, etc (which actually are also caused by obesity).**

Incidence of heart failure in obese patients

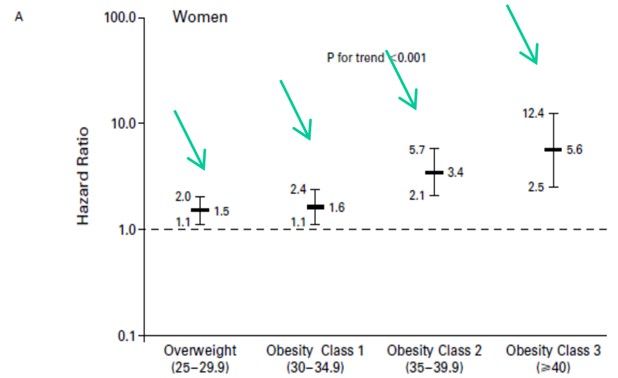


No. at Risk							
Normal	1729	1688	1634	1568	1477	1227	295
Overweight	955	929	880	815	757	634	248
Obese	493	477	448	409	372	296	104

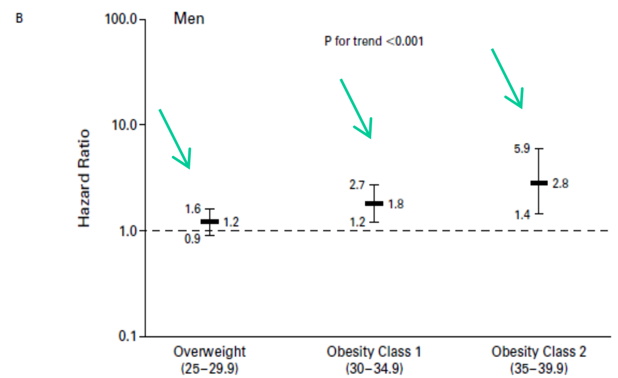


No. at Risk							
Normal	869	822	758	690	637	512	105
Overweight	1378	1322	1254	1163	1071	871	171
Obese	457	433	403	370	342	276	51

Figure 1. Cumulative Incidence of Heart Failure According to Category of Body-Mass Index at the Base-Line Examination. The body-mass index was 18.5 to 24.9 in normal subjects, 25.0 to 29.9 in overweight subjects, and 30.0 or more in obese subjects.



	Overweight	Obesity Class 1	Obesity Class 2	Obesity Class 3
No. of events	108	40	21	7
No. at risk	955	339	111	43
Person-yr of follow-up	14,232	4909	1540	595

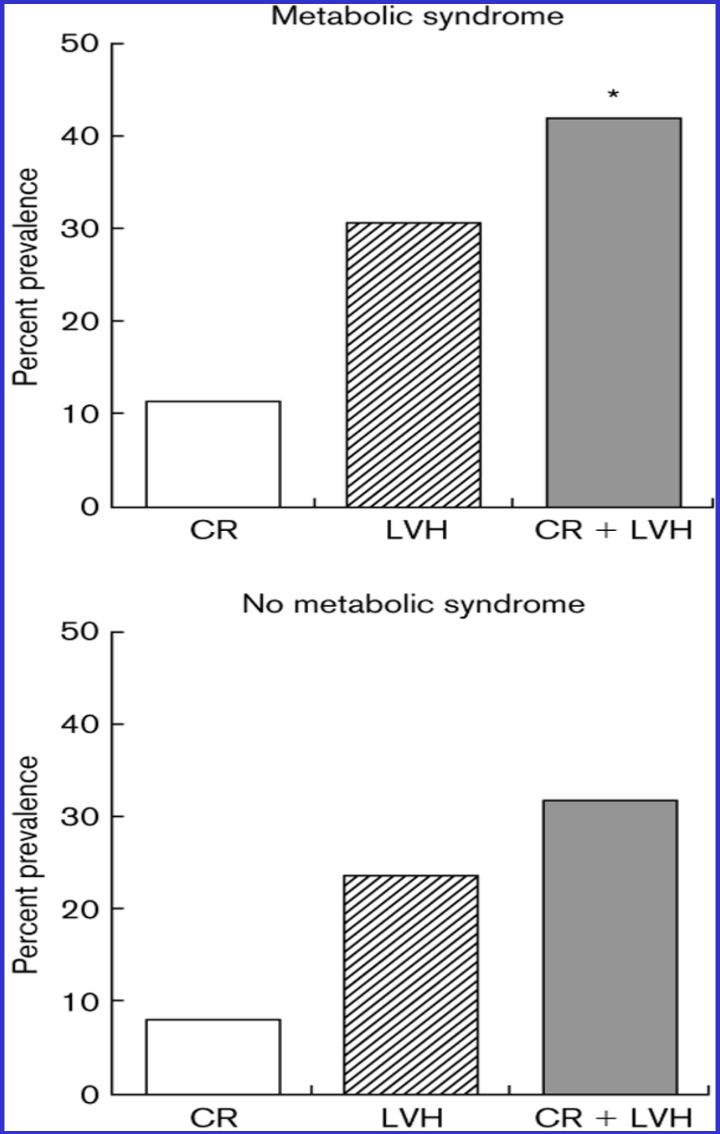


	Overweight	Obesity Class 1	Obesity Class 2
No. of events	125	45	9
No. at risk	1378	391	58
Person-yr of follow-up	19,358	5315	793

