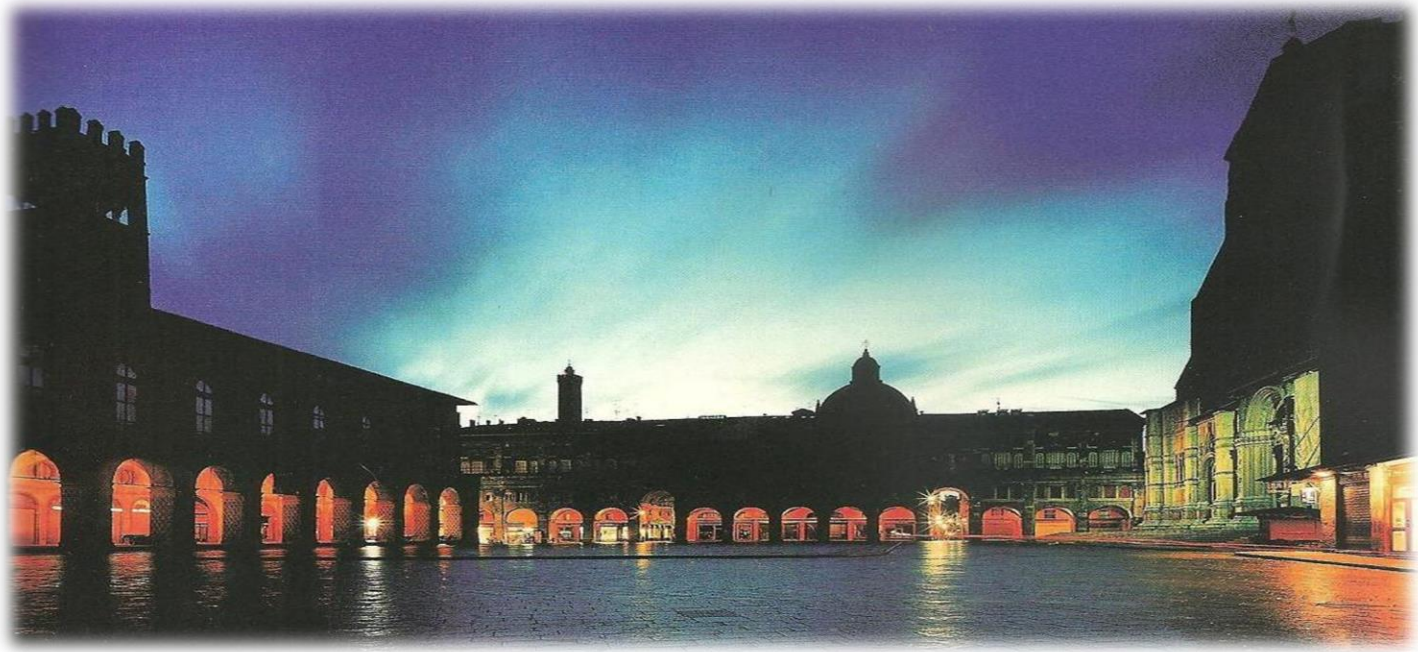
OSAS E IPERTENSIONE ARTERIOSA



Dott.ER Cosentino

Dipartimento Cardio-Toraco-Vascolare

Università degli Studi di Bologna

OSAS e rischio CV

- La prevalenza di OSAS è 2-3 volte maggiore nei cardiopatici rispetto alla popolazione di riferimento
- L'OSAS rappresenta un fattore di rischio indipendente
- Maggiore incidenza di ipertensione arteriosa, ictus, cardiopatia ischemica e scompenso

G Ital Cardiol 2008

Evidence on the Association between OSA and Hypertensionn

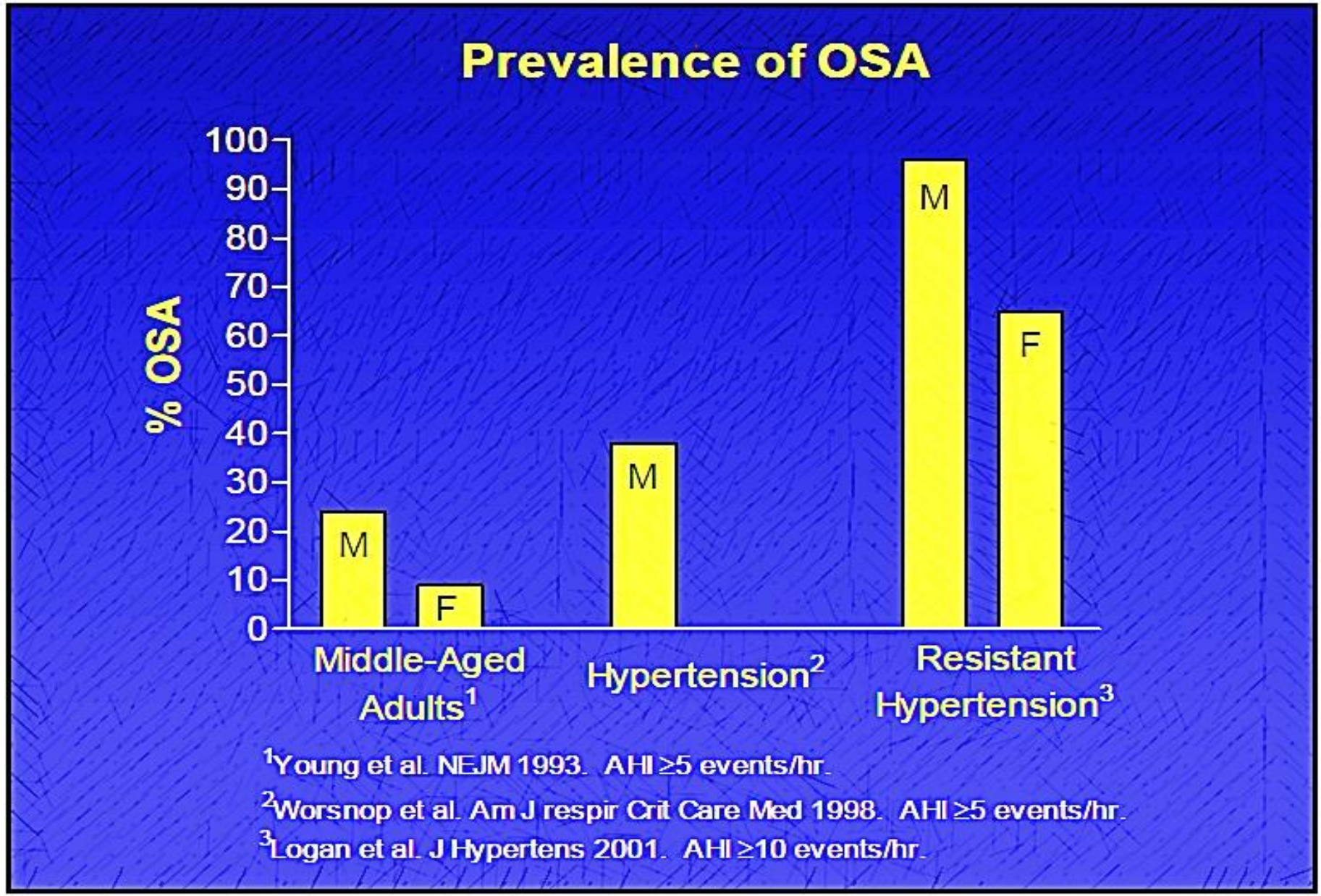
Recent Human Studies

- General population epidemiology studies
- Case control
- Intervention studies

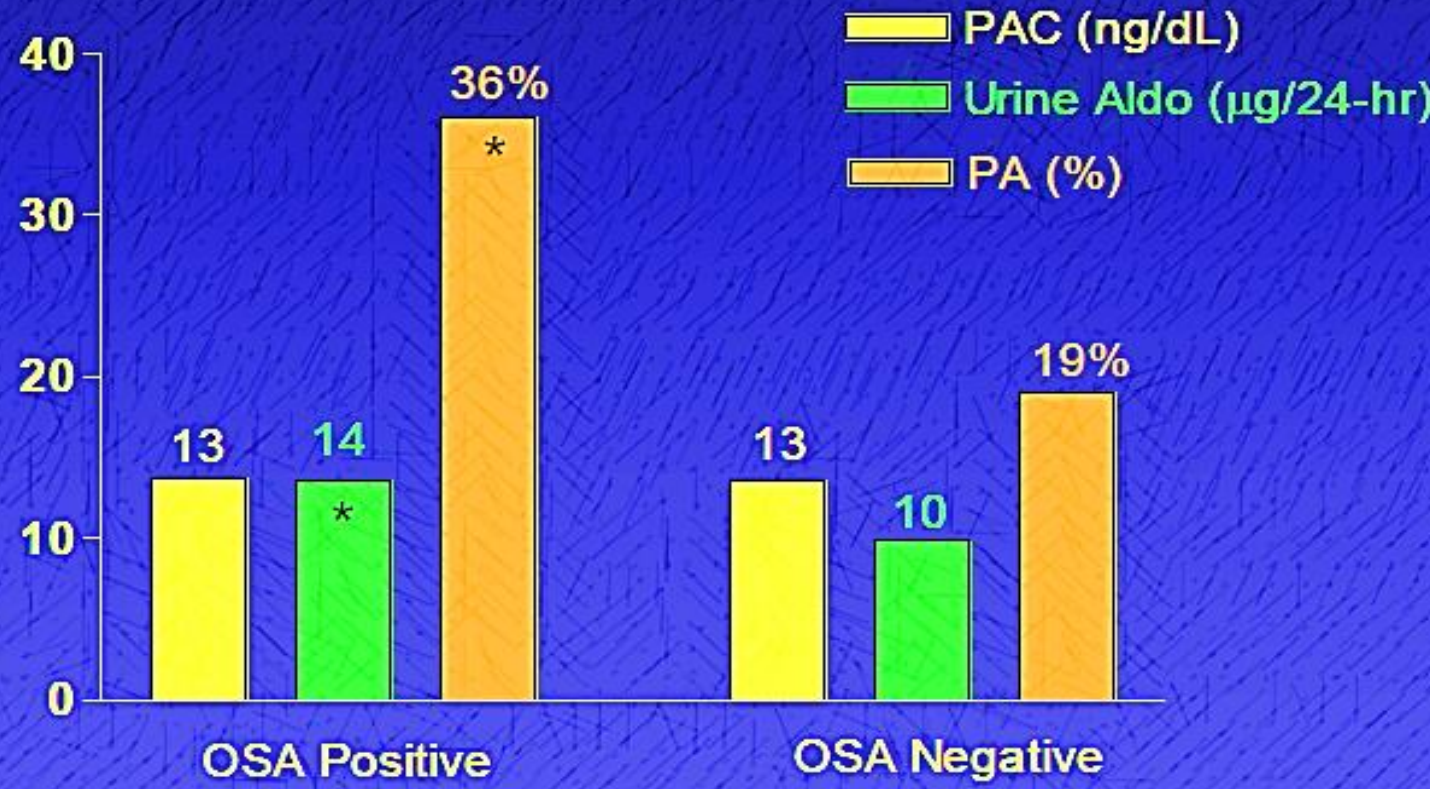
Evidence on the Association between OSA and Hypertensionn

- Il 96% degli uomini e il 65% delle donne con ipertensione resistente hanno OSA

- Gli ipertesi resistenti con OSA hanno livelli più alti di aldosterone plasmatico e incidenza più elevata di aldosteronismo primario, rispetto agli ipertesi resistenti senza OSA

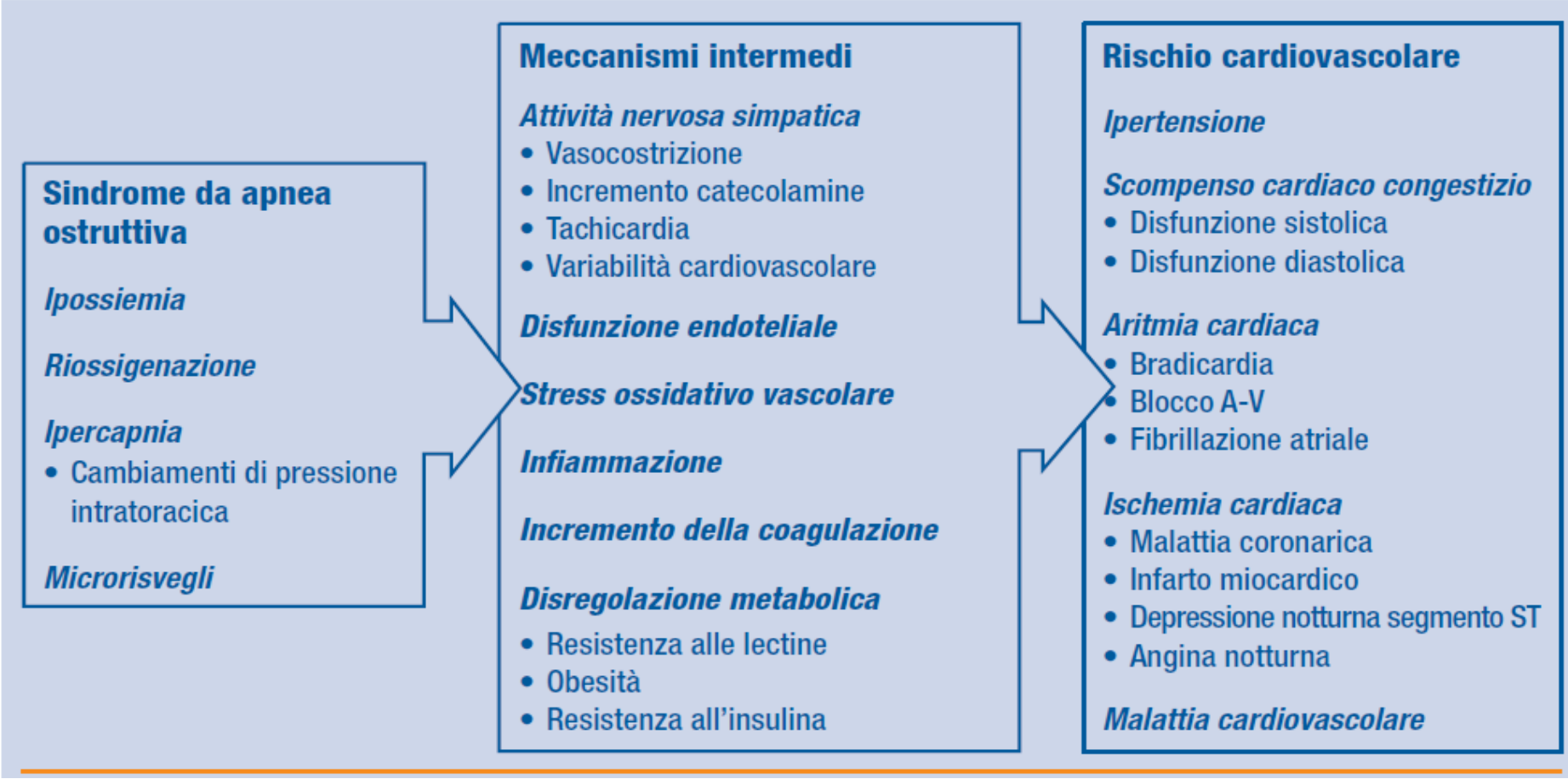

Prevalence of OSA
% OSA
100
90
80
70
60
50
40
30
20
10
0
M
F
M
M
F
Middle-Aged Adults[1]
Hypertension[2]
Resistant Hypertension[3]
[1]Young et al. NEJM 1993. AHI ≥5 events/hr.
[2]Worsnop et al. Am J respir Crit Care Med 1998. AHI ≥5 events/hr.
[3]Logan et al. J Hypertens 2001. AHI ≥10 events/hr.

Aldosterone Levels and Risk of OSA in Subjects with Resistant Hypertension



Calhoun et al. CHEST 2003

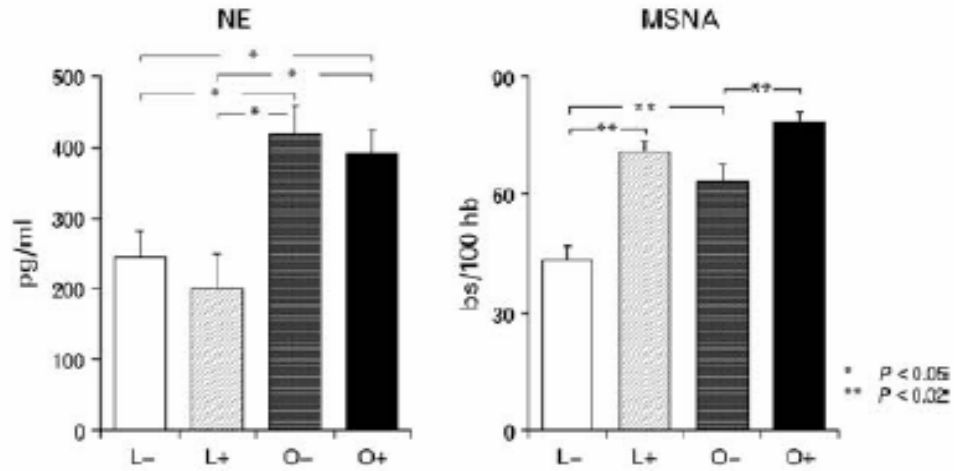
Meccanismi fisiopatologici associati all'OSAS che potenzialmente aumentano il rischio CV



Modificato da JACC 2008:52; 686-717

The sympathetic nervous system and the metabolic syndrome

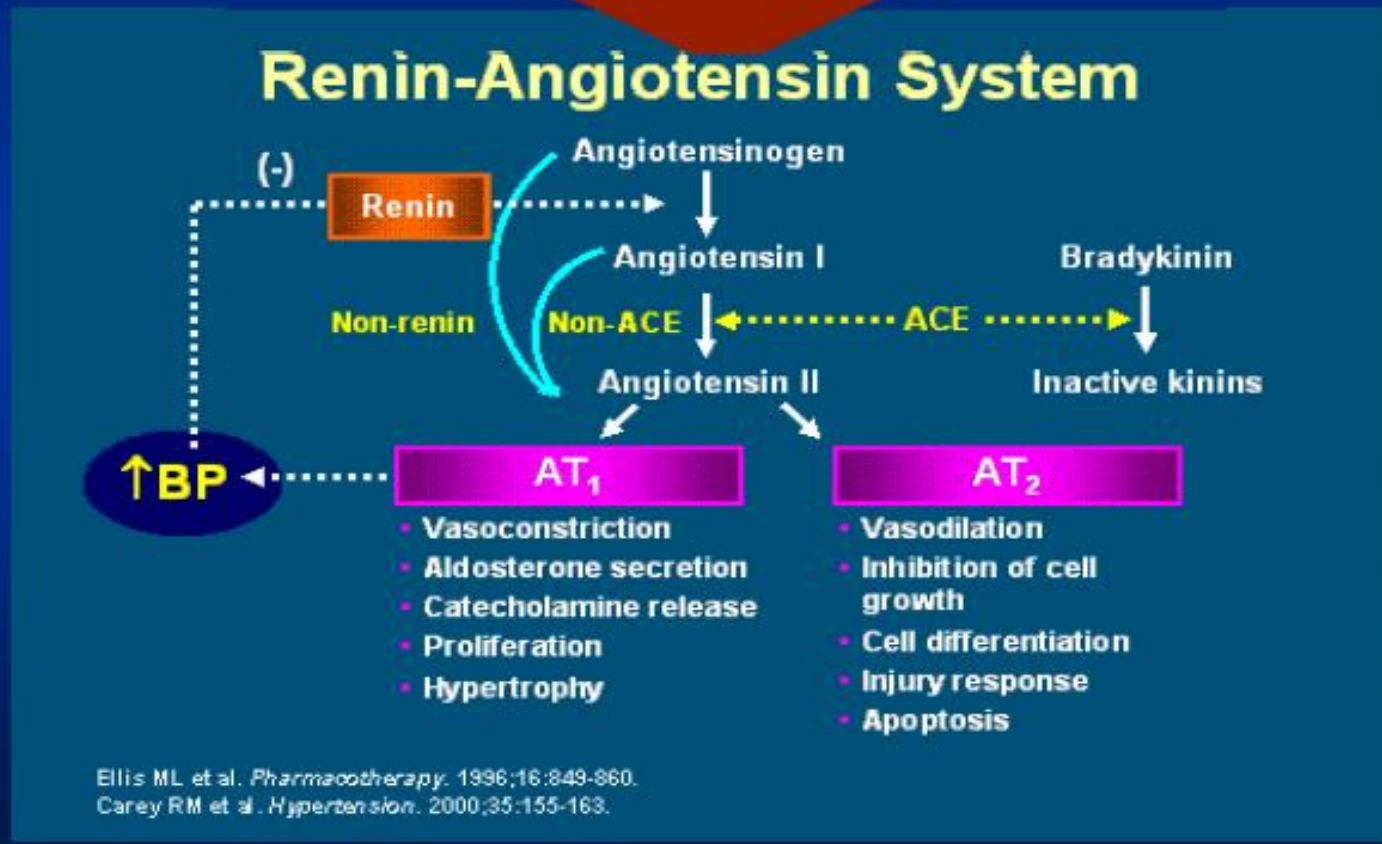
Giuseppe Mancia[a], Pascal Bousquet[b], Jean Luc Elghozi[c], Murray Esler[d], Guido Grassi[a], Stevo Julius[e], John Reid[f] and Peter A. Van Zwieten[g]



Plasma noradrenaline (NE) and muscle sympathetic nerve traffic (MSNA) values detected in lean subjects without (L–) and with (L+) sleep apnoea and in age-matched obese patients without (O–) and with (O+) sleep apnoea. Data are shown as means ± SEM. Asterisks (*$P < 0.05$, **$P < 0.01$) refer to the statistical significance between groups. Modified from Grassi *et al.* [93].

