Is OSAS responsible for coronary artery disease?

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GYNAECOLOGISTS' PERSPECTIVE OF THE HEART

"A uterus-shaped organ situated in the chest whose primary function is to pump blood to the ovaries"

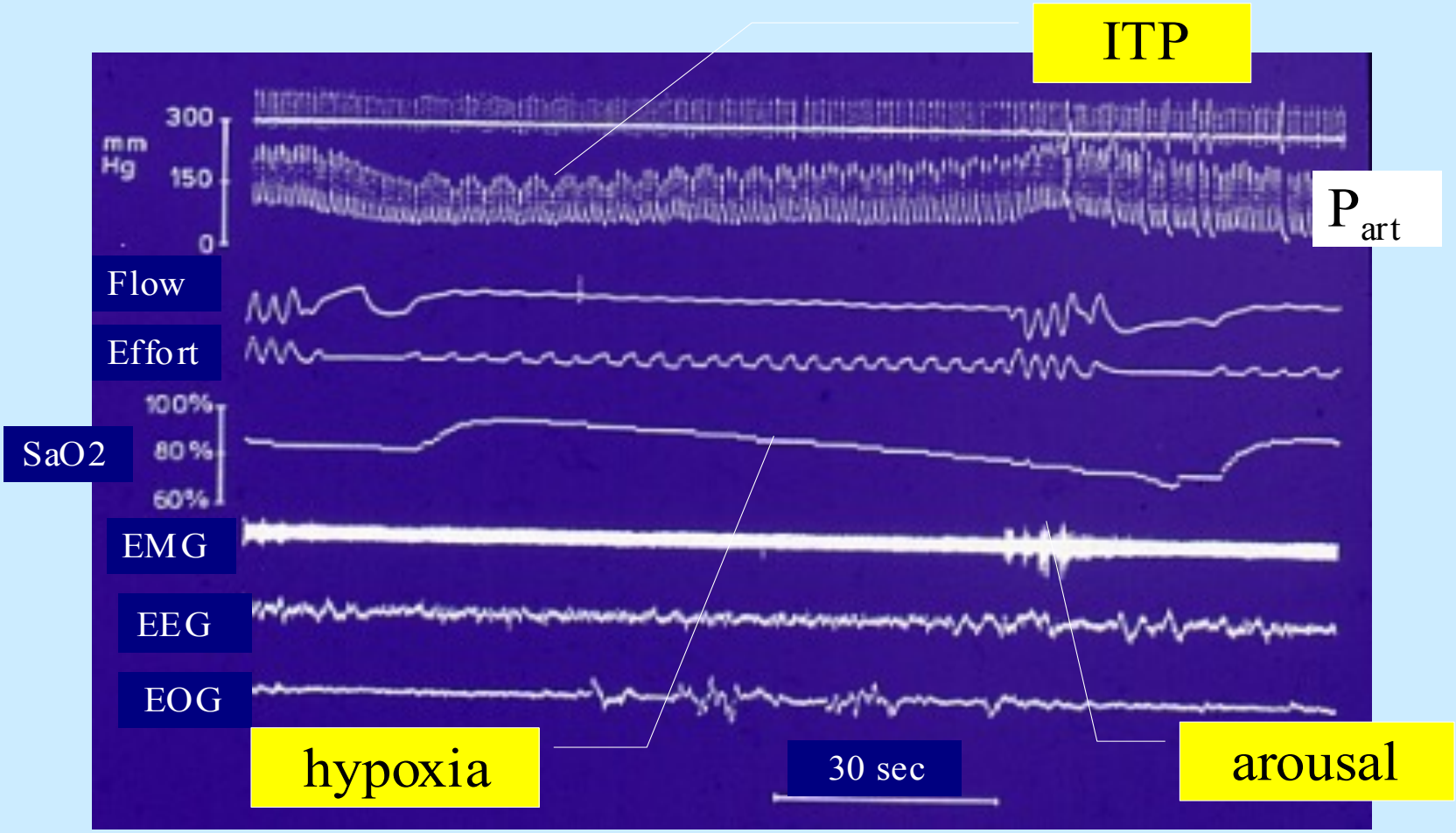
- OSA (Asymptomatic OSA; “Non-sleepy sleep apnoeics”)
- OSAS (Symptomatic OSA; “Sleepy sleep-apnoeics”)