Figure 2. Risk of Heart Failure in Obese Subjects, According to Category of Body-Mass Index at the Base-Line Examination.
I bars represent the 95 percent confidence intervals for the hazard ratios. Hazard ratios were adjusted for age, total serum cholesterol level, cigarette smoking, alcohol consumption, and presence or absence of valve disease, hypertension, diabetes mellitus, electrocardiographic evidence of left ventricular hypertrophy, and myocardial infarction at base line. Normal weight (body-mass index, 18.5 to 24.9) was the reference category. Hazard ratios on the y axis are shown on a logarithmic scale. Data for men in obesity class 3 are not provided because of the small sample (eight subjects).

Kenchaiahs et al N Engl J Med , 2002; 347:305-13

Left ventricular concentric remodeling and hypertrophy in the metabolic syndrome



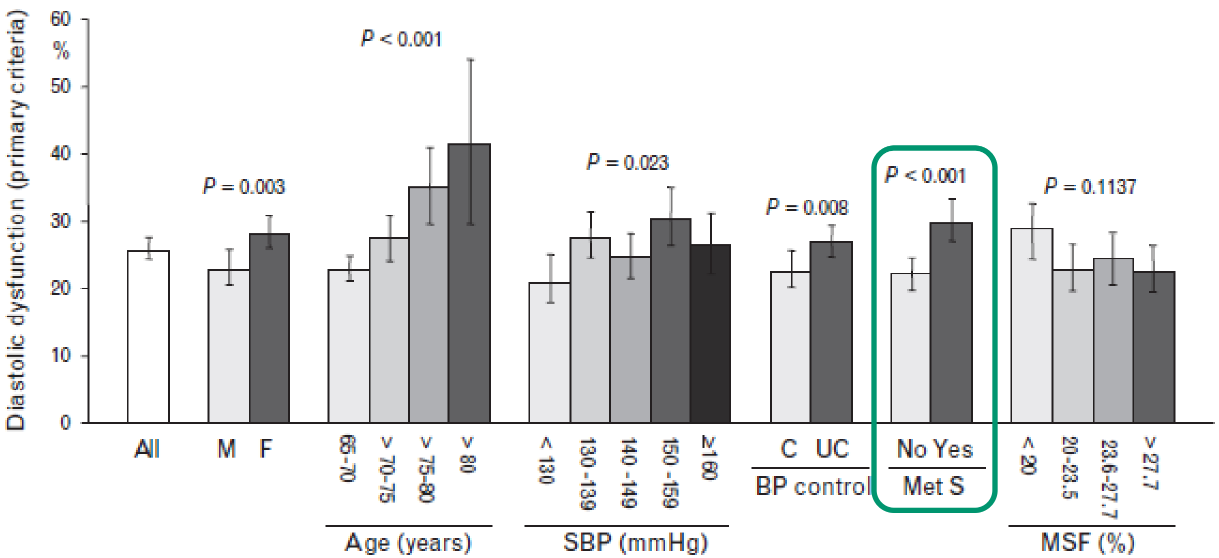
*P , 0.01.

Left ventricular concentric remodelling (CR)
Left ventricular hypertrophy (LVH)

Cuspidi C et al.
Journal of Hypertension
2004, 22:1991–1998

Diastolic dysfunction of the heart in old hypertensive patients: the role of obesity