Journal of Hypertension 2007, 25:909–920

IPERTONO SIMPATICO renale



Ellis ML et al. *Pharmacotherapy*. 1996;16:849-860.
Carey RM et al. *Hypertension*. 2000;35:155-163.

The New England
Journal of Medicine

VOLUME 342 MAY 11, 2000 NUMBER 19

PROSPECTIVE STUDY OF THE ASSOCIATION BETWEEN SLEEP-DISORDERED BREATHING AND HYPERTENSION

PAUL E. PEPPARD, PH.D., TERRY YOUNG, PH.D., MARI PALTA, PH.D., AND JAMES SKATRUD, M.D.

ABSTRACT

Background Sleep-disordered breathing is prevalent in the general population and has been linked to chronically elevated blood pressure in cross-sectional epidemiologic studies. We performed a prospective, population-based study of the association between objectively measured sleep-disordered breathing and hypertension (defined as a laboratory-measured blood pressure of at least 140/90 mm Hg or the use of antihypertensive medications).

Methods We analyzed data on sleep-disordered breathing, blood pressure, habitus, and health history at base line and after four years of follow-up in 709 participants of the Wisconsin Sleep Cohort Study (and after eight years of follow-up in the case of 184 of these participants). Participants were assessed overnight by 18-channel polysomnography for sleep-disordered breathing, as defined by the apnea–hypopnea index (the number of episodes of apnea and hypopnea per hour of sleep). The odds ratios for the presence of hypertension at the four-year follow-up study according to the apnea–hypopnea index at base line were estimated after adjustment for base-line hypertension status, body-mass index, neck and waist circumference, age, sex, and weekly use of alcohol and cigarettes.

TABLE 3. ADJUSTED ODDS RATIOS FOR HYPERTENSION AT A FOLLOW-UP SLEEP STUDY, ACCORDING TO THE APNEA–HYPOPNEA INDEX AT BASE LINE.*

BASE-LINE APNEA–HYPOPNEA INDEX	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS AND NONMODIFIABLE RISK FACTORS (AGE AND SEX)	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS, NONMODIFIABLE RISK FACTORS, AND HABITUS (BMI AND WAIST AND NECK CIRCUMFERENCE)	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS, NONMODIFIABLE RISK FACTORS, HABITUS, AND WEEKLY ALCOHOL AND CIGARETTE USE
	odds ratio (95% confidence interval)			
0 events/hr†	1.0	1.0	1.0	1.0
0.1–4.9 events/hr	1.66 (1.35–2.03)	1.65 (1.33–2.04)	1.42 (1.14–1.78)	1.42 (1.13–1.78)
5.0–14.9 events/hr	2.74 (1.82–4.12)	2.71 (1.78–4.14)	2.03 (1.29–3.19)	2.03 (1.29–3.17)
≥15.0 events/hr	4.54 (2.46–8.36)	4.47 (2.37–8.43)	2.89 (1.47–5.69)	2.89 (1.46–5.64)
P for trend‡	<0.001	<0.001	0.002	0.002

*Hypertension was defined as a blood pressure of at least 140/90 mm Hg or the use of antihypertensive medications. Data on 893 follow-up sleep studies from 709 participants were analyzed. The odds ratios and confidence intervals were adjusted for the fact that 184 participants completed two follow-up sleep studies. BMI denotes body-mass index.

†This category served as the reference group.

‡P values are for the linear trend of the logistic-regression coefficients ($\log_e$ of the odds ratios).

Renin–angiotensin–aldosterone system in patients with sleep apnoea: prevalence of primary aldosteronism

A. Di Murro, L. Petramala*, D. Cotesta*, L. Zinnamosca*, E. Crescenzi*, C. Marinelli*, M. Saponara† and C. Letizia**

Abstract

Obstructive sleep apnoea (OSA) is a sleep disorder characterized by recurrent episodes of oxygen desaturation during sleep, representing an independent risk factor for cardiovascular disease, such as myocardial infarction, stroke, congestive heart failure and resistant hypertension. Several neurohormonal mechanisms have been suggested to account for blood pressure increases, such as sympathetic nervous system hyperactivity, oxidative stress, renin–angiotensin–aldosterone system (RAAS) activation, endothelin system activation, and endothelial dysfunction. The aim of this study was to evaluate the behaviour of RAAS and the presence of primary aldosteronism (PA) in these patients and possible correlations between RAAS and the severity of OSA. From October 2007 to November 2008 we studied 325 consecutive newly diagnosed hypertensive patients; 71 patients (21.8%) presented with clinical signs of sleep disorders, evaluated also through a specific questionnaire (Epworth Sleepiness Scale). In hypertensive patients with sleep disorders, 53 patients were affected by OSA; in this group 18 patients were affected by PA (five with aldosterone-producing adenoma (APA) and 13 with bilateral hyperplasia (IHA)); obesity was also demonstrated (BMI > 30 kg/m^2). Overall, in patients with OSA PRA levels correlated positively with apnoea/hypopnoea index (AHI; $r = 0.35$; $p<0.01$), and in all groups the waist circumference and the neck circumference were correlated positively with AHI ($r = 0.3$ $p<0.02$ and $r = 0.3$ $p<0.03$, respectively). We revealed a high prevalence of PA in patients with OSA, and we can conclude that patients with hypertension and OSA, especially those who are newly diagnosed, must be evaluated for PA.

Introduction

Obstructive sleep apnoea (OSA) is characterized by recurrent episodes of partial or complete obstruction of the upper airways during sleep resulting in oxygen desaturation and arousal from sleep.[1] OSA is an independent risk factor for cardiovascular disease, including myocardial infarction, stroke, congestive heart failure and arterial hypertension.[2-10] Approximately 50–60% of patients with OSA are hypertensive, and it is estimated that 50% of these hypertensive patients have multi-drug-resistant hypertension.[11]

A variety of neurohormonal mechanisms have been suggested to account for blood pressure increases in patients with OSA, such as sympathetic nervous system hyperactivity, oxidative stress, renin–angiotensin–aldosterone system (RAAS) activation, endothelin system activation, and endothelial dysfunction.[12-14]

The aim of this study was to evaluate: (1) the behaviour of the RAAS in patients with OSA; (2) the prevalence of primary aldosteronism (PA) in these patients; and (3) the possible correlations between RAAS and severity of OSA.

Material and methods

We studied 325 consecutive newly hypertensive patients who were referred to the Day Hospital of Internal Medicine and Secondary Hypertension, Department of Clinical Sciences, University of Rome 'Sapienza', Italy, from October 2007 to November 2008. Some 254 hypertensive patients did not have any features of sleep disorders (154 male, 100 female; mean age 50.8 ± 7.5 years), and 71 patients (21.8%; 51 male, 20 female; mean age 51.5 ± 9.7 years) presented with clinical signs of sleep disorders (Table 1). The excessive daytime sleepiness was evaluated by the use of a specific questionnaire, the Epworth Sleepiness Scale.[15] If the score was equal to or greater than 10, patients were referred to Centre for Diagnosis and Cure of Roncopathy, where they underwent polysomnography for the validation of OSA. Patients without a diagnosis of OSA were classified as habitual snorers.

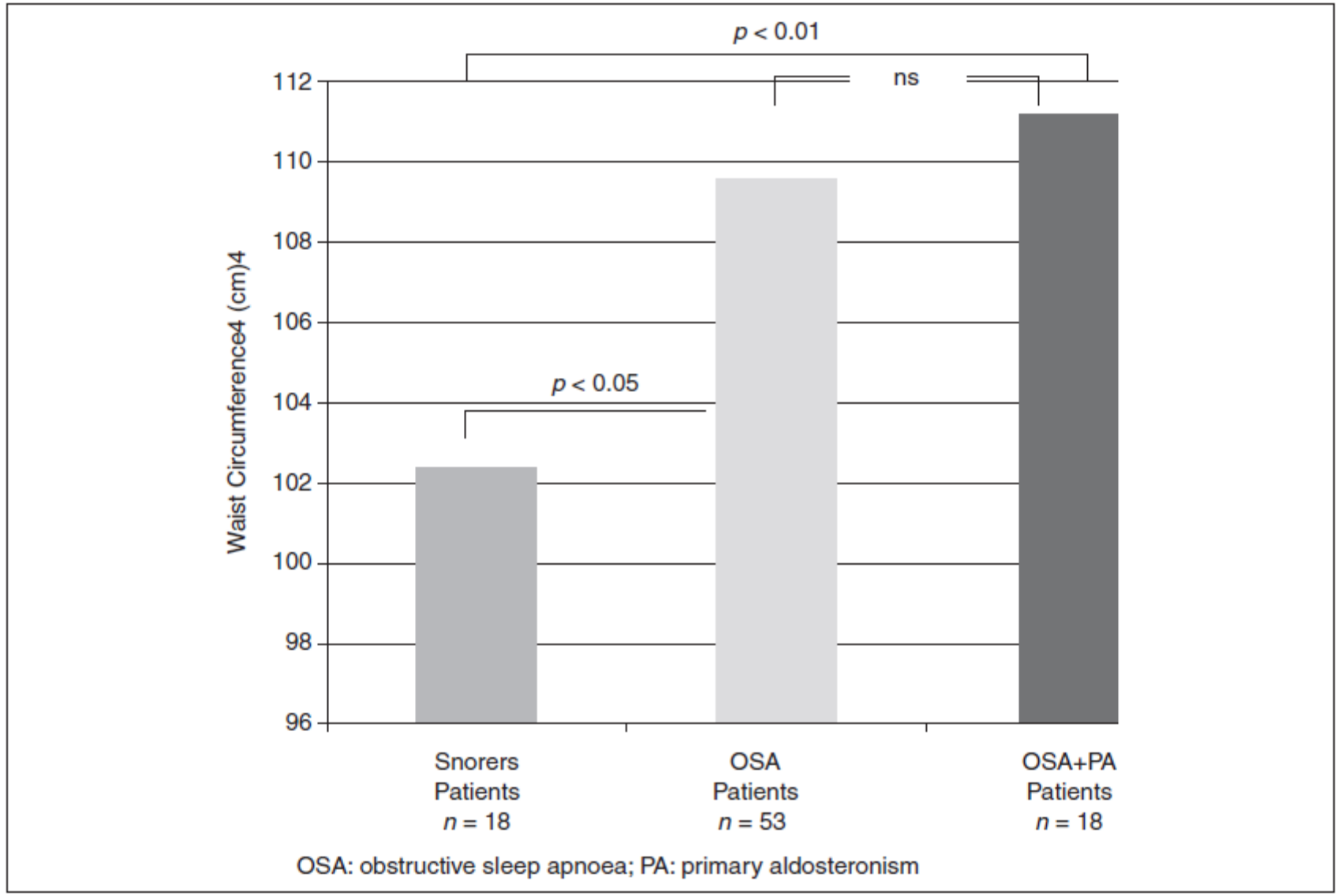


Figure 1
Waist circumference in studied groups.

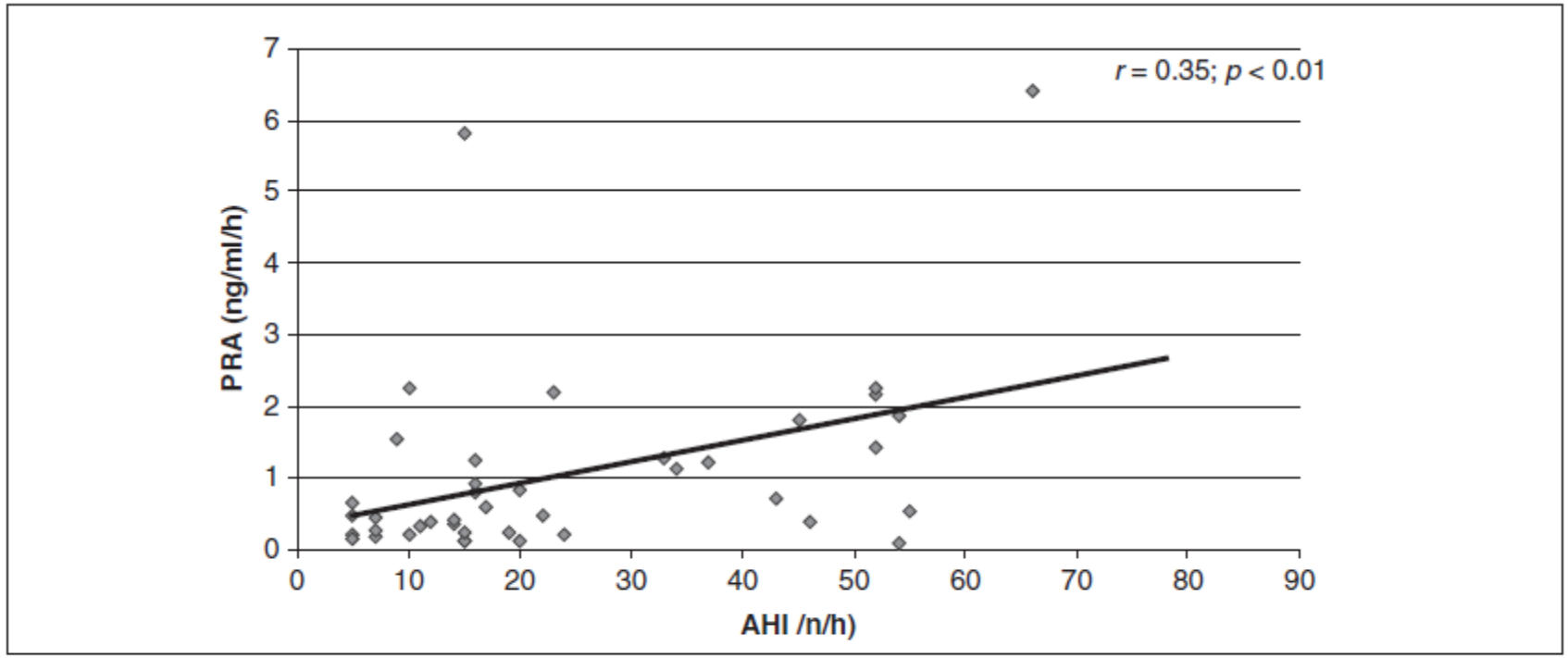


Figure 2
Correlation between plasma renin activity (PRA) levels and apnoea/hypopnoea index (AHI) in 53 patients with obstructive sleep apnoea **(Spearman test).**

NEW RESEARCH

JCSM
Journal of Clinical Sleep Medicine

Severity of Obstructive Sleep Apnea is Related to Aldosterone Status in Subjects with Resistant Hypertension

Carolina C. Gonzaga, M.D.[1]; Krishna K. Gaddam, M.D.[1]; Mustafa I. Ahmed, M.D.[1]; Eduardo Pimenta, M.D.[2]; S. Justin Thomas, B.S., R.P.S.G.T.[1]; Susan M. Harding, M.D.[3]; Suzanne Oparil, M.D.[1]; Stacey S. Cofield, Ph.D.[4]; David A. Calhoun, M.D.[1]

[1]Vascular Biology and Hypertension Program, Division of Cardiovascular Disease, University of Alabama at Birmingham, AL; [2]Endocrine Hypertension Research Center and Clinical Center of Research Excellence in Cardiovascular Disease and Metabolic Disorders, University of Queensland School of Medicine, Princess Alexandra and Greenslopes Hospitals, Brisbane, QLD, Australia; [3]Sleep/Wake Disorders Center, Division of Pulmonary, Allergy and Critical Care Medicine, University of Alabama at Birmingham, AL; [4]Department of Biostatistics, University of Alabama at Birmingham, AL

Background: We previously described a significant correlation between plasma aldosterone concentration (PAC) and severity of obstructive sleep apnea (OSA) in patients with resistant hypertension. This investigation examines the relationship between aldosterone status and OSA in patients with resistant hypertensive—with and without hyperaldosteronism.

Methods and Results: One hundred and nine consecutive patients with resistant hypertension were prospectively evaluated with plasma renin activity (PRA), PAC, 24-hour urinary aldosterone excretion (UAldo), and polysomnography. Hyperaldosteronism (PRA < 1 $ng \cdot mL^{-1} \cdot h^{-1}$ and UAldo ≥ 12 µg/24-h) prevalence was 28% and OSA prevalence was 77%. In patients with hyperaldosteronism, OSA prevalence was 84%, compared with 74% in hypertensive patients with normal aldosterone levels. There were no significant differences in body mass index or neck circumference between aldosterone groups. PAC and UAldo were both significantly correlated with apnea-hypopnea index (AHI) in the high-aldosterone group ($\rho = 0.568$, $p = 0.0009$; $\rho = 0.533$, $p = 0.002$, respectively). UAldo correlated weakly with apnea-hypopnea index in the normal-aldosterone group, but there was no significant correlation between PAC and AHI in the normal-aldosterone group ($\rho = 0.224$, $p = 0.049$; $\rho = 0.015$, $p = 0.898$, respectively).