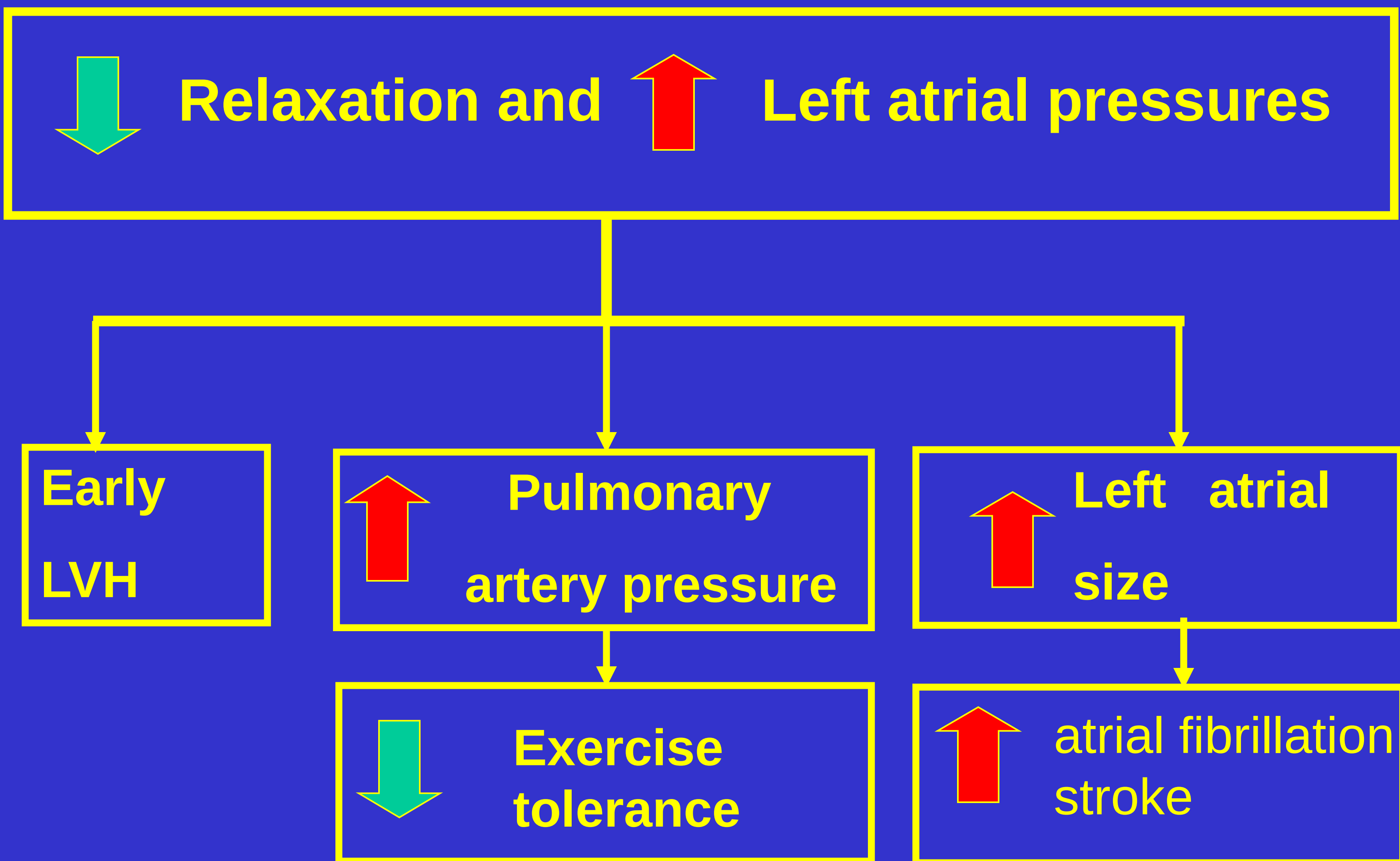
Fig. 2



Prevalence of diastolic dysfunction, defined according to primary criteria. All, all participants; M, men; F, women; Age, patients at different ages; SBP, patients with different systolic blood pressure values; BP control, patients with blood pressure <140/90 mmHg (C) or with blood pressure >140/90 mmHg (UC); Met S, patients with (Yes) or without (No) metabolic syndrome; MSF (%): patients at different quartiles of midwall shortening fraction.