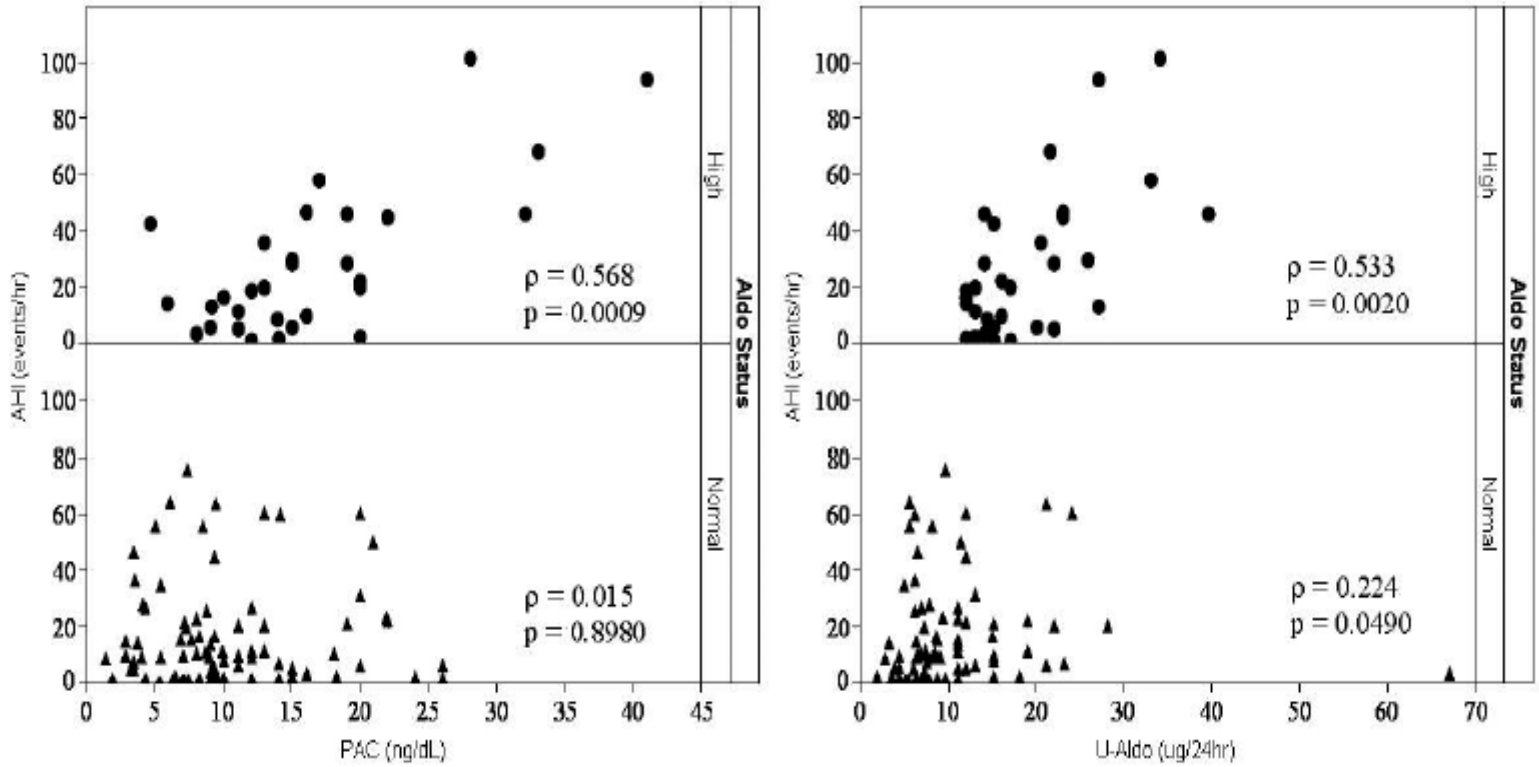
Conclusions: Our analysis of patients with resistant hypertension confirms a markedly high prevalence of OSA in this group. Furthermore, severity of OSA was greater in those patients with hyperaldosteronism and related to the degree of aldosterone excess. The correlation between OSA severity and aldosterone supports the hypothesis that aldosterone excess contributes to greater severity of OSA.

Keywords: Obstructive sleep apnea, aldosterone, resistant hypertension, sleep disorder, cardiovascular disease

Citation: Gonzaga CC; Gaddam KK; Ahmed MI; Pimenta E; Thomas SJ; Harding SM; Oparil S; Cofield SS; Calhoun DA. Severity of obstructive sleep apnea is related to aldosterone status in subjects with resistant hypertension. *J Clin Sleep Med* 2010;6(4):363-368.

SCIENTIFIC INVESTIGATIONS

Figure 1—Correlation between apnea-hypopnea index (AHI), plasma-aldosterone concentration (PAC), and 24-h urinary aldosterone excretion (UAldo) in high (H-Aldo) and normal (N-Aldo) aldosterone subjects



PAC and UAldo were positively and significantly correlated with AHI in the H-Aldo group (Spearman's ρ = 0.568, p = 0.0009; Spearman's ρ = 0.533, p = 0.0020, respectively). To a lesser degree, UAldo was correlated with AHI in the N-Aldo subjects (Spearman's ρ = 0.224, p = 0.0490). PAC was not significantly correlated with AHI in the N-Aldo group (Spearman's ρ = 0.015, p = 0.8980).

OSA e IPERTENSIONE ARTERIOSA

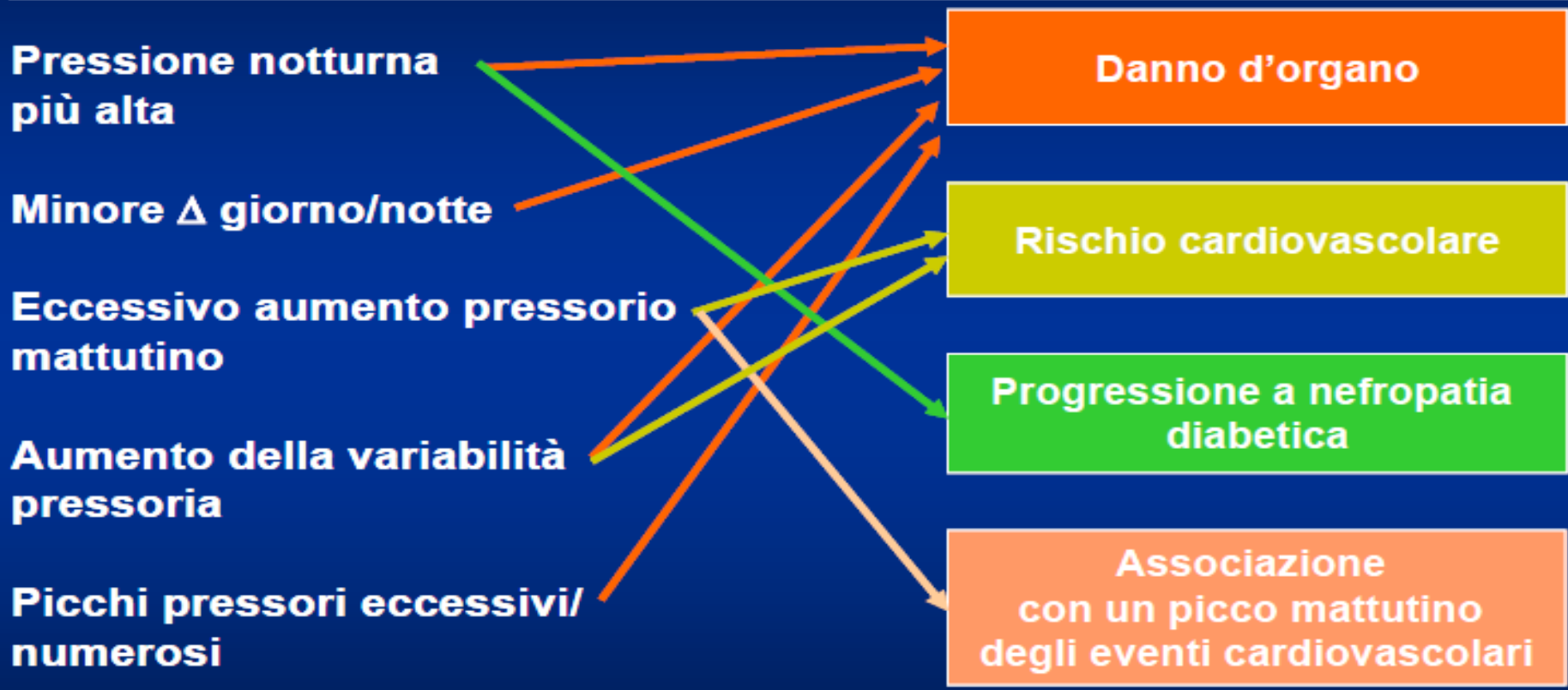
Monitoraggio ambulatorio della PA 24 ore

e

rialzo pressorio al risveglio

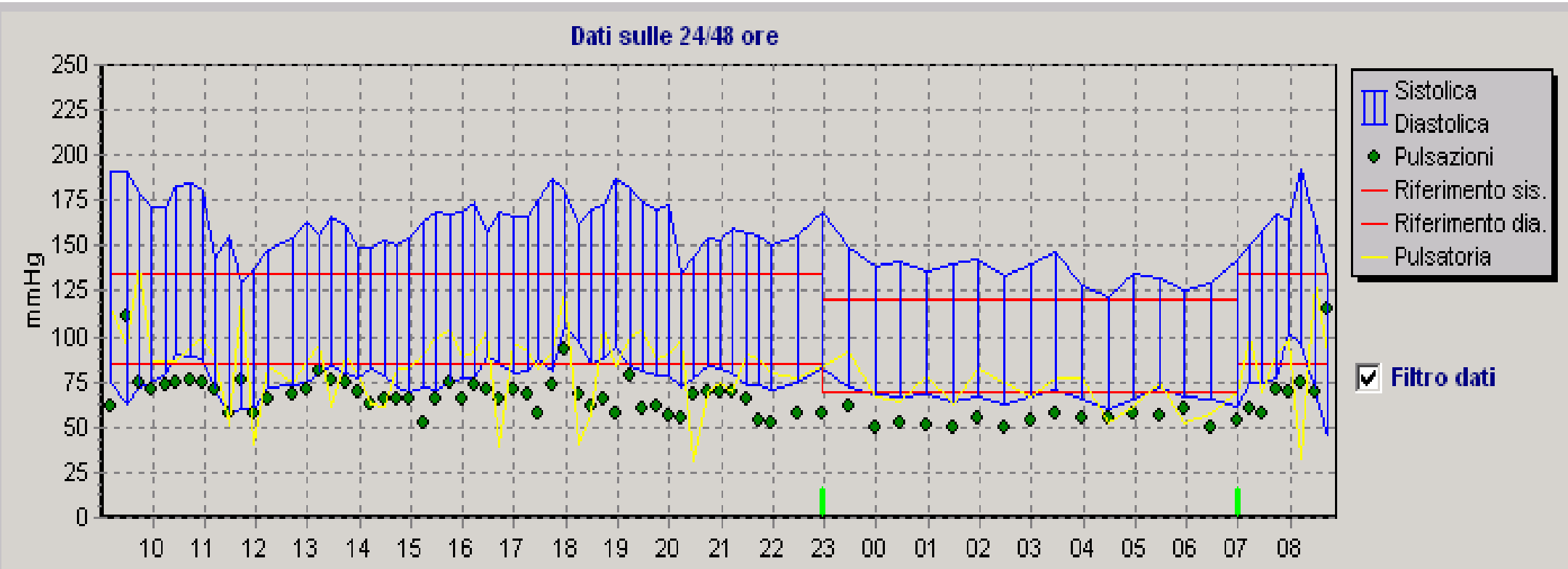
(morning surge pressure)

Rilevanza clinica dei fenomeni pressori nelle 24 ore

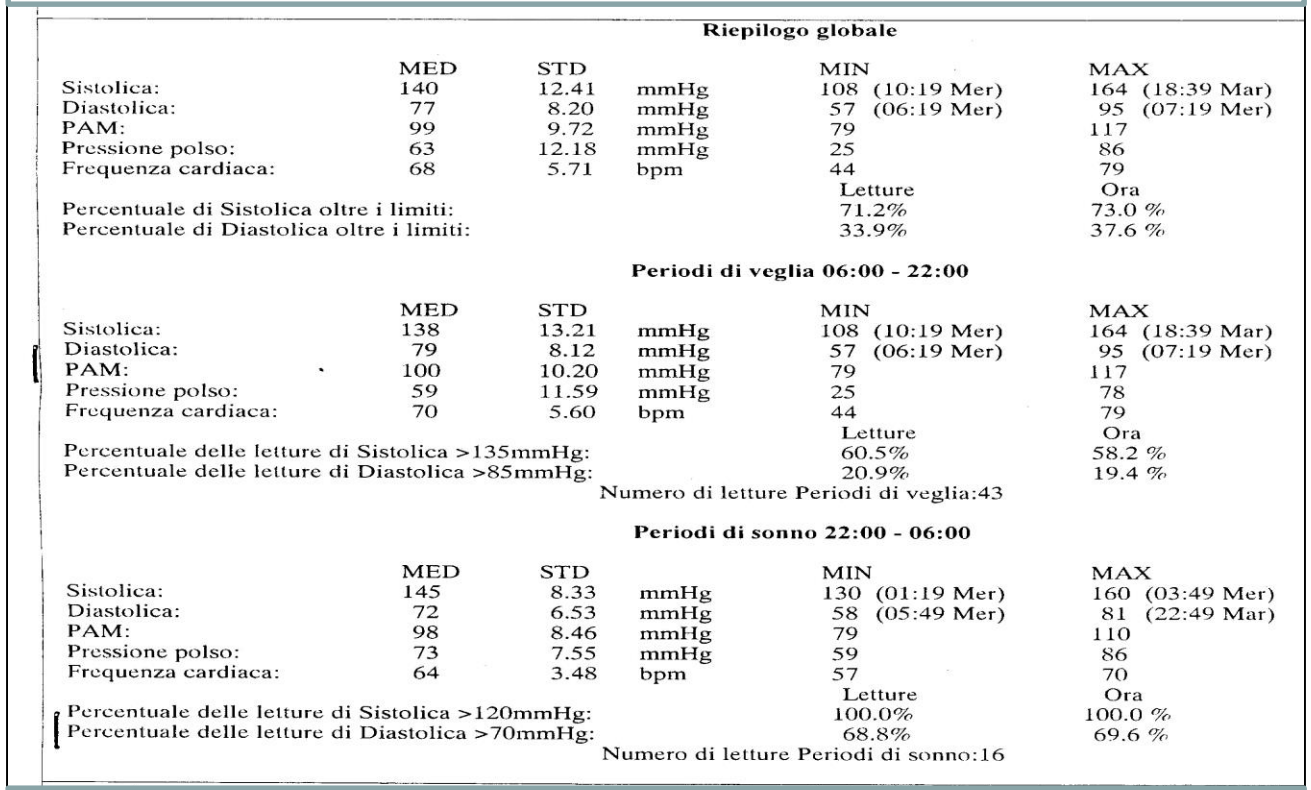


NON DIPPER

Riduzione notturna della pressione inferiore al 10% dei valori medi diurni.



ABPM



Riepilogo globale

	MED	STD		MIN	MAX
Sistolica:	140	12.41	mmHg	108 (10:19 Mer)	164 (18:39 Mar)
Diastolica:	77	8.20	mmHg	57 (06:19 Mer)	95 (07:19 Mer)
PAM:	99	9.72	mmHg	79	117
Pressione polso:	63	12.18	mmHg	25	86
Frequenza cardiaca:	68	5.71	bpm	44	79
				Letture	Ora
Percentuale di Sistolica oltre i limiti:				71.2%	73.0 %
Percentuale di Diastolica oltre i limiti:				33.9%	37.6 %

Periodi di veglia 06:00 - 22:00

	MED	STD		MIN	MAX
Sistolica:	138	13.21	mmHg	108 (10:19 Mer)	164 (18:39 Mar)
Diastolica:	79	8.12	mmHg	57 (06:19 Mer)	95 (07:19 Mer)
PAM:	100	10.20	mmHg	79	117
Pressione polso:	59	11.59	mmHg	25	78
Frequenza cardiaca:	70	5.60	bpm	44	79
				Letture	Ora
Percentuale delle letture di Sistolica >135mmHg:				60.5%	58.2 %
Percentuale delle letture di Diastolica >85mmHg:				20.9%	19.4 %

Numero di letture Periodi di veglia:43

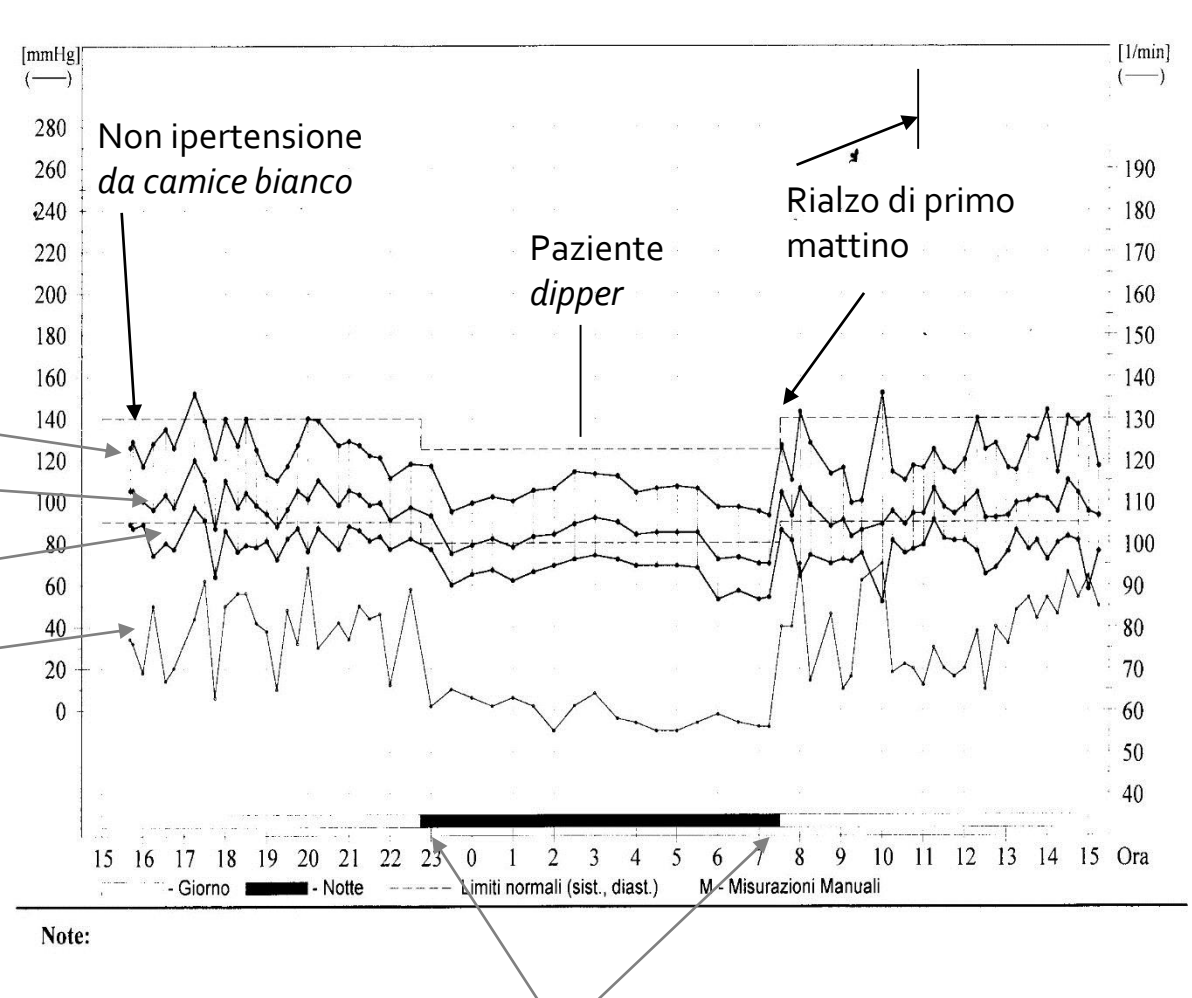
Periodi di sonno 22:00 - 06:00

	MED	STD		MIN	MAX
Sistolica:	145	8.33	mmHg	130 (01:19 Mer)	160 (03:49 Mer)
Diastolica:	72	6.53	mmHg	58 (05:49 Mer)	81 (22:49 Mar)
PAM:	98	8.46	mmHg	79	110
Pressione polso:	73	7.55	mmHg	59	86
Frequenza cardiaca:	64	3.48	bpm	57	70
				Letture	Ora
Percentuale delle letture di Sistolica >120mmHg:				100.0%	100.0 %
Percentuale delle letture di Diastolica >70mmHg:				68.8%	69.6 %