Zanchetti A et al, J Hypertens 2007;25:2158–2167

Clinical Importance of Diastolic Dysfunction of the heart



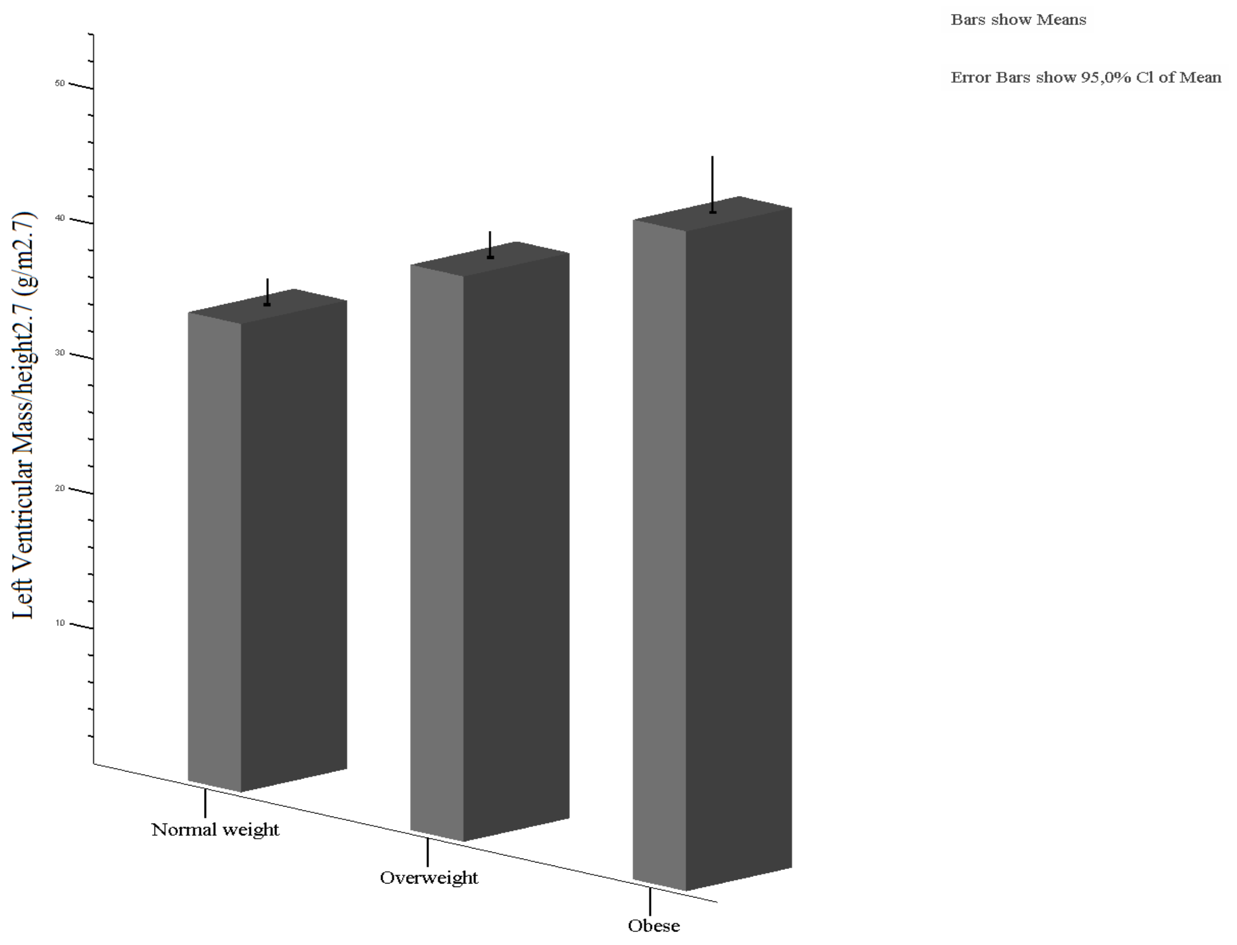
Obesity and daytime pulse pressure are predictors of left ventricular hypertrophy in true normotensive individuals

- **J Hypertens. 2010 May;28(5):1065-73.**

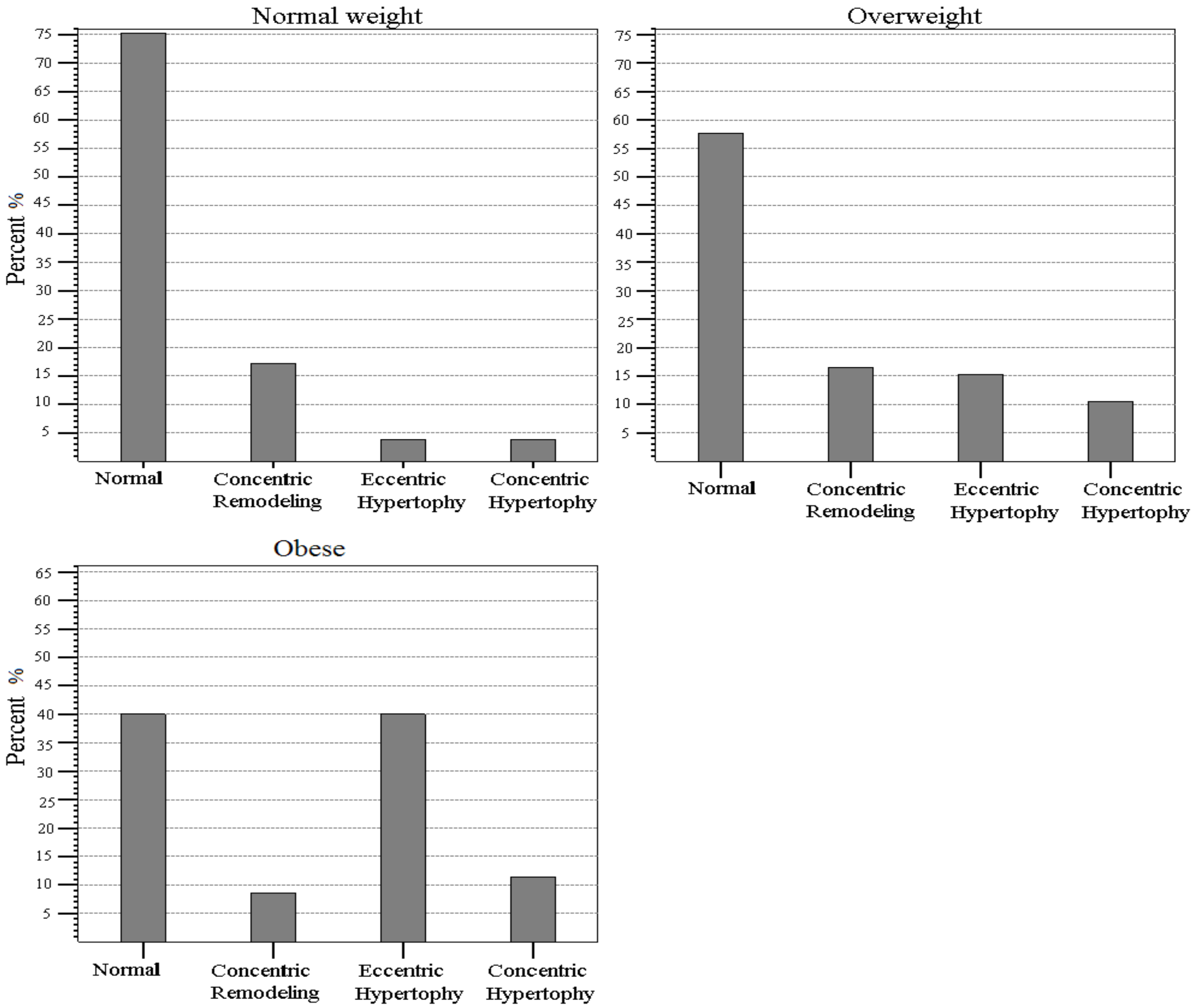
- Kotsis V, Stabouli S, Toumanidis S, Tsivgoulis G, Rizos Z, Trakateli C, Zakopoulos N, Sion M.
- Hypertension Center, Third Department of Medicine, Papageorgiou Hospital, Aristotle University of Thessaloniki, Hippokration Hospital, Thessaloniki, Greece.

- **Abstract**
- OBJECTIVE: To investigate predictors of left ventricular mass corrected for height2.7 (LVMI) and left ventricular hypertrophy in patients who were found to be normotensive with both office and 24-h ambulatory blood pressure (BP) measurements.
- METHODS: A total of 805 consecutive patients were analyzed. All patients underwent office BP measurements, 24-h ambulatory BP monitoring, laboratory measurements for cardiovascular risk factors and echocardiography. Individuals with both office and ambulatory normotension were characterized as true normotensive.
- RESULTS: LVMI was found to be 34.5 +/- 10.9 g/m2.7 in normal-weight patients and 48.7 +/- 13.0 g/m2.7 in obese patients (P < 0.0001). LVMI was found to be 41.7 +/- 10 g/m2.7 in overweight patients, significantly lower than the values of obese patients (P < 0.005) and higher than the values of normal-weight patients (P < 0.001). These results remained significant even after adjustment for age, sex, daytime and nighttime SBP, daytime and nighttime DBP, daytime and nighttime BP variability and daytime and nighttime pulse pressure (PP). In a multivariate analysis model, in which LVMI was the dependent variable and office SBP, office DBP, daytime and nighttime SBP and DBP, daytime and nighttime PPs and variabilities, day-night SBP ratio, fasting serum glucose, triglycerides, total cholesterol, age and BMI were inserted as independent variables with weighted least squares regression by sex, the predictors of LVMI were age, BMI and daytime PP (r2 = 0.31). Left ventricular hypertrophy was 17.67 times more likely in obese patients as compared with normal-weight true normotensive individuals.
- CONCLUSION: Obesity may represent a significant cardiovascular risk factor even in normotensive individuals. Other predictors of LVMI were ageing and daytime PP.