Numero di letture Periodi di sonno:16

NON DIPPER

GRAFICO DELL'ANDAMENTO PRESSORIO OSAS

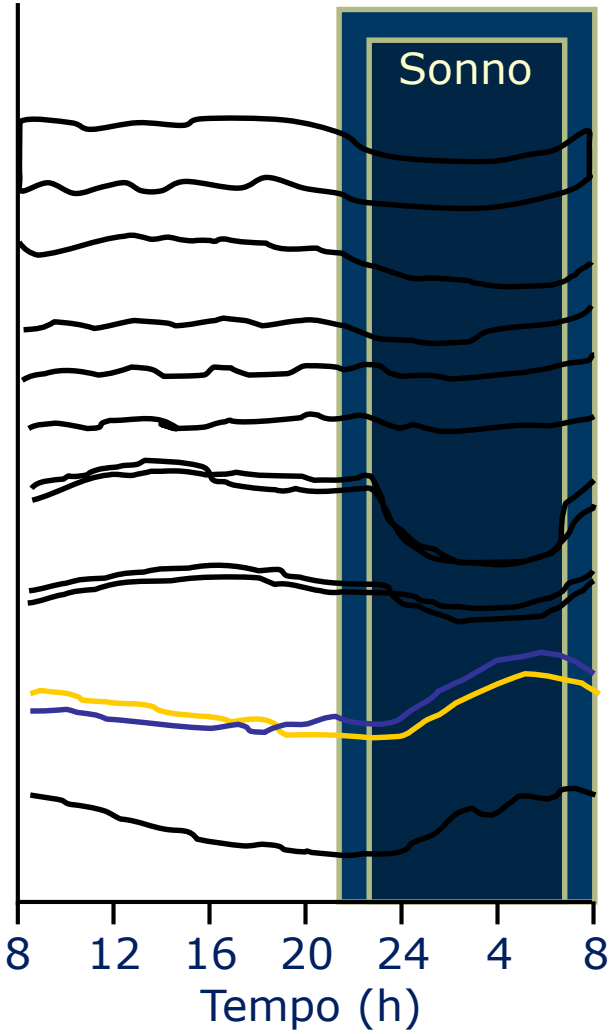


DURANTE LA REGISTRAZIONE
SI TIENE UN DIARIO

Periodo notturno

Ritmo circadiano

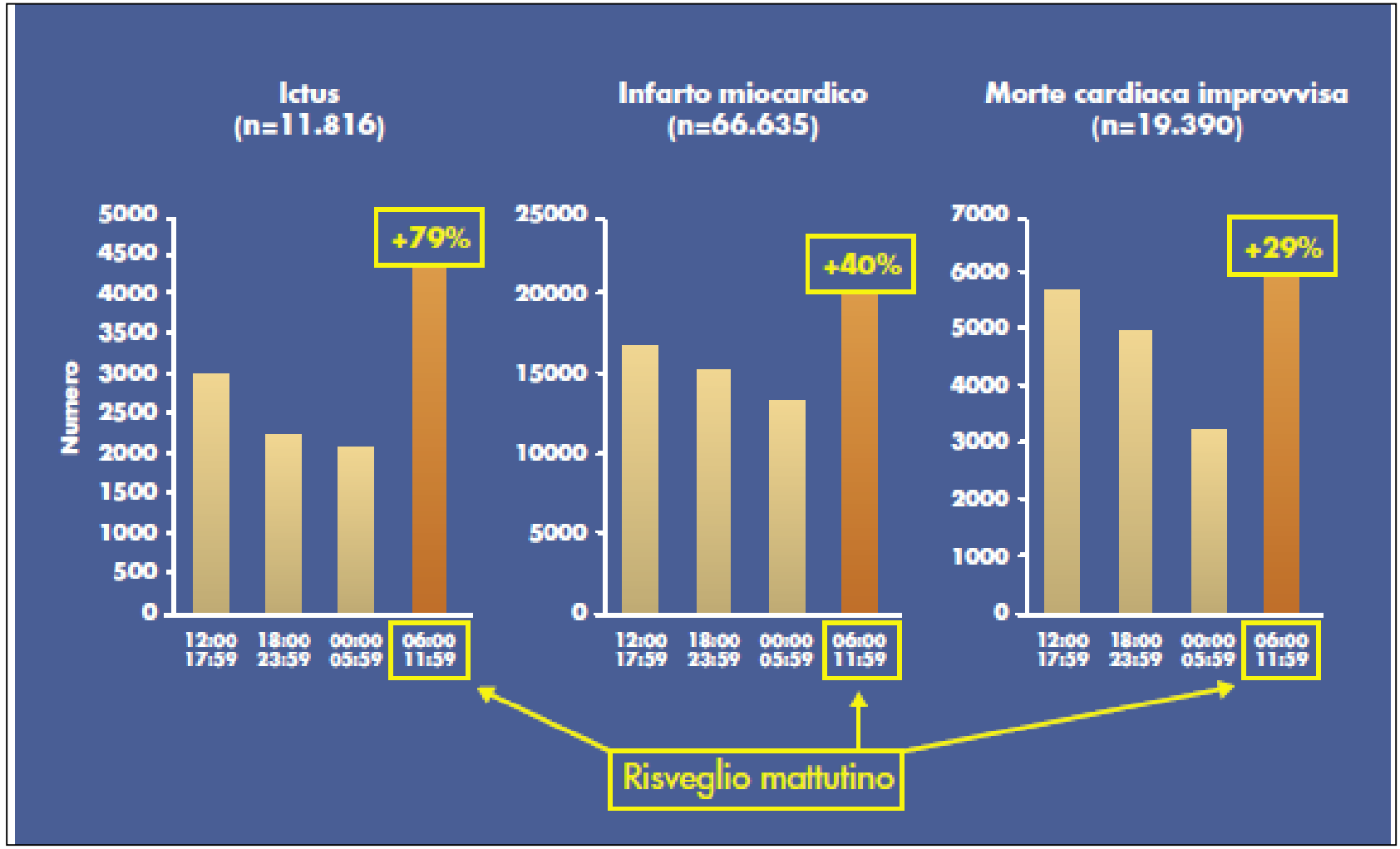
Attivazione del SRAA durante le prime ore del mattino



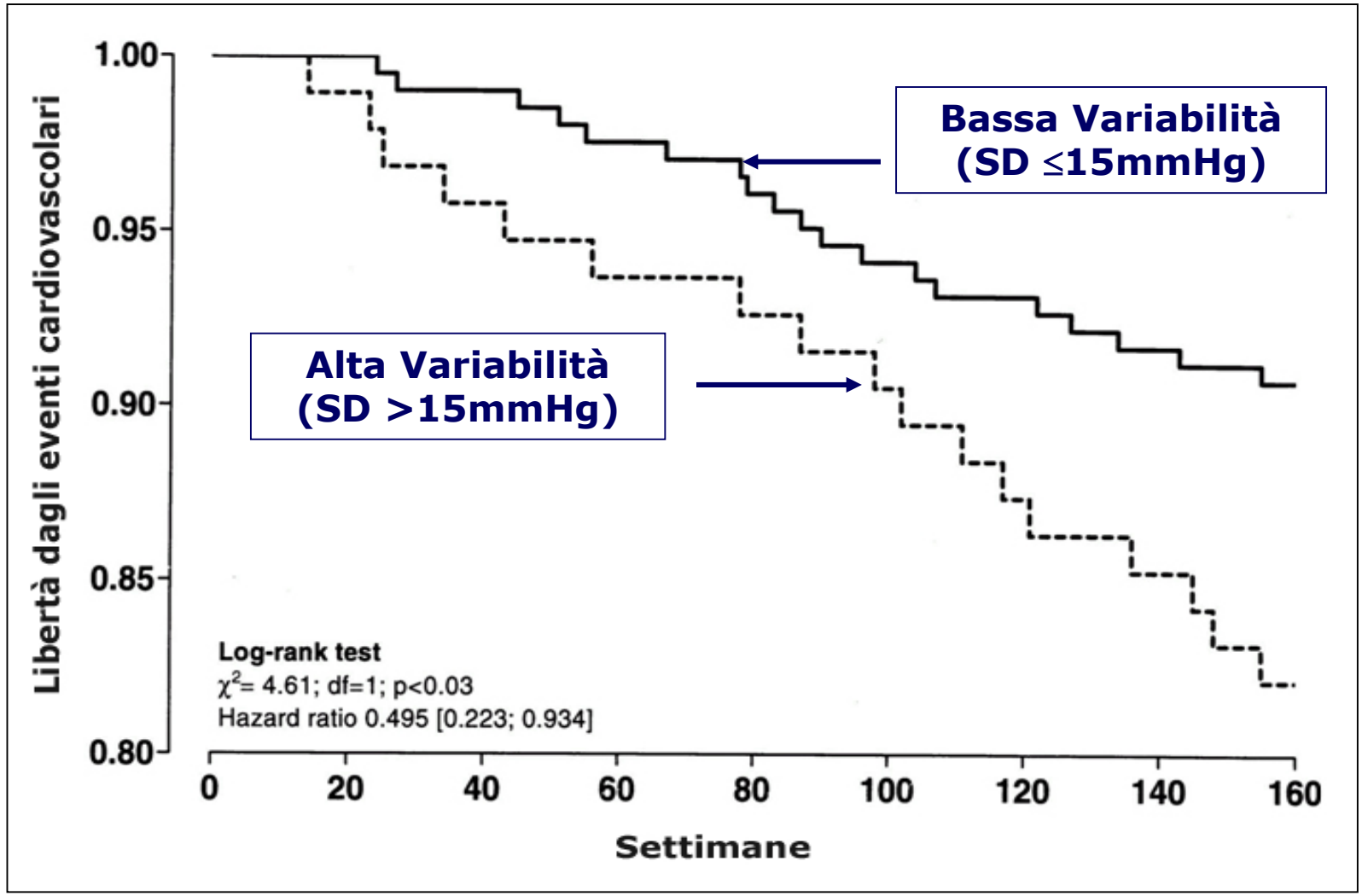
Pressione arteriosa	-15%	**Emodinamica**
Frequenza cardiaca	-10%	
Resistenze periferiche totali	-10%	
Gittata cardiaca	-5%	
Tasso di filtrazione renale	-5%	
NaCl	-67%	**Escrezione elettroliti**
$KHCO_3$	-50%	
Attività reninica plasmatica	+200%	**Ormonale**
Aldosterone plasmatico		
Cortisolo	+100%	

White. *J Hypertens* 2003;21 (Suppl 6):S9–S15

ANDAMENTO CIRCADIANO DEGLI EVENTI CARDIOVASCOLARI

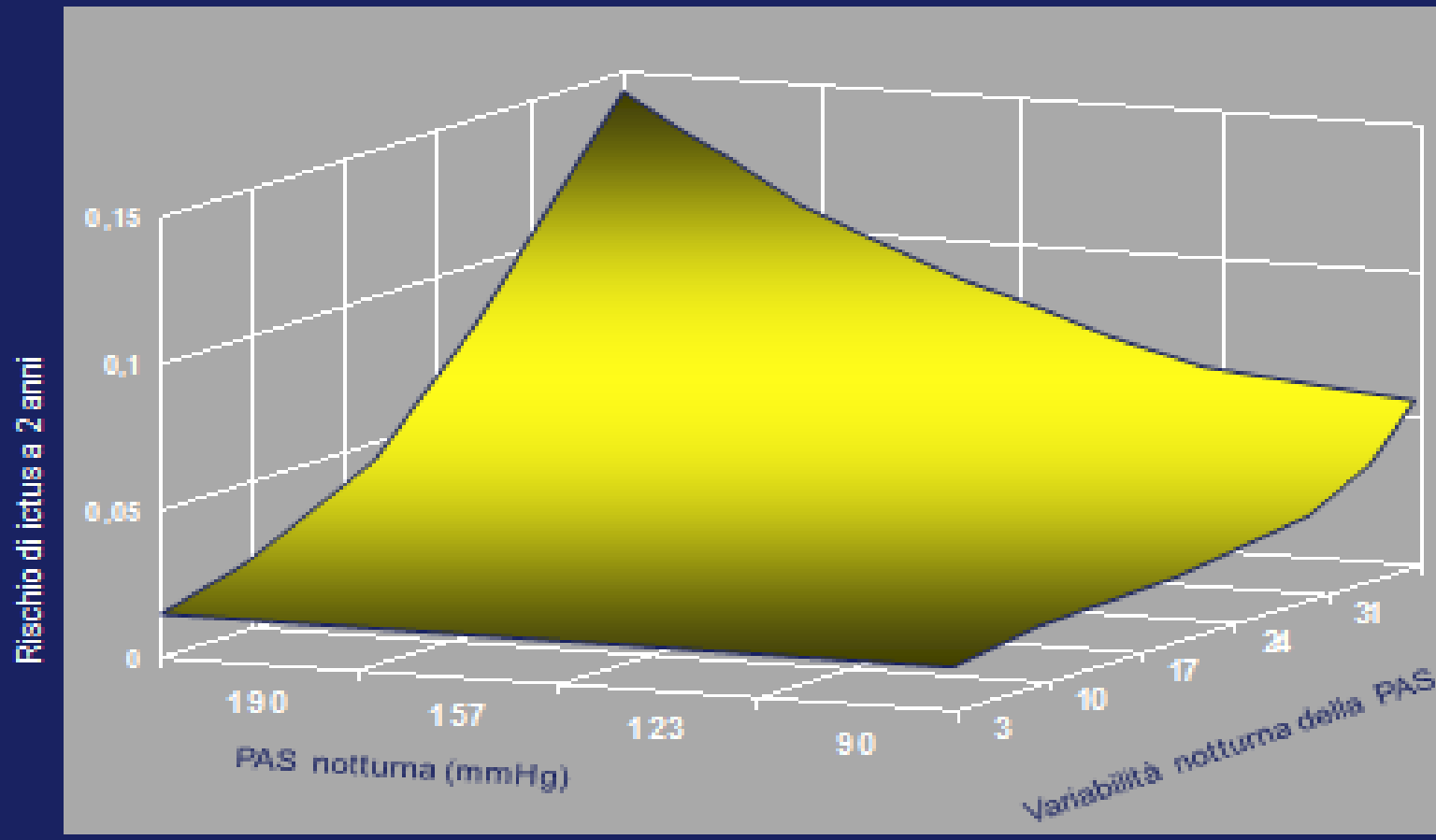


Analisi della sopravvivenza in 286 pazienti con alta e bassa variabilità della PA Sistolica



Sander D et al, Circulation 2000;102:1536

Variabilità della pressione sistolica come fattore di rischio per ictus e mortalità cardiovascolare negli ipertesi anziani



Journal of Hypertension 2003; 21: 1-7

Le patologie cerebrovascolari e l'ictus sono correlate con l'aumento pressorio al risveglio

	Aumento pressorio mattutino > 55 mmHg (n= 53)	Aumento pressorio mattutino ≤ 55 mmHg (n= 466)
Età (gruppi di pari età)	**76 ± 6,9**	**76 ± 6,9**
Infarto cerebrale silente (valutato con risonanza magnetica)	**70%** RR= 2,0 (*p* = 0,04)	**49%**
Ictus clinico	**17%** RR= 2,7 (*p* = 0,04)	**7%**

Kario. Circulation 2003; 107: 1401-1406

Riepilogo globale

	MED	STD		MIN	MAX	Dipping
Sistolica:	144	16.78	mmHg	114 (04:42 Gio)	184 (15:14 Mer)	14.1%
Diastolica:	91	16.61	mmHg	58 (04:42 Gio)	118 (10:57 Mer)	26.6%
PAM:	109	15.64	mmHg	80	146	20.7%
Pressione polso:	53	10.34	mmHg	28	86	
Frequenza cardiaca:	93	15.73	bpm	43	112	

	Letture	Ora
Percentuale di Sistolica oltre i limiti:	80.0%	80.4 %
Percentuale di Diastolica oltre i limiti:	80.0%	79.2 %

Periodi di veglia 06:00 - 22:00

	MED	STD		MIN	MAX
Sistolica:	150	14.72	mmHg	124 (06:12 Gio)	184 (15:14 Mer)
Diastolica:	98	12.51	mmHg	62 (06:32 Gio)	118 (10:57 Mer)
PAM:	116	12.35	mmHg	83	146
Pressione polso:	51	11.37	mmHg	28	86
Frequenza cardiaca:	98	14.57	bpm	43	112

	Letture	Ora
Percentuale delle letture di Sistolica >135mmHg:	79.5%	77.5 %
Percentuale delle letture di Diastolica >85mmHg:	87.2%	84.5 %

Numero di letture Periodi di veglia:39

Periodi di sonno 22:00 - 06:00

	MED	STD		MIN	MAX
Sistolica:	129	11.76	mmHg	114 (04:42 Gio)	155 (22:42 Mer)
Diastolica:	72	8.01	mmHg	58 (04:42 Gio)	90 (22:12 Mer)
PAM:	92	7.12	mmHg	80	104
Pressione polso:	57	5.69	mmHg	47	71
Frequenza cardiaca:	80	9.70	bpm	63	96

	Letture	Ora
Percentuale delle letture di Sistolica >120mmHg:	81.3%	79.3 %
Percentuale delle letture di Diastolica >70mmHg:	62.5%	62.9 %

Numero di letture Periodi di sonno:16

Misure di CENTRALITA'

- I valori normali della D.S. sono:
  - 10-12% per la PA diastolica
  - 12-15% per la PA sistolica

Age and Ageing 2008; **37:** 201–206
doi:10.1093/ageing/afm193

The value of ambulatory blood pressure in older adults: the Dublin outcome study

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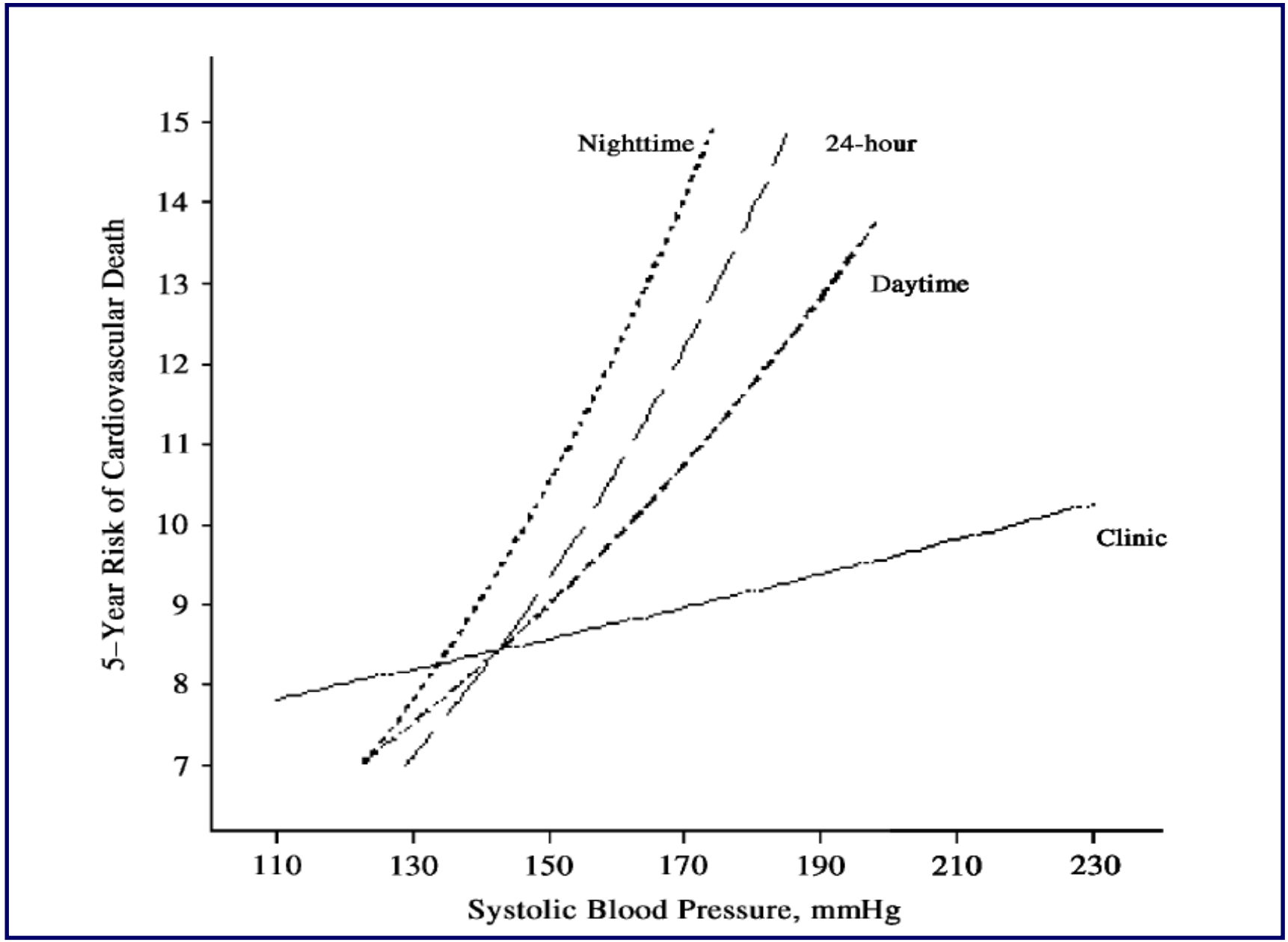
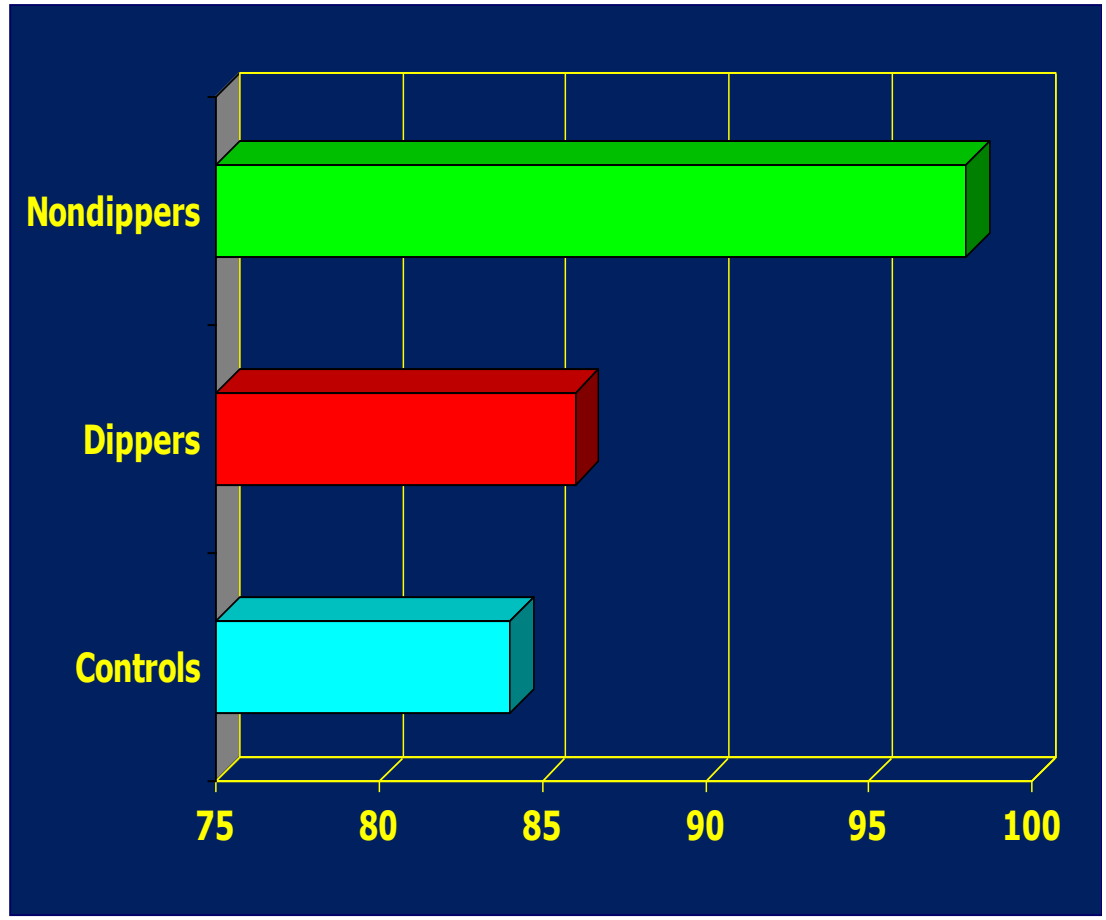
[1] The Lewin Stroke and Rehabilitation Unit, Cambridge University Hospitals NHS Foundation Trust, Addenbrooke's Hospital, Hills Road, Cambridge, UK
[2] The Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Belfield, Dublin 4, Ireland
[3] Blood Pressure Unit, Beaumont Hospital, and Department of Clinical Pharmacology, Royal College of Surgeons in Ireland, Dublin, Ireland



Burr M.L. et all, Age and Ageing 2008

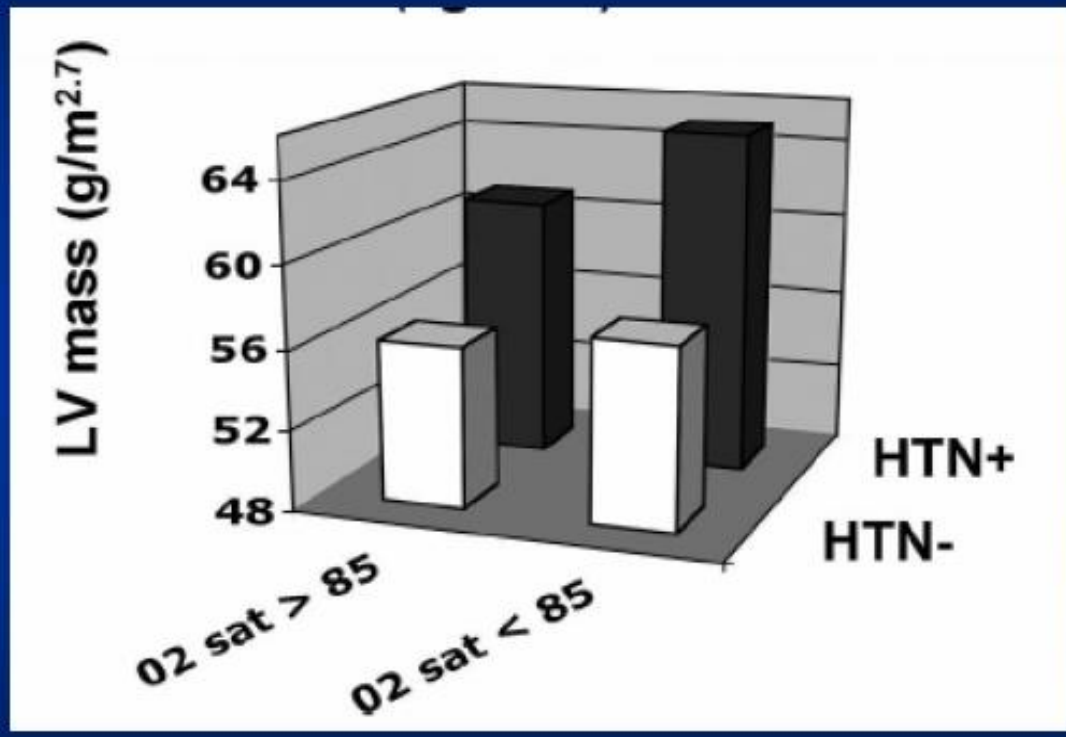
Circadian Blood Pressure Changes and Left Ventricular Hypertrophy in Essential Hypertension



LVMI (g/m^2)

Verdecchia et al. Circulation 1990; 81:528-536

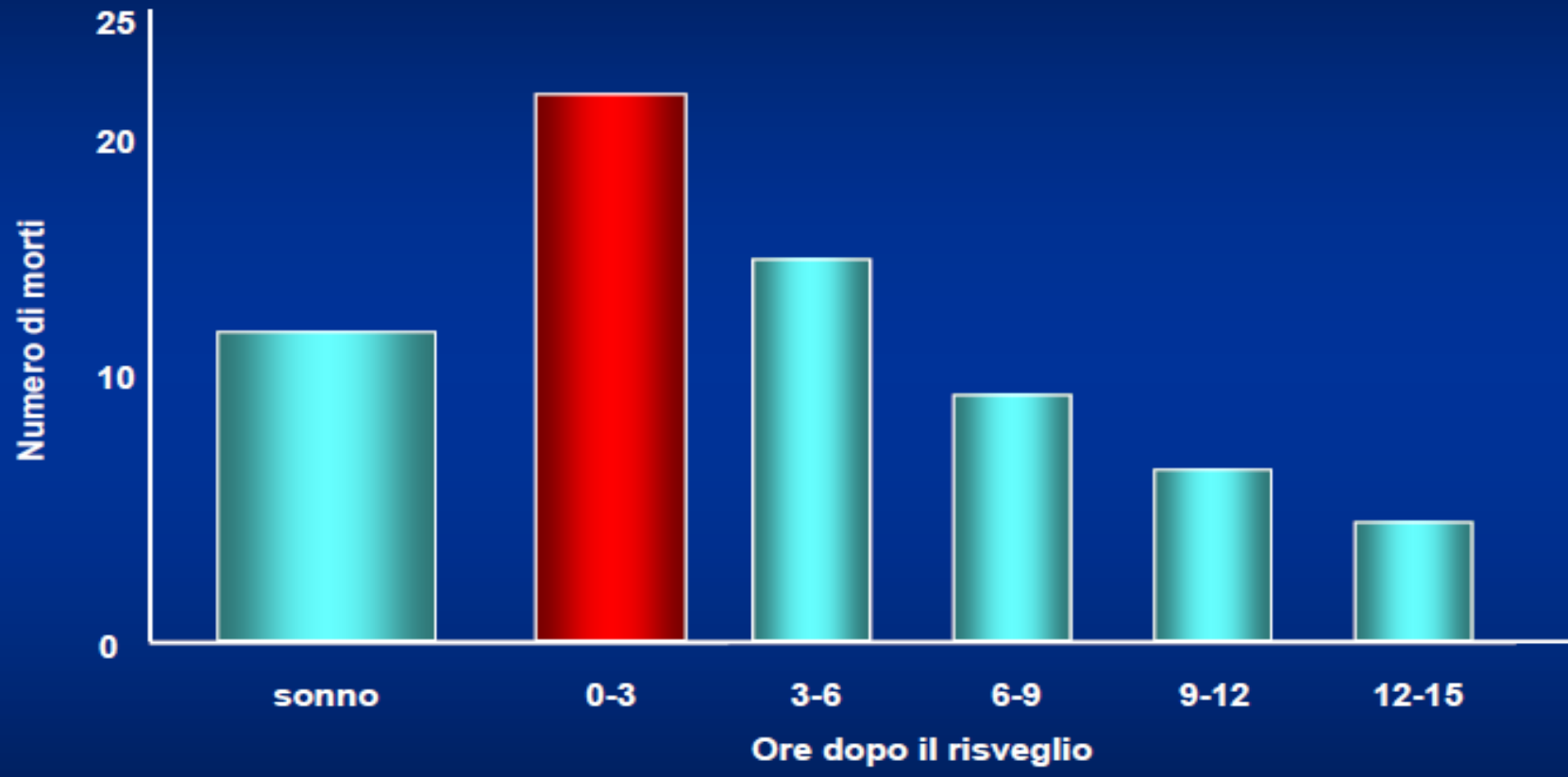
SO_2 e Massa Ventricolare sinistra



Data supporting a possible cause and effect relationship between OSA and LVH.
6 months of nocturnal CPAP to patients with severe OSA was associated with a significant reduction in LV wall thickness.
Chest 2003;124

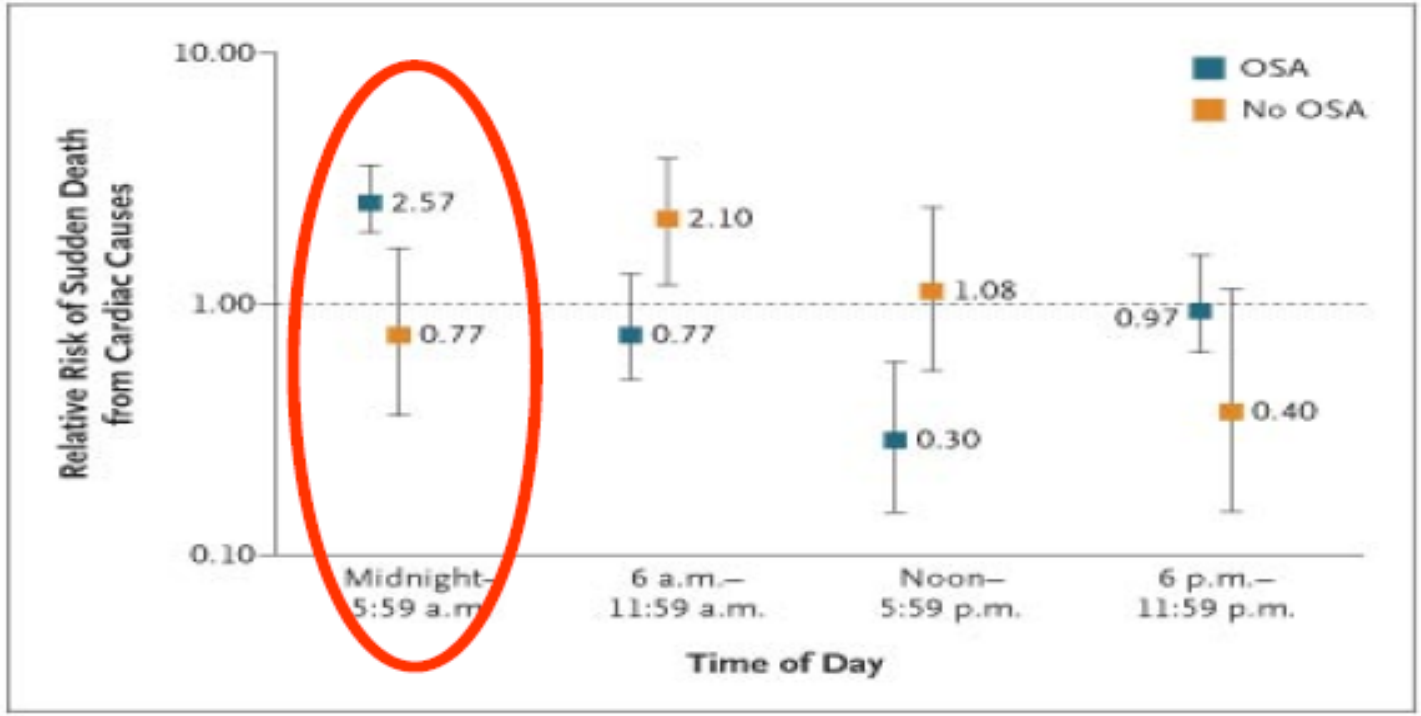
Hypertension 2007;49:34-39

Mortalità nelle prime tre ore dopo il risveglio



Willich. Am J Cardiol 1992; 70: 65-68

Sudden cardiac death and OSA



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VIA MEDICA

ORIGINAL ARTICLE

Cardiology Journal
2013, Vol. 20, No. 5, pp. 519–525
DOI: 10.5603/CJ.2013.0043

ISSN 1897–5593

Early left ventricular functional alterations in patients with obstructive sleep apnea syndrome

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Abstract

Background: *The knowledge regarding myocardial alterations in patients with obstructive sleep apnea syndrome (OSAS) in the absence of any known cardiovascular disorders including hypertension is limited. The aim of this study was to assess the early alterations of left ventricular (LV) functions caused by OSAS before the development of hypertension and other cardiovascular manifestations of OSAS.*

Methods: *Eighty consecutive patients who underwent polysomnography (PSG) were enrolled in the study. Patients with hypertension, diabetes mellitus or any other known cardiac diseases were excluded from the study. Subjects were separated into two groups by their apnea/hypopnea index (AHI) (group 1: AHI < 15, and group 2: AHI ≥ 15). Fourty-three patients with normal polysomnographic examination or mild OSAS (group 1) and 37 patients with moderate to severe OSAS (group 2) were compared. After PSG examination, LV functions were assessed by using the conventional and tissue Doppler echocardiographic methods.*

Results: *The mean age was similar between the groups. The ratio of male patients was higher in group 2 (male/female: 31/12 in group 1 vs. 34/3 in group 2, $p = 0.04$). Body mass index was higher in group 2 ($p = 0.05$). Conventional echocardiography showed that interventricular septum thickness was 9.5 ± 1.1 mm in group 1, and 10.5 ± 1.4 mm in group 2 ($p = 0.02$). Mean left atrial diameter was 35.6 ± 4.1 mm in group 2, and 33.8 ± 3.1 mm in group 1 ($p = 0.04$). Ratio of early to late transmitral diastolic velocities was lower in group 2 ($p = 0.01$), indicating that impairment of diastolic function was more frequent in moderate to severe OSAS patients. Tissue Doppler echocardiography showed that early diastolic myocardial velocity was lower in group 2 (21.1 ± 5.6 cm/s in group 1 vs. 18.3 ± 5.3 cm/s in group 2, $p = 0.01$).*

Conclusions: *Left ventricular diastolic dysfunction, LV hypertrophy and left atrial dilatation occur in patients with OSAS even before the development of hypertension and other cardiovascular diseases.* (Cardiol J 2013; 20, 5: 519–525)

Key words: diastolic dysfunction, obstructive sleep apnea

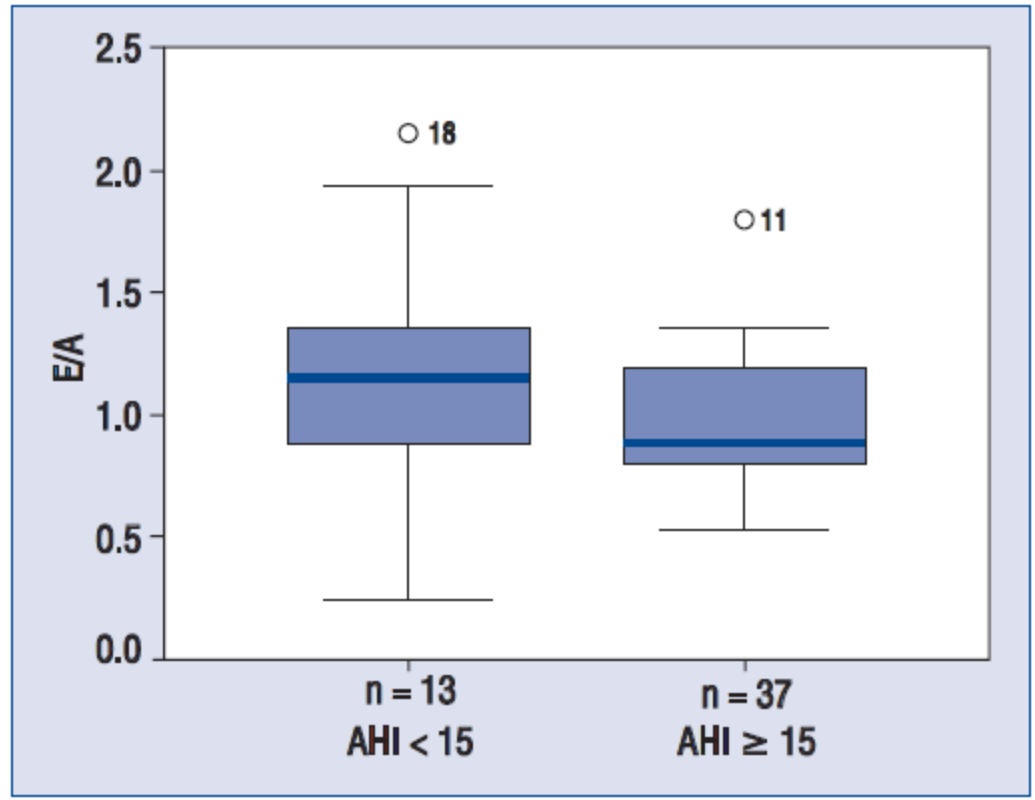

Figure 1. Boxplot graph demonstrates that E/A ratio is lower in patients with moderate-severe obstructive sleep apnea syndrome (OSAS) compared to mild OSAS patients and normal subjects; AHI — apnea/hypopnea index.