Left ventricular hypertrophy in true normotensive individuals

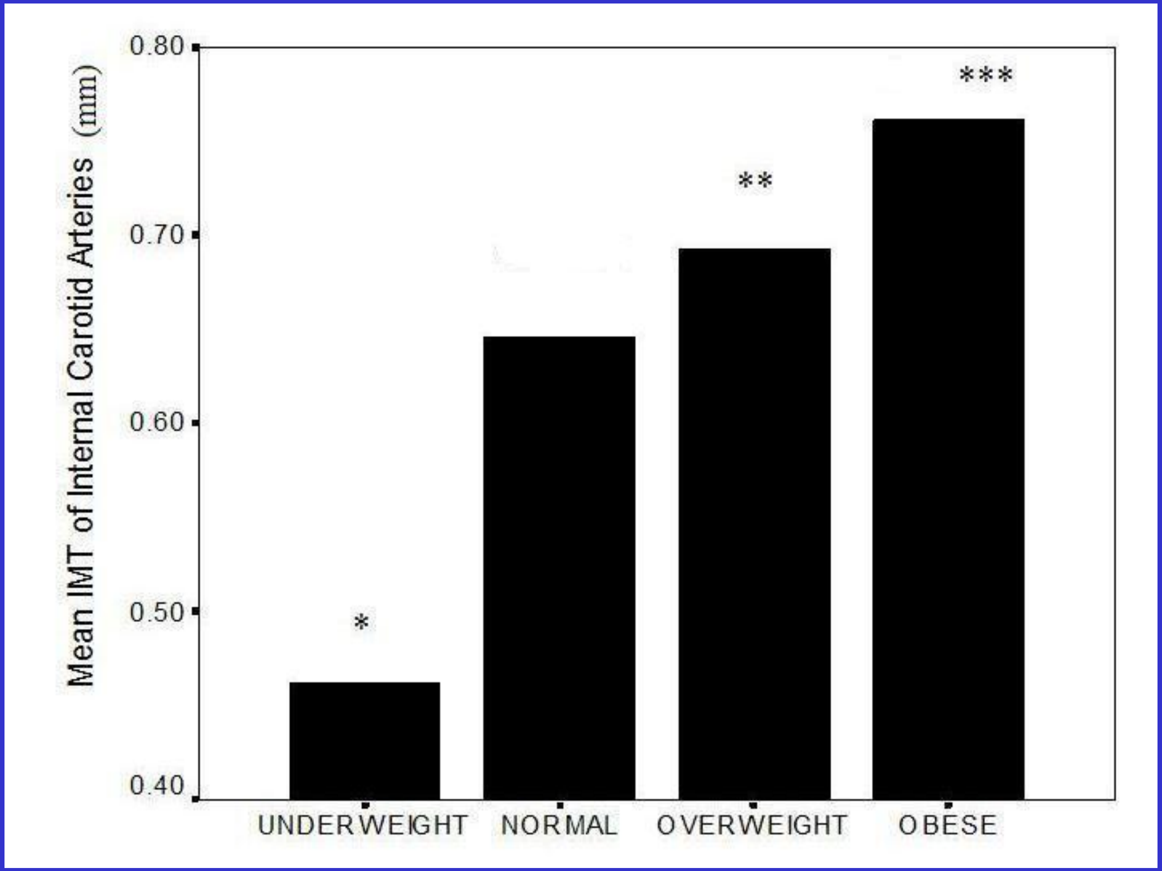


Eccentric and concentric hypertrophy in obese subjects



Kotsis et al
J Hypertens
2010

Obesity and carotid atherosclerosis

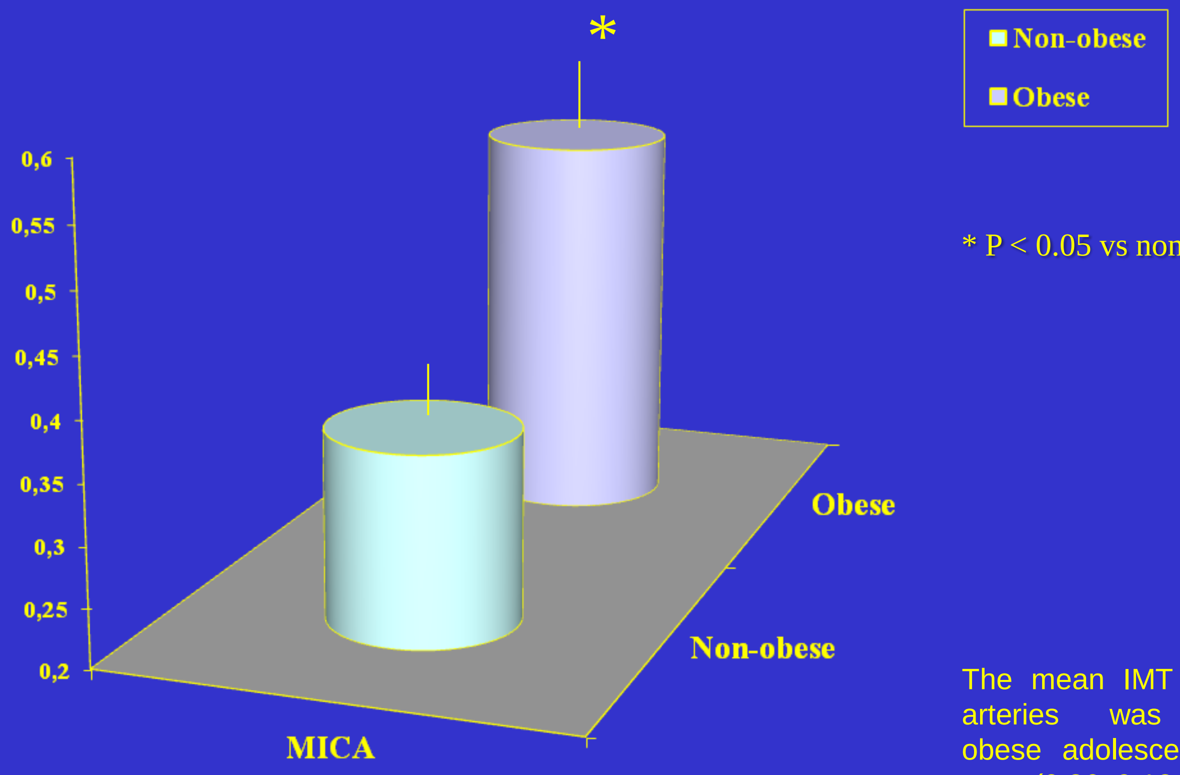


536 subjects matched for age, gender and mean 24h blood pressures values were included in the analysis

Kotsis et al Obesity 2005

Adolescent obesity is associated with high ABP and increased cIMT

Stabouli et al, The Journal of Pediatrics 2005;147:651-6



* P < 0.05 vs non Obese

The mean IMT of the internal carotid arteries was significantly thicker in obese adolescents than in non-obese ones (0.36±0.12 vs 0.53±0.11, p<0.05).

A Guide to Selecting Treatment

	BMI category				
Treatment	25–26.9	27–29.9	30-34.9	35–39.9	≥ 40
Diet, physical activity, and behavior therapy	With comorbidities	With comorbidities	+	+	+
Pharmacotherapy		With comorbidities	+	+	+
Surgery				With comorbidities	

- Prevention of weight gain with lifestyle therapy is indicated in any patient with a BMI ≥ 25 kg/m², even without comorbidities, while weight loss is not necessarily recommended for those with a BMI of 25–29.9 kg/m² or a high waist circumference, unless they have two or more comorbidities.
- Combined therapy with a low-calorie diet (LCD), increased physical activity, and behavior therapy provide the most successful intervention for weight loss and weight maintenance.
- Consider pharmacotherapy only if a patient has not lost 1 pound per week after 6 months of combined lifestyle therapy.

The + represents the use of indicated treatment regardless of comorbidities.

Adapted from the Practical Guide Identification, Evaluation, and Treatment of Overweight and Obesity in Adults , National institute of health, USA

Low-Calorie Step I Diet

Nutrient	Recommended Intake
Calories[1]	Approximately 500 to 1,000 kcal/day reduction from usual intake
Total fat[2]	30 percent or less of total calories
Saturated fatty acids[3]	8 to 10 percent of total calories
Monounsaturated fatty acids	Up to 15 percent of total calories
Polyunsaturated fatty acids	Up to 10 percent of total calories
Cholesterol[3]	<300 mg/day
Protein[4]	Approximately 15 percent of total calories
Carbohydrate[5]	55 percent or more of total calories
Sodium chloride	No more than 100 mmol/day (approximately 2.4 g of sodium or approximately 6 g of sodium chloride)
Calcium[6]	1,000 to 1,500 mg/day
Fiber[5]	20 to 30 g/day

Adapted from the Practical Guide Identification, Evaluation, and Treatment of Overweight and Obesity in Adults , National institute of health, USA

Increase physical activity

Examples of Moderate Amounts of Physical Activity*		
Common Chores	**Sporting Activities**	
Washing and waxing a car for 45–60 minutes	Playing volleyball for 45–60 minutes	Less Vigorous, More Time† ↑
Washing windows or floors for 45–60 minutes	Playing touch football for 45 minutes	
Gardening for 30–45 minutes	Walking 1¾ miles in 35 minutes (20 min/mile)	
Wheeling self in wheelchair for 30–40 minutes	Basketball (shooting baskets) for 30 minutes	
Pushing a stroller 1½ miles in 30 minutes	Bicycling 5 miles in 30 minutes	
Raking leaves for 30 minutes	Dancing fast (social) for 30 minutes	
Walking 2 miles in 30 minutes (15 min/mile)	Water aerobics for 30 minutes	
Shoveling snow for 15 minutes	Swimming laps for 20 minutes	
Stairwalking for 15 minutes	Basketball (playing a game) for 15–20 minutes	
	Jumping rope for 15 minutes	↓ More Vigorous, Less Time
	Running 1½ miles in 15 minutes (15 min/mile)	

All adults should set a long-term goal to accumulate at least 30 minutes or more of moderate-intensity physical activity on most, and preferably all, days of the week.

Adapted from the Practical Guide Identification, Evaluation, and Treatment of Overweight and Obesity in Adults , National institute of health, USA