Table 2. Echocardiography and tissue Doppler results (nonparametric results are indicated with an*).

	Group (n = 43); mean ± SD [median (min–max)]	Group 2 (n = 37); mean ± SD [median (min-max)]	P
Left ventricular diastolic diameter [mm]	47.4 ± 3.8	47.5 ± 5.9	0.9
Ejection fraction [%]	66.2 ± 4.5	66.8 ± 5.6	0.11
Intraventricular septum thickness [mm]	9.5 ± 1.06	10.5 ± 1.4	**0.02**
Left ventricle posterior wall thickness [mm]	9.07 ± 0.8	9.4 ± 1.3	0.1
Left atrial diameter [mm]	33.8 ± 3.1	35.6 ± 4.05	**0.04**
Transmitral early diastolic flow (E) [cm/s]	63.1 ± 16.7	60.4 ± 14.6	0.4
Transmitral late diastolic flow (A) [cm/s]	57.1 ± 12.2	63.8 ± 12.1	**0.01**
E/A ratio	1.1 ± 0.3	0.9 ± 0.2	**0.01**
Deceleration time [ms]	189.7 ± 42.2 [190 (117–304)]	201.8 ± 59.1 [212 (21–327)]	0.127*
Systolic myocardial velocity from lateral mitral annulus [cm/s]	15.4 ± 3.7	15.5 ± 4.2	0.8
Early diastolic myocardial velocity from lateral mitral annulus [cm/s]	21.1 ± 5.6	18.3 ± 5.3	**0.02**
Late diastolic myocardial velocity from lateral mitral annulus [cm/s]	19.7 ± 5.7	20.2 ± 5.5	0.6

Progressione della malattia renale

- I non-dippers hanno una più rapida riduzione della clearance della creatinina vs i dippers (0,37 +/- 0,26 vs 0,27 +/- 0,09 ml/min/mese P < 0.002)

- L'aumento della proteinuria è maggiore nei non-dippers vs i dippers (993 +/- 438 vs 691 +/- 222 mg/24 h P < 0.009)

- Un pattern di tipo non-dipper dell'ABPM è associato con una più rapida progressione della insufficienza renale. Un migliore controllo della PA notturna è un aiuto aggiuntivo della terapia antiipertensiva".

Timio et al. Clin Nephrol 1995 3(6) : 382-7

Arrhythmias associated with SDB

- The following have been associated with SDB:
  - Classically severe bradycardia (sinus arrest, AV block)
  - Atrial and ventricular ectopics
  - SVT, Atrial flutter, AF
  - Sustained and nonsustained VT
- Causality is not proven but tend to occur most with severe OSA and hypoxia

Association of Nocturnal Arrhythmias with Sleep-disordered Breathing

The Sleep Heart Health Study

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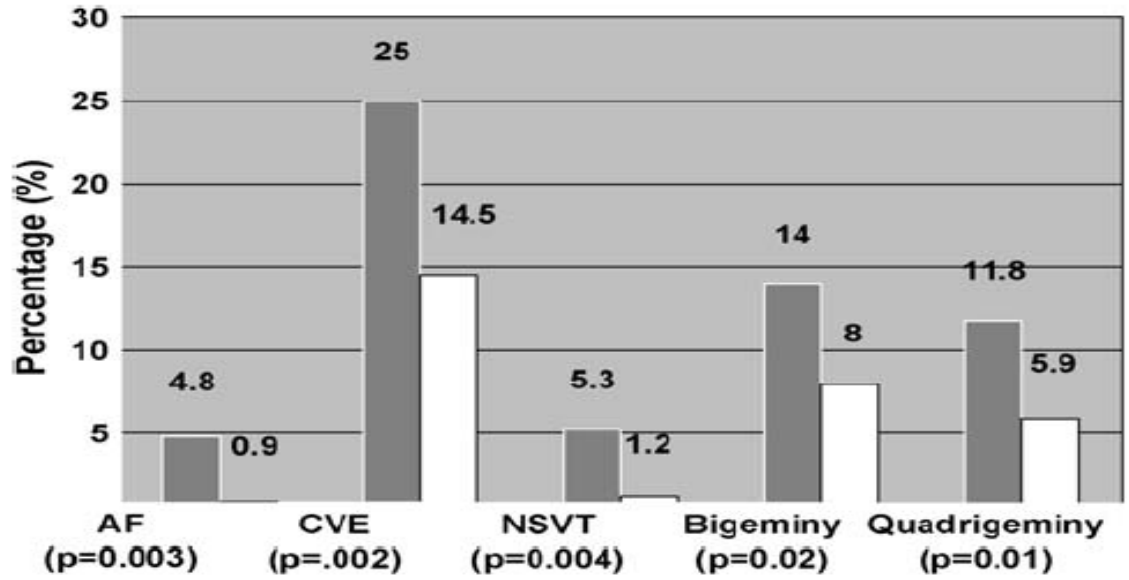
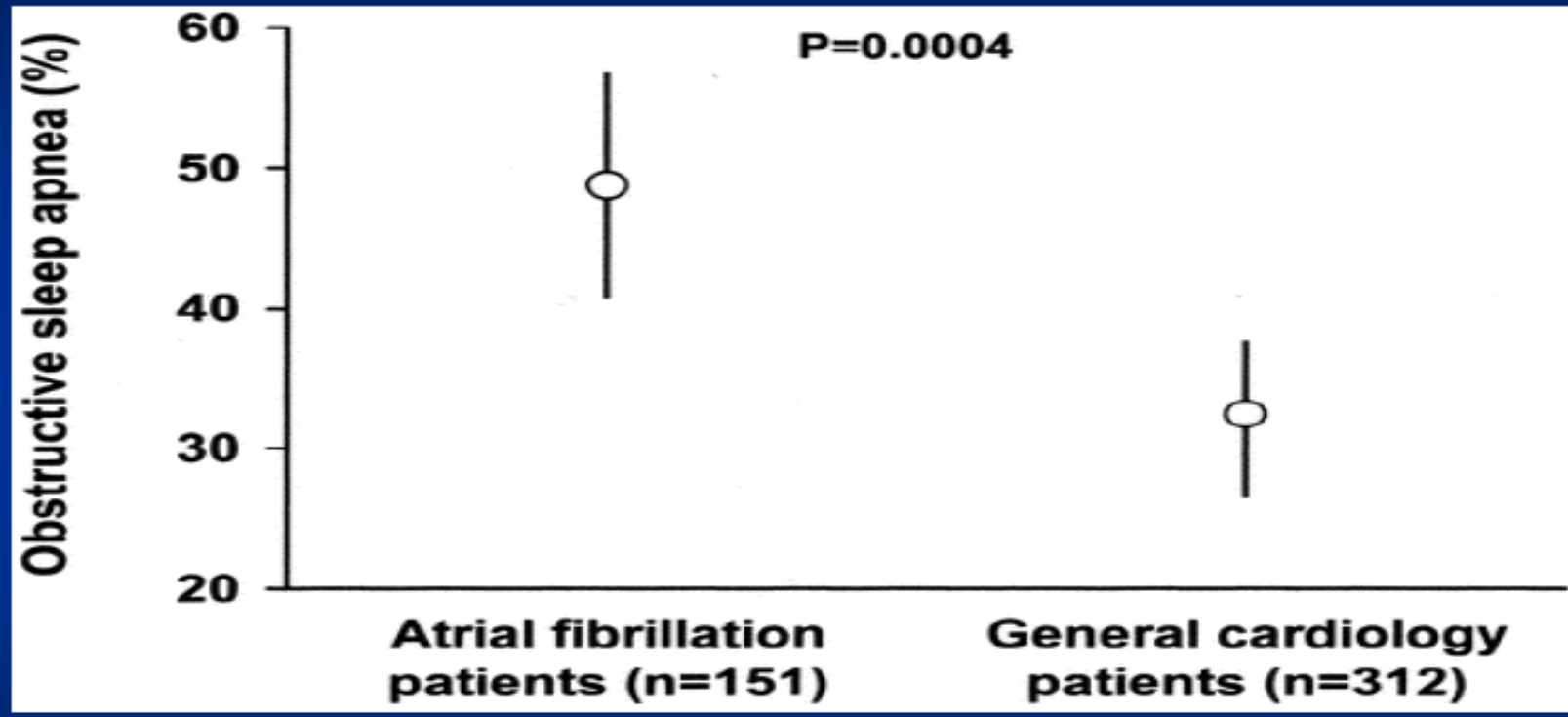


Figure 1. Arrhythmia prevalence (%) according to sleep-disordered breathing (SDB) status. *Shaded bars*, SDB; *open bars*, non-SDB. AF, atrial fibrillation; CVE, complex ventricular ectopy; NSVT, nonsustained ventricular tachycardia. n = 228 with SDB and n = 338 without SDB.

OSA e FA



Gami AS Circulation 2004;110:364-7

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Obstructive Sleep Apnea, Obesity, and the Risk of Incident Atrial Fibrillation

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Rochester, Minnesota

Objectives This study sought to identify whether obesity and obstructive sleep apnea (OSA) independently predict incident atrial fibrillation/flutter (AF).

Background Obesity is a risk factor for AF, and OSA is highly prevalent in obesity. Obstructive sleep apnea is associated with AF, but it is unknown whether OSA predicts new-onset AF independently of obesity.

Methods We conducted a retrospective cohort study of 3,542 Olmsted County adults without past or current AF who were referred for an initial diagnostic polysomnogram from 1987 to 2003. New-onset AF was assessed and confirmed by electrocardiography during a mean follow-up of 4.7 years.

Results Incident AF occurred in 133 subjects (cumulative probability 14%, 95% confidence interval [CI] 9% to 19%). Univariate predictors of AF were age, male gender, hypertension, coronary artery disease, heart failure, smoking, body mass index, OSA (hazard ratio 2.18, 95% CI 1.34 to 3.54) and multiple measures of OSA severity. In subjects <65 years old, independent predictors of incident AF were age, male gender, coronary artery disease, body mass index (per 1 kg/m^2, hazard ratio 1.07, 95% CI 1.05 to 1.10), and the decrease in nocturnal oxygen saturation (per 0.5 U log change, hazard ratio 3.29, 95% CI 1.35 to 8.04). Heart failure, but neither obesity nor OSA, predicted incident AF in subjects ≥65 years of age.

Conclusions Obesity and the magnitude of nocturnal oxygen desaturation, which is an important pathophysiological consequence of OSA, are independent risk factors for incident AF in individuals <65 years of age. (J Am Coll Cardiol 2007;49:565–71) © 2007 by the American College of Cardiology Foundation

Obstructive Sleep Apnea, Obesity, and the Risk of Incident Atrial Fibrillation

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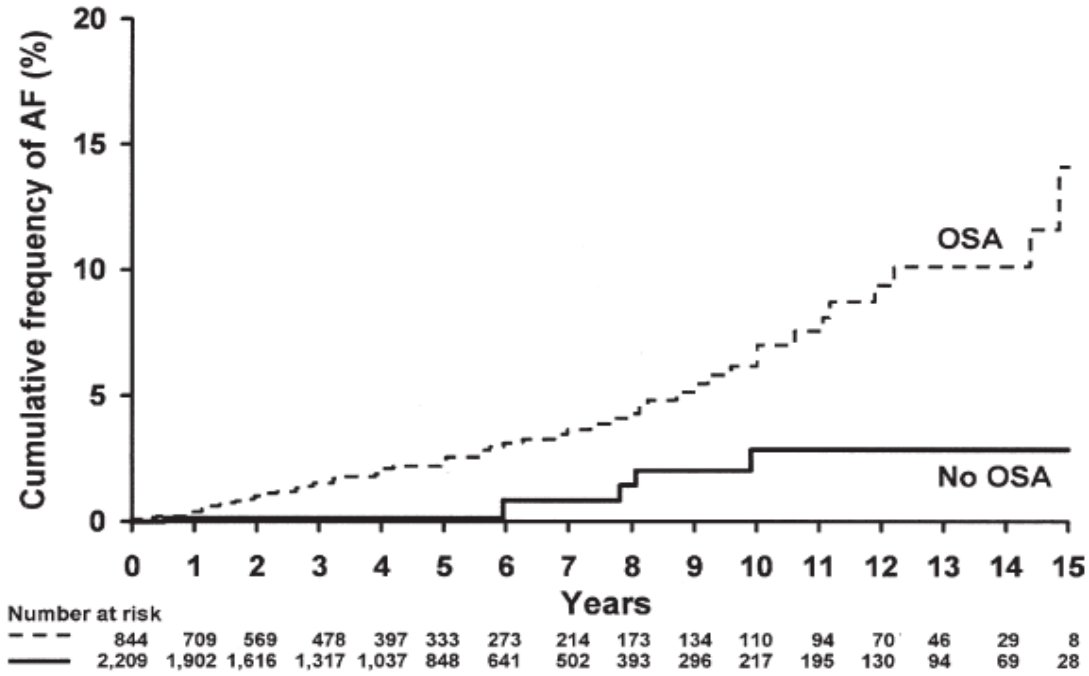

Figure 1 **Incidence of AF Based on Presence or Absence of OSA**

Cumulative frequency curves for incident atrial fibrillation (AF) for subjects <65 years of age with and without obstructive sleep apnea (OSA) during an average 4.7 years of follow-up. $p = 0.002$.

Obstructive Sleep Apnea, Obesity, and the Risk of Incident Atrial Fibrillation

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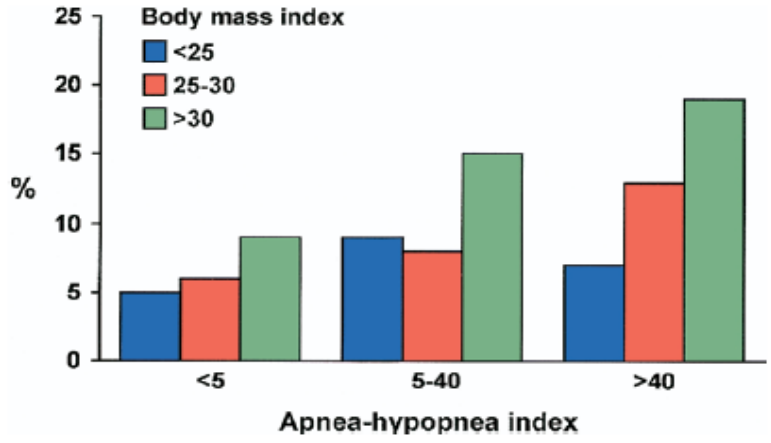
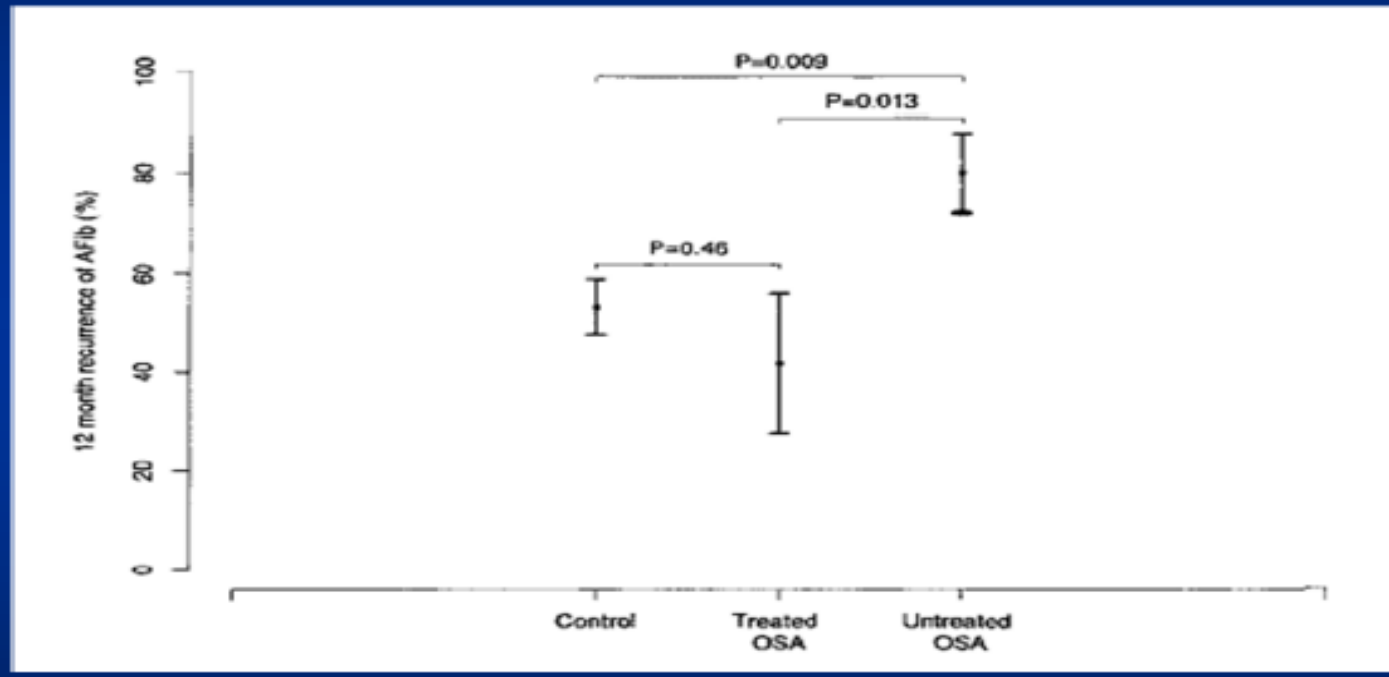


Figure 2 **Incidence of AF Based on the Severity of OSA and Obesity**

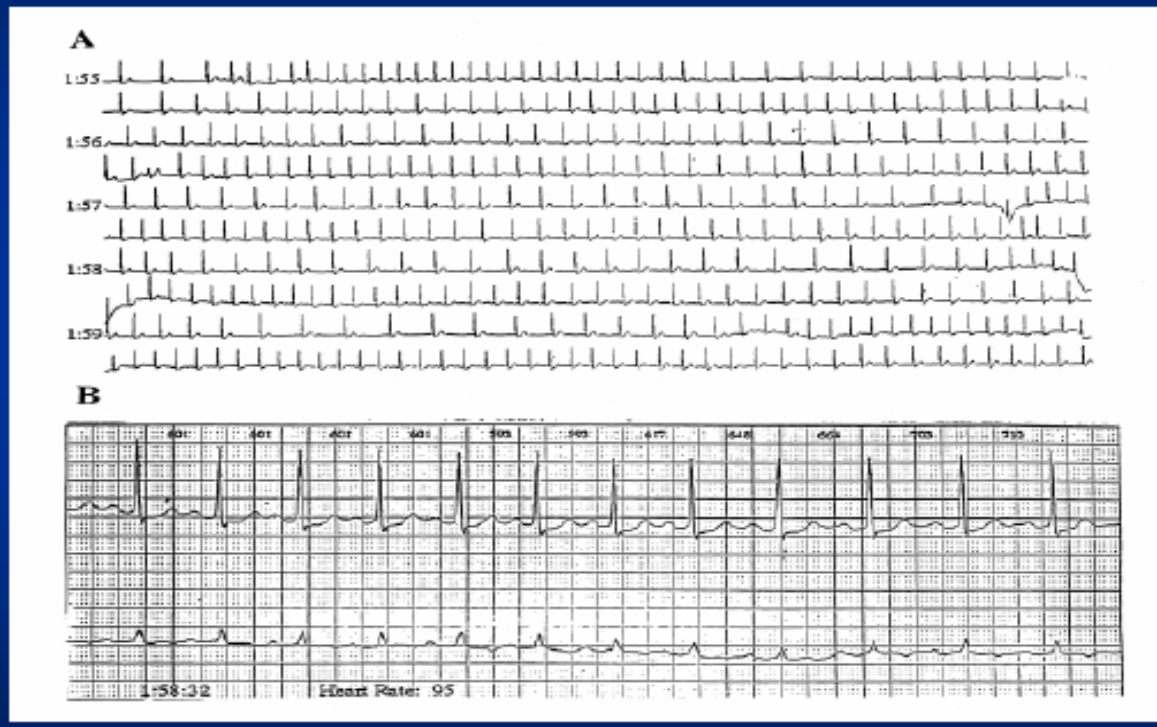
Cumulative frequency of incident atrial fibrillation (AF) during an average 4.7 years of follow-up, based on interactions between the body mass index (BMI) and the apnea-hypopnea index (AHI). An AHI <5 represents no obstructive sleep apnea (OSA), an AHI 5 to 40 represents mild to moderate OSA, and an AHI >40 represents severe OSA. A BMI <25 represents normal weight, a BMI 25 to 30 kg/m^2 represents overweight, and a BMI >30 kg/m^2 represents obesity.

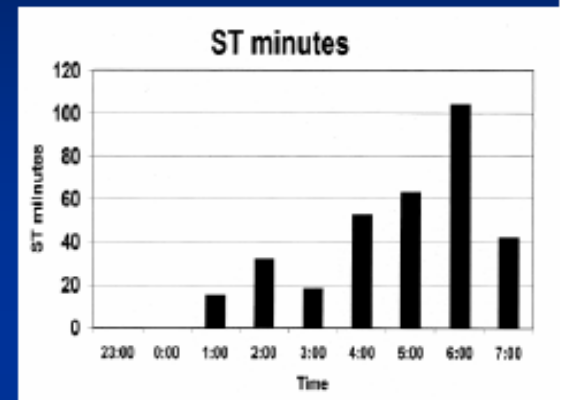
Recurrence of AF 12 months after cardioversion

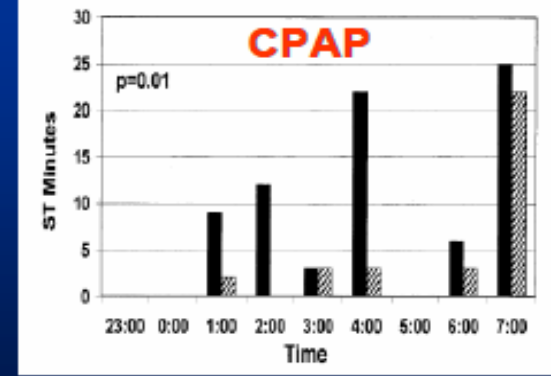


Kanagala R Circulation 2003;107:2589-94

Nocturnal Ischemic Events in Patients With Obstructive Sleep Apnea Syndrome. Effects of Continuous Positive Air Pressure Treatment.







10/51 paz. con OSA

J Am Coll Cardiol 1999;34

Integrated Blood Pressure Control

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REVIEW

Effectiveness of continuous positive airway pressure in lowering blood pressure in patients with obstructive sleep apnea: a critical review of the literature

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Integrated Blood Pressure Control
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Abstract: Obstructive sleep apnea (OSA) is an extremely common comorbid condition in patients with hypertension, with a prevalence of ~50%. There is growing evidence suggesting that OSA is a secondary cause of hypertension, associated with both poor blood pressure (BP) control and target organ damage in patients with hypertension. The application of continuous positive airway pressure (CPAP) during sleep is the gold standard treatment of moderate-to-severe OSA and very effective in abolishing obstructive respiratory events. However, several meta-analyses showed that the overall impact of CPAP on BP is modest (~2 mmHg). There are several potential reasons for this disappointing finding, including the heterogeneity of patients studied (normotensive patients, controlled, and uncontrolled patients with hypertension), non-ideal CPAP compliance, clinical presentation (there is some evidence that the positive impact of CPAP on lowering BP is more evident in sleepy patients), and the multifactorial nature of hypertension. In this review, we performed a critical analysis of the literature evaluating the impact of CPAP on BP in several subgroups of patients. We finally discussed perspectives in this important research area, including the urgent need to identify predictors of BP response to CPAP and the importance of precision medicine in this scenario.

Keywords: cardiovascular disease, CPAP, hypertension, sleep apnea, treatment

Table 1 Summary of BP effects of CPAP on patients with OSA derived from randomized studies[a]

Patients' profile	BP effects of CPAP	Comments
Normotensive[9,11]	No or very mild effect	BP is already optimal and any intervention may have a minimal or neutral effect on BP levels
Prehypertension/ masked hypertension[19]	Mild effect	• One small randomized trial showed 5 mmHg drop in systolic BP after CPAP and a significant reduction in the frequency of prehypertension and masked hypertension in patients with severe OSA[19] • More randomized trials are needed
Controlled hypertensives[22,23,26]	No or modest effect	• Results are variable • No ideal CPAP compliance in some studies
Uncontrolled hypertensives (with or without resistant hypertension diagnosis)[24,25,27,29]	Modest effect (~2 mmHg)	• Results are variable (from no effect to 8 mmHg drop in BP) • The effects seem to be more evident in sleepy patients • No ideal CPAP compliance in some studies • More randomized trials are needed
Resistant hypertension[32–37]	Mild effect (3–5 mmHg)	• Only one study showed no effect on BP[36] • Results are variable (from no effect to 10 mmHg drop in BP). Overall, the proportion of patients who reach BP goal (<140/90 mmHg) is low • A recent report found biomarkers of BP response to CPAP in patients with good device adherence[41]

The NEW ENGLAND JOURNAL of MEDICINE

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CPAP for Prevention of Cardiovascular Events in Obstructive Sleep Apnea

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ABSTRACT

BACKGROUND

Obstructive sleep apnea is associated with an increased risk of cardiovascular events; whether treatment with continuous positive airway pressure (CPAP) prevents major cardiovascular events is uncertain.

METHODS

After a 1-week run-in period during which the participants used sham CPAP, we randomly assigned 2717 eligible adults between 45 and 75 years of age who had moderate-to-severe obstructive sleep apnea and coronary or cerebrovascular disease to receive CPAP treatment plus usual care (CPAP group) or usual care alone (usual-care group). The primary composite end point was death from cardiovascular causes, myocardial infarction, stroke, or hospitalization for unstable angina, heart failure, or transient ischemic attack. Secondary end points included other cardiovascular outcomes, health-related quality of life, snoring symptoms, daytime sleepiness, and mood.

RESULTS

Most of the participants were men who had moderate-to-severe obstructive sleep apnea and minimal sleepiness. In the CPAP group, the mean duration of adherence to CPAP therapy was 3.3 hours per night, and the mean apnea–hypopnea index (the number of apnea or hypopnea events per hour of recording) decreased from 29.0 events per hour at baseline to 3.7 events per hour during follow-up. After a mean follow-up of 3.7 years, a primary end-point event had occurred in 229 participants in the CPAP group (17.0%) and in 207 participants in the usual-care group (15.4%) (hazard ratio with CPAP, 1.10; 95% confidence interval, 0.91 to 1.32; P=0.34). No significant effect on any individual or other composite cardiovascular end point was observed. CPAP significantly reduced snoring and daytime sleepiness and improved health-related quality of life and mood.

CONCLUSIONS

Therapy with CPAP plus usual care, as compared with usual care alone, did not prevent cardiovascular events in patients with moderate-to-severe obstructive sleep apnea and established cardiovascular disease. (Funded by the National Health and Medical Research Council of Australia and others; SAVE ClinicalTrials.gov number, NCT00738179; Australian New Zealand Clinical Trials Registry number, ACTRN12608000409370.)

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. McEvoy at the Adelaide Institute for Sleep Health, Flinders University and Respiratory and Sleep Services, Southern Adelaide Local Health Network, Repatriation General Hospital, Daw Park, Adelaide SA 5041, Australia, or at doug.mcevoy@flinders.edu.au; or to Dr. Luo at the First Affiliated Hospital of Guangzhou Medical University, State Key Laboratory of Respiratory Disease, Guangzhou, China, or at yuanmingluo9431@yahoo.co.uk.

*A complete list of sites and trial investigators and coordinators in the Sleep Apnea Cardiovascular Endpoints (SAVE) study is provided in the Supplementary Appendix, available at NEJM.org.

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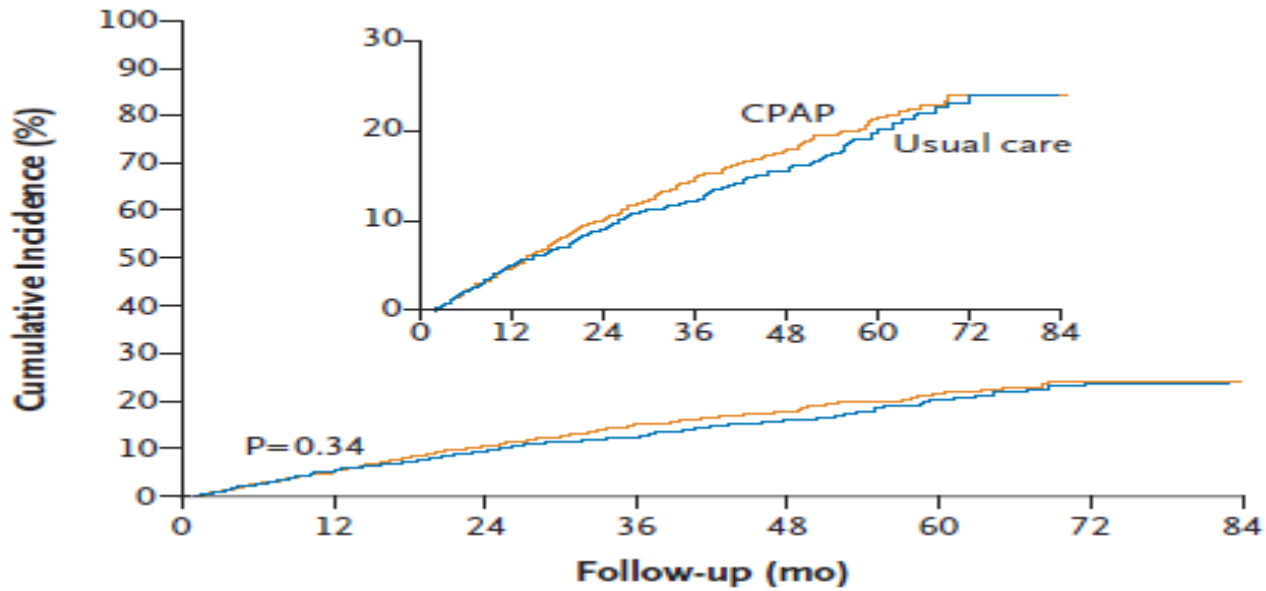
DOI: 10.1056/NEJMoa1606599



No. at Risk								
CPAP	1346	1222	1118	754	482	278	146	146
Usual care	1341	1211	1108	727	499	290	103	103

Figure 2. Cumulative Event Curve of the Primary End Point.

Shown is the cumulative incidence of a first primary end point (a composite of death from cardiovascular causes, myocardial infarction, stroke, or hospitalization for heart failure, unstable angina, or transient ischemic attack) in the group that received CPAP plus usual care (CPAP group) and in the group that received usual care alone (usual-care group). The inset shows the same data on an enlarged y axis.

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Blood pressure effects of CPAP in nonresistant and resistant hypertension associated with OSA: A systematic review of randomized clinical trials

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ABSTRACT

Obstructive sleep apnea (OSA) is a rather common chronic disorder, associated with increased prevalence of hypertension. The pathophysiological mechanisms for hypertension in OSA are at least in part linked to intermittent hypoxia developed during nightly hypopneas and apneas. Hypoxemia stimulates sympathetic overactivity, systemic inflammation, oxidative stress, and endothelial dysfunction. However, it appears that intermittent hypoxemia is not the only factor in the development of hypertension in OSA. Supplemental oxygen therapy that improved oxyhemoglobin saturation to similar levels to those achieved with CPAP treatment did not reduce BP. In this scenario, it could be proposed that hypoxemia acts as a trigger of sympathetic overdrive, which when set is the main factor in the development of hypertension in OSA. This review appraises evidence provided by randomized controlled trials on the BP-lowering effectiveness of continuous positive airway pressure (CPAP) treatment of OSA patients with nonresistant and resistant hypertension. It suggests that CPAP treatment is more effective in treating resistant hypertension than nonresistant hypertension. A possible explanation is that sympathetic overactivity and altered vascular reactivity in OSA could be more severe in resistant hypertension than in nonresistant hypertension. An intricate interaction among compliance, adherence, and their interaction with demographic characteristics, genetic factors, and comorbidities of the population included might explain the differences found between trials on their influence over the antihypertensive effectiveness of CPAP. Further long-term trials are needed in hypertensive OSA patients to assess whether CPAP treatment in OSA patients consistently restores physiological nocturnal BP fall and adjusts resting and circadian heart rate.

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KEYWORDS
Antihypertensive effects; CPAP; OSA; pathophysiology; therapeutics

Table 2. RCTs on BP Effects of CPAP in OSA patients with resistant hypertension.

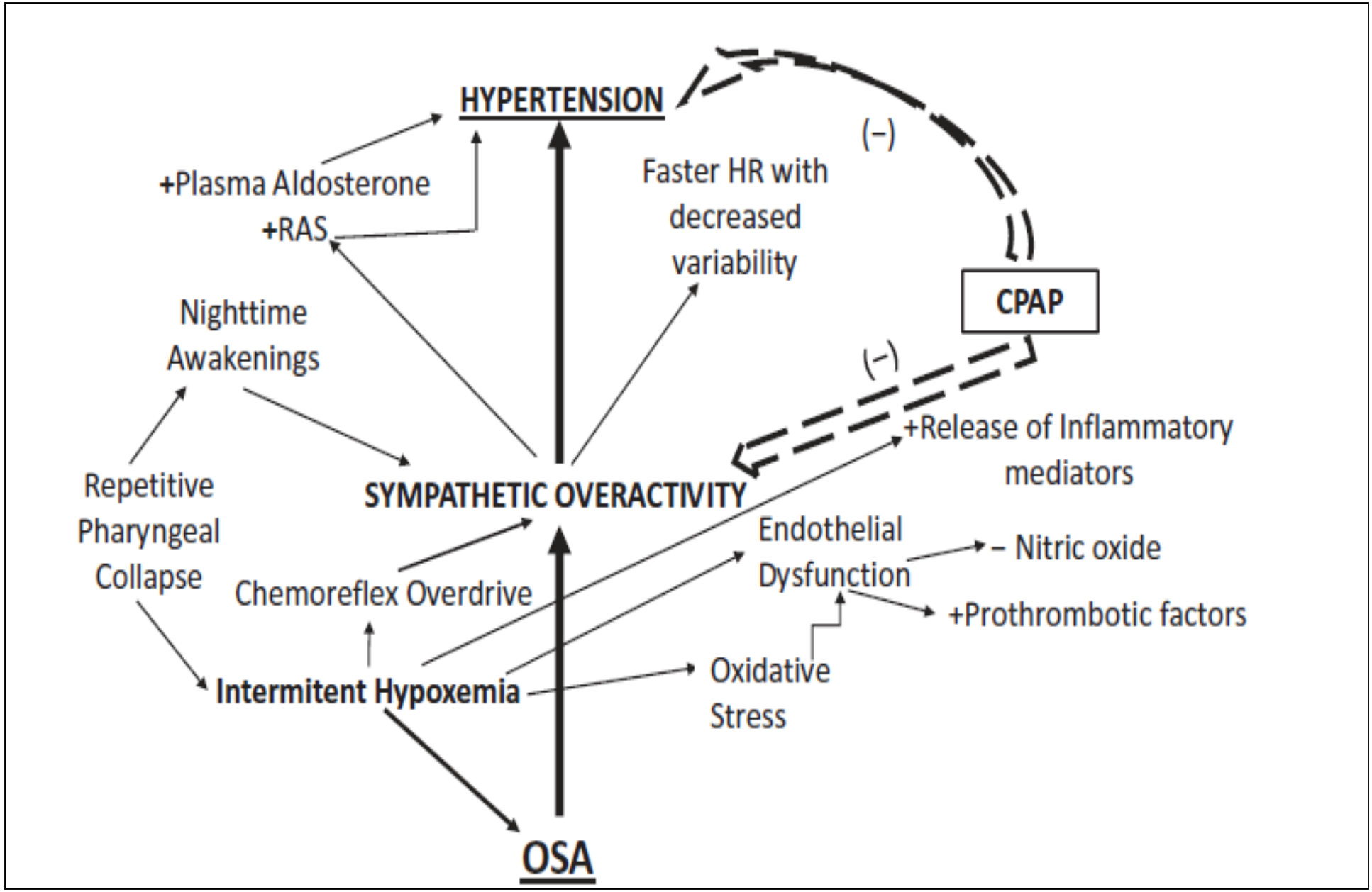
Study	Sample age/ gender	^AIH	CPAP treatment	24-h BP change in control group (mm Hg)	24-h BP change in CPAP group (mm Hg)	Nighttime BP change in control group (mm Hg)	Nighttime BP change in CPAP group (mm Hg)	Difference in BP change between Groups OR (95%CI)	Comments
Lozano et al. (35)	*n* = 64 59 years Males (%) 76	CPAP plus ATH: ^60 ATH: ^47	12 weeks; 5.6 h per night	SBP/DBP: +0.6/ +0.1	SBP/DBP: −7.6/ −4.9	SBP/DBP: +3.8/+1.5	SBP/DBP −1.9/−3.1	24-h DBP: −6.98 (−1.86 to −12.1) 24-h SBP: −9.71 (−0.20 to −19.22)	CPAP treatment significantly decreased daytime MBP/DBP, and nighttime MBP/SBP/DBP
Martinez Garcia et al. (36)	*n* = 194 56 years Males (%) 72	CPAP plus ATH:^ 41.3 ATH: ^ 39.5	12 Weeks 5 h per night	MBP: −0.8 SBP/DBP: −1.2/ −0,5	MBP: −4.1 SBP/DBP: −4.7/ −3.9	SBP/DBP: −2.6/−1.1	SBP/DBP: −6.6/−3.1	24-h MBP: −3.1 (−0.6 to −5.6) 24-h DBP: −3.2 (−1.0 to −5.4)	CPAP therapy reduced 24-h MBP and DBP in patients with moderate-to-severe OSA
Pedrosa et al. (42)	*n* = 35 56 years Males (%) 81	CPAP plus ATH: ^36 ATH: ^ 28	24 weeks; 6.01 h per night	SBP/DBP: +2.6/ −3.0	SBP/DBP: −6.9/ −9.7	SBP/DBP: +2.4/+1.9	SBP/DBP: +1.8/+0.8	NR	Treatment of moderate-to-severe OSA with CPAP reduced daytime SBP and DBP but not nocturnal BP
D'Oliveira et al. (43)	*n* = 47 59 years Males (%) 58	CPAP: ^20.5 Sham CPAP:^20	8 weeks 5.3 h per night	NR	NR	NR	NR	24-h SBP −9.3 (−17.9 to −0.4)	CPAP treatment in patients with moderate OSA and resistant hypertension reduced significantly 24-h SBP
Muxfeldt et al. (44)	*n* = 117 60 years Males (%) 40%	CPAP: ^44.5 Sham CPAP: ^42.5	12 weeks; 4.5 h per night	SBP/DBP: +0.4/ −0.2	SBP/DBP +0.8/− 0.2	SBP/DBP +1.8/+1	SBP/DBP +1.2/+0.6	Nighttime SBP: −1.7 (−7.0 to +3.6) Nighttime DBP: −0.4 (−3.7 to +3.0)	In a mainly female sample, CPAP treatment had no significant effect on BP in moderate-to-severe OSA patients

AHI: apnea-hypopnea index; ATH: antihypertensive treatment; CPAP: continuous positive airway pressure; BP: blood pressure; MBP: mean BP; SBP: systolic blood pressure; DBP: diastolic blood pressure; HT: hypertension; OR: odds ratio; CI: confidence interval; NR: not reported.