Weight Loss Drugs*

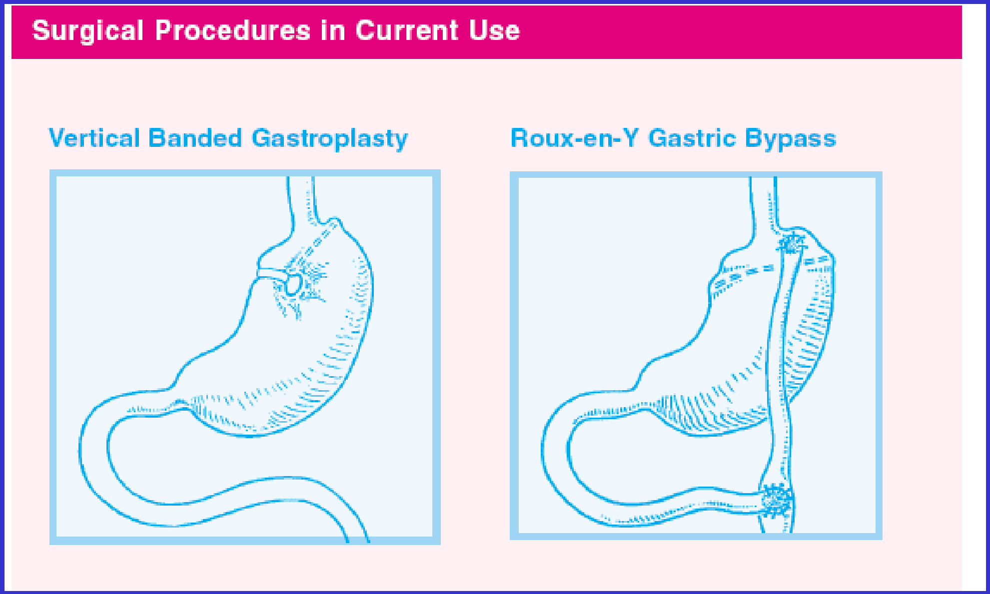
Drug	Dose	Action	Adverse Effects
Sibutramine	5, 10,15 mg 10 mg po qd to start, may be increased to 15 mg or decreased to 5 mg	Norepinephrine, dopamine, and serotonin reuptake inhibitor	Increase in heart rate and blood pressure.
Orlistat	120 mg 120 mg po tid before meals	Inhibits pancreatic lipase, decreases fat absorption.	Decrease in absorption of fat-soluble vitamins; soft stools and anal leakage.

In Europe sibutramine has been withdrawn from EMEA because of the cardiovascular side effects

* Ephedrine plus caffeine, and fluoxetine have also been tested for weight loss but are not approved for use in the treatment of obesity. Mazindol, diethylpropion, phentermine, benzphetamine, and phendimetrazine are approved for only short-term use for the treatment of obesity. Herbal preparations are not recommended as part of a weight loss program. These preparations have unpredictable amounts of active ingredients and unpredictable, and potentially harmful, effects.

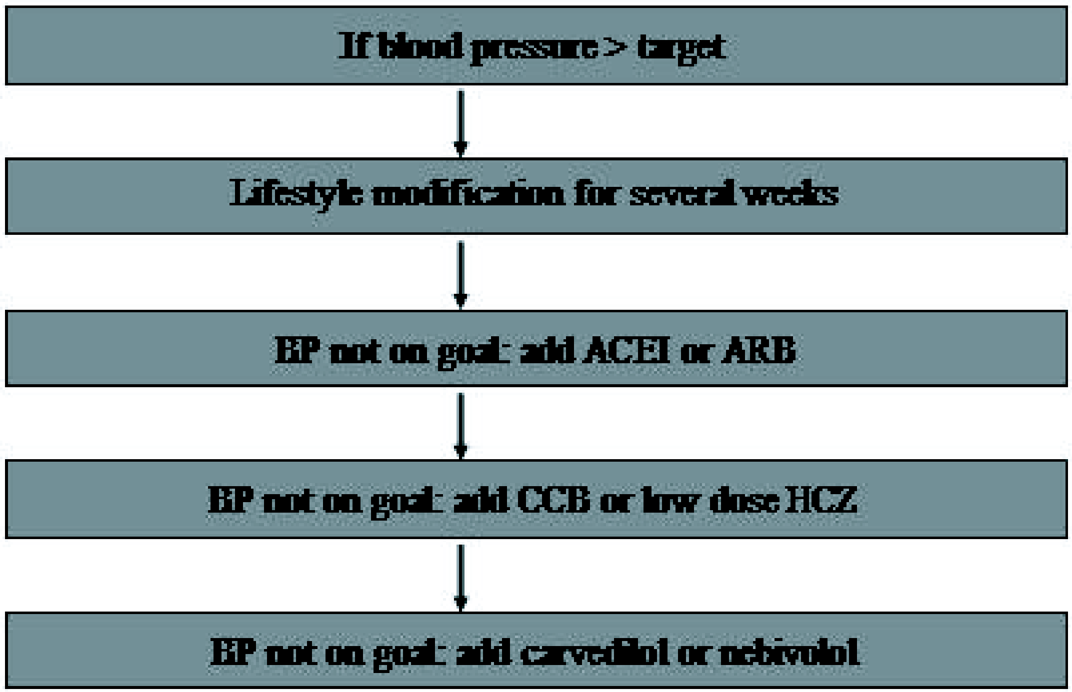
Adapted from the Practical Guide Identification, Evaluation, and Treatment of Overweight and Obesity in Adults , National institute of health, USA

Surgical procedures



Adapted from the Practical Guide Identification, Evaluation, and Treatment of Overweight and Obesity in Adults , National institute

Treatment approach for patients with obesity associated hypertension



Kotsis et al Hypertension Research 2010

Conclusions: Hypertension, obesity and metabolic syndrome

- Obesity is often associated with hypertension and multiple metabolic abnormalities that include dyslipidemia, glucose intolerance and insulin resistance

- The co-existence of these features compose the metabolic syndrome

- Obesity, especially centrally distributed, has a key role in the pathogenesis of HTN and other components of the metabolic syndrome

- **Thank you very much**