Table 1. Characteristics of RCT on BP Effects of CPAP in OSA patients with nonresistant hypertension.

Study	Sample age/ gender	^AIH ^^Oxygen Saturation Dips >4	CPAP treatment	24-h BP change in control group (mm Hg)	24-h BP change in CPAP group (mm Hg)	Nighttime BP change in in control group (mm Hg)	Nighttime BP change in CPAP group (mm Hg)	Difference in BP change between groups OR(95%CI)	Comments
Norman et al. (31)	*n*: 46 49 years Males (%) 83	CPAP: ^66 ^Sham CPAP: ^59	2 weeks; 6.7 h per night	24-h MBP:+3.6 24-h SBP/DBP: +3.8/+3	24-hMBP: −3 24-h SBP/DBP: −2.1/−2.5	MBP: +2.8 SBP/DBP: +3/+2.5	MBP: −5 SBP/DBP: −6/−3	NR	CPAP treatment significantly decreased daytime MBP and DBP, and nighttime MBP, SBP, and DBP
Robinson et al. (32)	*n*: 35 54 years Males (%) 89	Whole sample: ^^28.1	4 weeks; CPAP: 5.2 h per night	24-h MBP: −1.2 24-h SBP/DBP: −3.7/+0.1	24-h MBP: −2 24-h SBP/DBP: −3.3/−1.1	MBP: −0.2	−2.7	NS	CPAP therapy did not reduce 24-h MBP in patients with moderate-to-severe OSA
Campos Rodriguez et al. (33)	*n*: 68 55 years Males (%) 55.8	CPAP: ^58.3 Sham CPAP: ^59.5	4 weeks; 4.7 h per night.	24-h SBP/DBP: −0.6/−0.8	24-h MBP: −3 24h SBP/DBP: −1.9/−1.5	MBP: −0.4	MBP: −1.5	NS	CPAP therapy did not reduce 24-h MBP/SBP/DBP
Duran Cantolla et al. (34)	*n*: 340 53 years Males (%) 79	CPAP: ^44.5 Sham CPAP: ^42.5	12 weeks; 4.5 h per night	24-h MBP: 0 24-h SBP/DBP: −1/ 0	24-h MBP: −2 24-h SBP/DBP: −3/ −2	MBP: −1 SBP/DBP: 0/−1	MBP: −3 SBP/DBP: −4/−2	24- h MBP: −1.5 (−0.4 to −2.7), 24 −h SBP: −2.1 (−0.4 to −3.7), 24-h DBP: −1.3(−0.2 to −2.3)	CPAP treatment modestly but significantly decreased 24-h MBP and 24-h SBP/DBP in OSA patients

AHI: apnea-hypopnea index; CPAP: continuous positive airway pressure; BP: blood pressure; MBP: mean BP; SBP: systolic blood pressure; DBP: diastolic blood pressure; HT: hypertension; NS: nonsignificant; OR: odds ratio; CI: confidence interval; NR: not reported.


HYPERTENSION
(–)
+Plasma Aldosterone
+RAS
Faster HR with decreased variability
CPAP
Nighttime Awakenings
(–)
+Release of Inflammatory mediators
Repetitive Pharyngeal Collapse
SYMPATHETIC OVERACTIVITY
Endothelial Dysfunction
– Nitric oxide
Chemoreflex Overdrive
+Prothrombotic factors
Intermitent Hypoxemia
Oxidative Stress
OSA

Vascular Health and Risk Management

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ORIGINAL RESEARCH

Effects of CPAP on "vascular" risk factors in patients with obstructive sleep apnea and arterial hypertension

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Background: The aim of this study was to assess the effects of continuous positive airway pressure (CPAP) on arterial stiffness, central blood pressure, and reflected pulse wave characteristics in patients with severe obstructive sleep apnea (OSA) and stage 2–3 arterial hypertension.

Methods: Forty-four patients with hypertension and severe OSA (apnea/hypopnea index > 30) received stepped dose titration of antihypertensive treatment, consisting of valsartan 160 mg + amlodipine 5–10 mg + hydrochlorothiazide 25 mg. CPAP therapy was added after 3 weeks of continuous antihypertensive treatment with BP $< 140/90$ mmHg or after adjusting triple treatment in patients with resistant arterial hypertension. The patients were randomized to effective CPAP (4–15 mm H_2O) or placebo CPAP (pressure 4 mm H_2O) for three weeks, then crossed over to the alternative treatment in a single-blind manner. Office blood pressure (BP), ambulatory BP monitoring, ambulatory arterial stiffness index (AASI), aortic BP, carotid-femoral pulse wave velocity (cfPWV), and systolic wave augmentation index were measured using a Sphygmocor® device at baseline, after antihypertensive treatment, placebo CPAP, and effective CPAP.

Results: Baseline cfPWV was above the normal range in 94% of patients. After reaching target BP, the cfPWV decreased by 1.9 ± 1.0 msec ($P = 0.007$). Effective CPAP achieved a further cfPWV reduction of 0.7 msec ($P = 0.03$). Increased arterial stiffness (pulse wave velocity > 12 msec) persisted in 35% of patients on antihypertensive treatment and effective CPAP, in 56% of patients on antihypertensive treatment alone, and in 53% of patients on placebo CPAP. Only the combination of antihypertensive treatment with effective CPAP achieved a significant reduction in augmentation index and AASI, along with a further reduction in aortic and brachial BP.

Conclusion: Effective CPAP for 3 weeks resulted in a significant additional decrease in office BP, ambulatory BP monitoring, central BP, and augmentation index, together with an improvement in arterial stiffness parameters, ie, cfPWV and AASI, in a group of hypertensive patients with OSA.

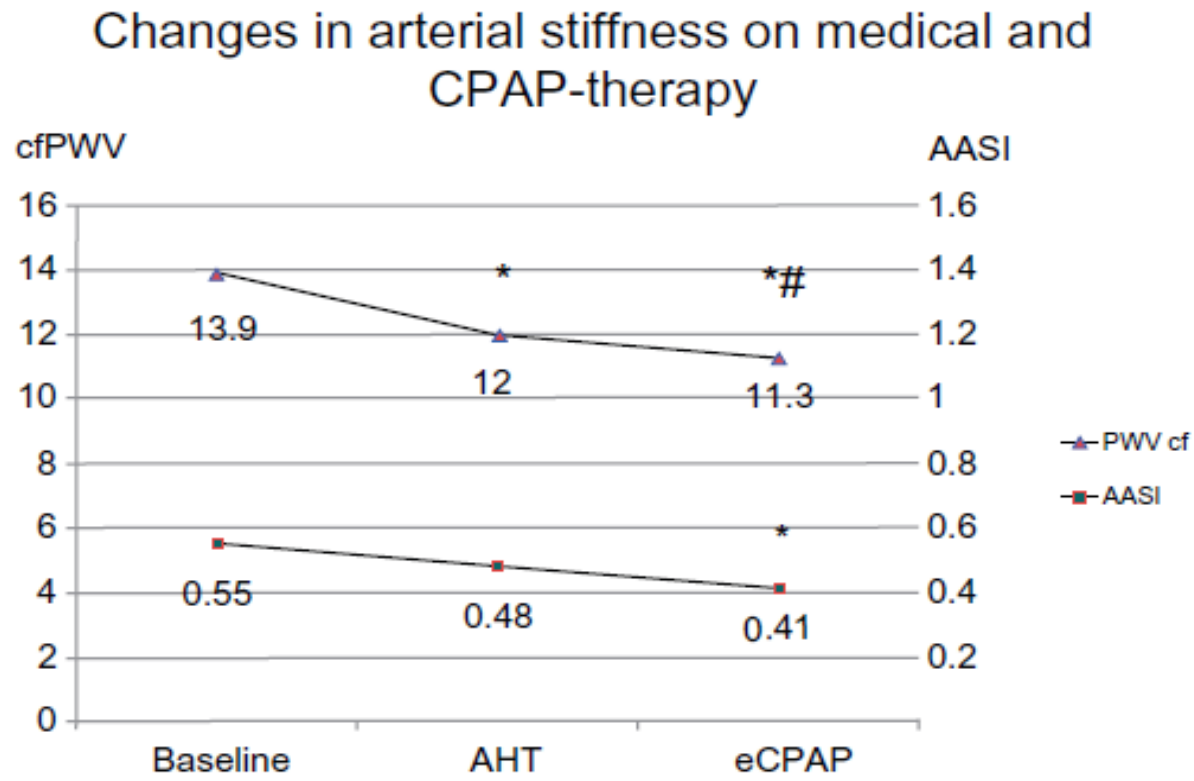

Figure 3 Changes in carotid-femoral PWV and AASI after antihypertensive therapy and CPAP therapy.

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PLOS | ONE

Relationship between Aldosterone and the Metabolic Syndrome in Patients with Obstructive Sleep Apnea Hypopnea Syndrome: Effect of Continuous Positive Airway Pressure Treatment

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Abstract

Background: Metabolic syndrome (MS) occurs frequently in patients with obstructive sleep apnea-hypopnea syndrome (OSAHS). We hypothesized that aldosterone levels are elevated in OSAHS and associated with the presence of MS.

Methods: We studied 66 patients with OSAHS (33 with MS and 33 without MS) and 35 controls. The occurrence of the MS was analyzed according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) clinical criteria. Measurements of plasma renin activity (PRA), aldosterone, aldosterone:PRA ratio, creatinine, glucose, triglycerides, cholesterol and HDL cholesterol were obtained at baseline and after CPAP treatment.

Results: Aldosterone levels were associated with the severity of OSAHS and higher than controls ($p = 0.046$). Significant differences in aldosterone levels were detected between OSAHS patients with and without MS ($p = 0.041$). A significant reduction was observed in the aldosterone levels in patients under CPAP treatment ($p = 0.012$).

Conclusion: This study shows that aldosterone levels are elevated in OSAHS in comparison to controls, and that CPAP therapy reduces aldosterone levels. It also shows that aldosterone levels are associated with the presence of metabolic syndrome, suggesting that aldosterone excess might predispose or aggravate the metabolic and cardiovascular complications of OSAHS.

Trial registration: The study is not a randomized controlled trial and was not registered.

Table 2. Changes in components of the metabolic syndrome and in aldosterone, PRA and aldosterone/PRA ratio after 12 month of CPAP treatment (n = 51).

	Baseline	Follow-up	p value
BMI (Kg.m $^{-2}$)	30.5±4.5	30.9±4.5	0.191
Waist circumference (cm)	106.1	107.5	0.706
Glucose (mg/dL)	108±22	106±33	0.246
Triglycerides (mg/dL)	193±62	179±75	0.288
HDLc (mg/dL)	51±10	54±11	0.022
SBP (mmHg)	134±16	138±20	0.252
DBP (mmHg)	83±11	81±10	0.311
Creatinine (mg/dL)	0.95±0.15	0.94±0.15	0.855
PRA (ng/mL/h)	1.4±1.1	1.3±0.9	0.765
Aldosterone (ng/dL)	16.7±8.7	12.6±9.4	0.012
Aldosterone/PRA ratio	19±15	17±13	0.274
Hyperaldosteronism (n,%)	9, 19%	2, 4%	0.120

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Spironolactone Reduces Severity of Obstructive Sleep Apnea in Patients with Resistant Hypertension: a Preliminary Report

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Abstract

Introduction—Obstructive sleep apnea (OSA) and hyperaldosteronism are very common in subjects with resistant hypertension. We hypothesized that aldosterone mediated chronic fluid retention may influence OSA severity in patients with resistant hypertension. We tested this in an open label evaluation by assessing the changes in the severity of OSA in patients with resistant hypertension following treatment with spironolactone.

Methods—Subjects with resistant hypertension [clinic blood pressure (BP) ≥140/90 mm Hg on ≥3 antihypertensive medications, including a thiazide diuretic and OSA [defined as an apneahypopnea index (AHI) ≥ 15] had full diagnostic, polysomnography before and 8 weeks after spironolactone (25–50 mg/day) was added to their ongoing antihypertensive therapy.

Results—Twelve patients (mean age 56 years and body mass index 36.8 kg/m^2) were evaluated. Following treatment with spironolactone, the AHI (39.8±19.5 vs. 22.0±6.8 events/hr; $p < 0.05$) and hypoxic index (13.6±10.8 vs. 6.7±6.6 events/hr; $p < 0.05$), weight, clinic and ambulatory BP were significantly reduced. Plasma renin activity and serum creatinine were significantly higher.

Conclusion—This study provides preliminary evidence that treatment with a mineralocorticoid receptor antagonist substantially reduces the severity of OSA. If confirmed in a randomized assessment it will support aldosterone-mediated chronic fluid retention as an important mediator of OSA severity in patients with resistant hypertension.

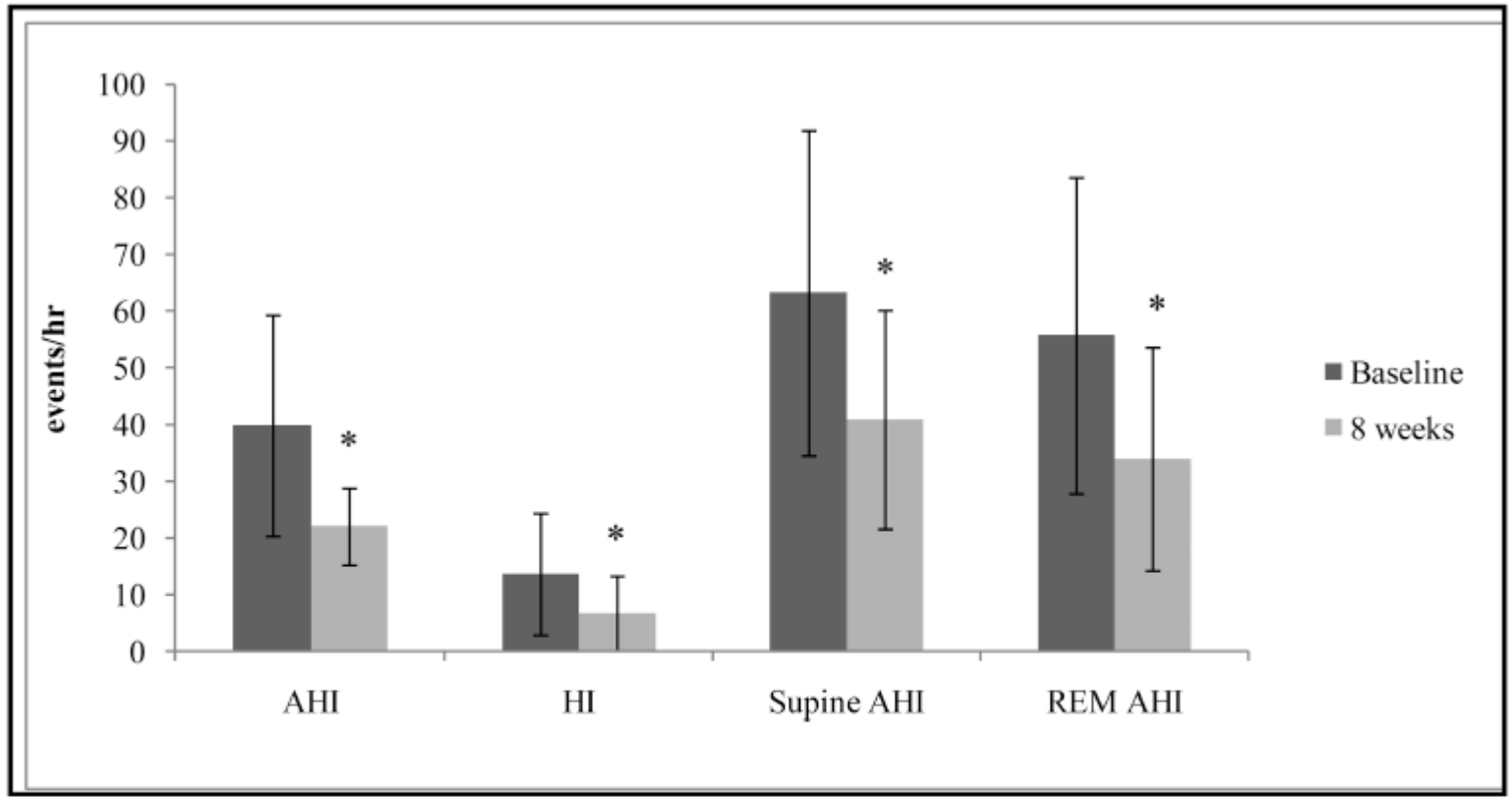

Figure.
Changes in apnea-hypopnea index (AHI) (39.8 ± 19.5 vs. 22.0 ± 6.8); hypoxic index (HI) (13.6 ± 10.8 vs. 6.7 ± 6.6); supine AHI (63.2 ± 28.7 vs. 40.8 ± 19.3); rapid eye movement sleep (REM) AHI (55.7 ± 27.9 vs. 33.9 ± 19.7) at 8 weeks (light grey bars) compared to baseline (dark grey bars). Values, mean ± SD. *Different compared to baseline, $P < .05$.

Table 2

Characteristics before and after spironolactone treatment

Characteristics	Baseline	8 Weeks	p-value
Weight, lbs	243.0 ± 32.4	239.9 ± 29.4	0.03
Neck, cm	42.1 ± 3.5	41.2 ± 3.4	0.195
Clinic SBP, mm Hg	145 ± 18	124 ± 16	<0.001
Clinic DBP, mm Hg	81 ± 16	72 ± 9	0.04
Ambulatory daytime SBP, mm Hg†	150 ± 14	134 ± 18	0.04
Ambulatory daytime DBP, mm Hg†	85 ± 15	75 ± 11	0.06
Ambulatory nighttime SBP, mm Hg†	142 ± 16	120 ± 23	0.02
Ambulatory nighttime DBP, mm Hg†	77 ± 12	64 ± 13	0.016
24-h systolic blood pressure, mm Hg†	147 ± 13	130 ± 19	0.025
24-h diastolic blood pressure, mm Hg†	82 ± 14	72 ± 11	0.051
No. of antihypertensive medications	4.3 ± 1.1	4.5 ± 1.0	0.76
Serum creatinine,	1.2 ± 0.3	1.3 ± 0.2	0.035
Serum potassium, mEq/L	4.0 ± 0.3	4.4 ± 0.5	0.05
Plasma renin activity, ng/mL/h	1.4 ± 2.1	14.3 ± 13.8	0.005
BNP, pg/mL	17.3 ± 12.7	12.6 ± 18.8	0.24
AHI, events/h	39.8 ± 19.5	22.0 ± 6.8	<0.001
Hypoxic index, %	13.6 ± 10.8	6.7 ± 6.6	0.04
Supine AHI, events/h	63.2 ± 28.7	40.8 ± 19.3	0.007
REM AHI, events/h†	55.7 ± 27.9	33.9 ± 19.7	0.003

Values, mean ± SD. SBP, systolic blood pressure; DBP, diastolic blood pressure; BNP, brain natriuretic peptide; AHI, apnea-hypopnea index; REM, rapid eye movement sleep.

† n = 11 due to one subject having no REM sleep during the baseline study.

CONCLUSIONI

- La sindrome delle apnee ostruttive notturna è uno dei disturbi respiratori più frequenti nella popolazione
- Risulta sempre più chiara la relazione tra essa e malattie cardiovascolari, prima fra tutte l'ipertensione
- L'ipertensione ha spesso un profilo non dipper ed è caratterizzato da una estrema variabilità pressoria
- L'OSAS si associa a danno d'organo CV come (IVS, aritmie, CIC e nefropatia)
- I valori di aldosterone sono spesso aumentati
- La CPAP è efficace solo nelle forme di ipertensione resistente

Thanks for your attention