AHI 30
AHI 30
AHI 30
AHI 30
AHI 30
AHI 30

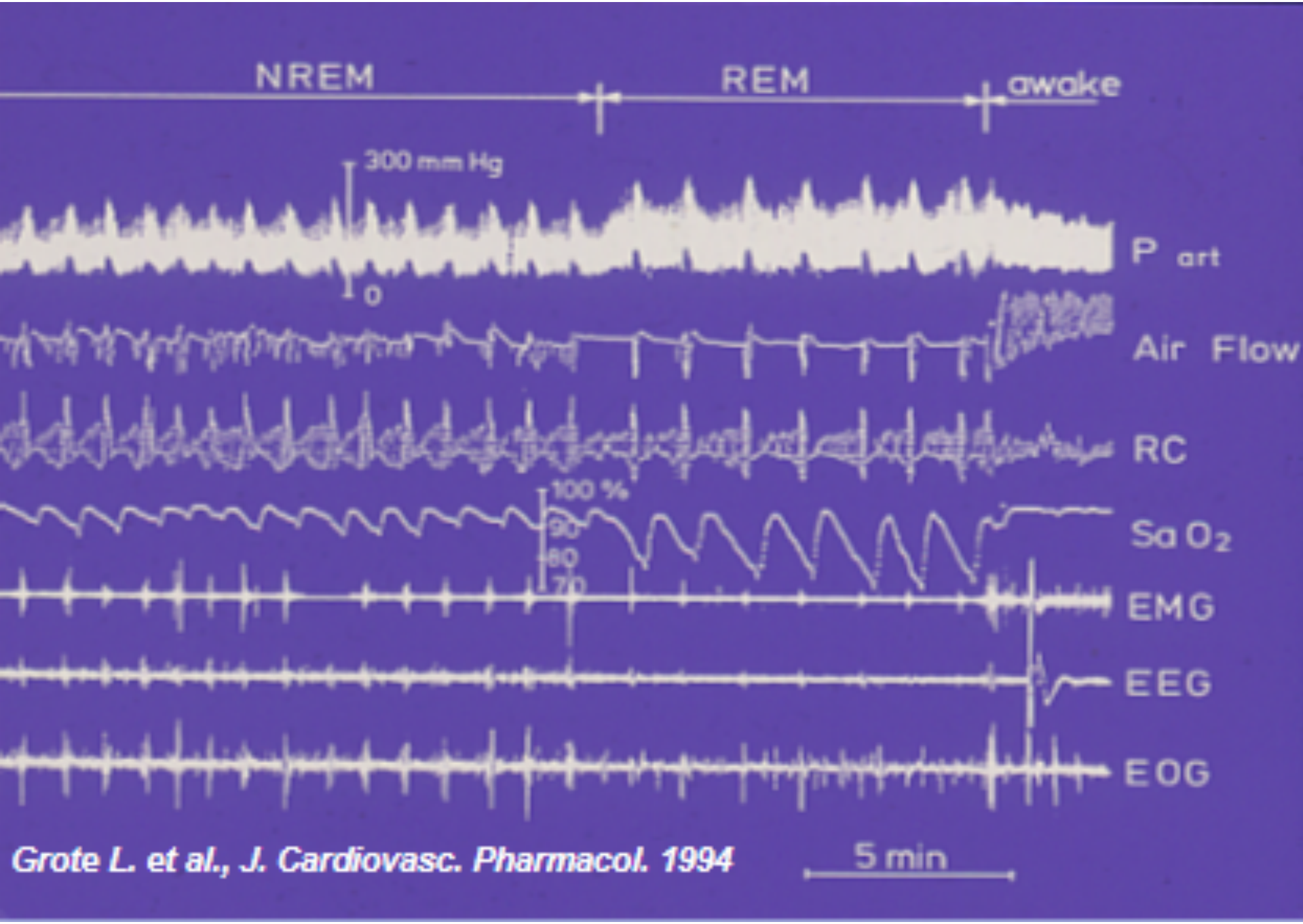
OSA

- Immediate changes
- Long-term effects

Acute Blood Pressure Changes in OSA
- Mechanisms -



Modified from Grote L, Schneider H, 1997



Grote L. et al., J. Cardiovasc. Pharmacol. 1994

Circadian distribution of acute myocardial infarction and sudden cardiac death

Increased risk during the late hours of sleep or in the early morning after awakening

Muller JE et al, Circulation 1989

Day-night pattern of sudden death in sleep-disordered breathing

- Sudden cardiac death (n=112)
- SDB (n=78), non-SDB (n=34)
- Death between midnight and 6.00 am:
- Solely by chance in each quarter of the day: % 25
- Historical control group: % 16
- Mayo Sleep Clinic - SDB: % 46; non-SDB: % 21

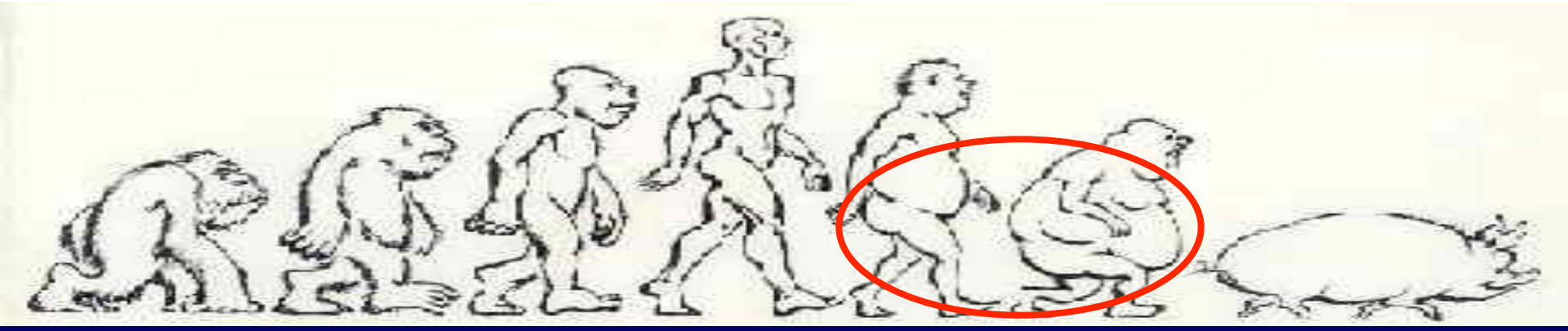
Gami AS et al, N Engl J Med 2005


P
Sleeping
Prohibited
11pm-6am

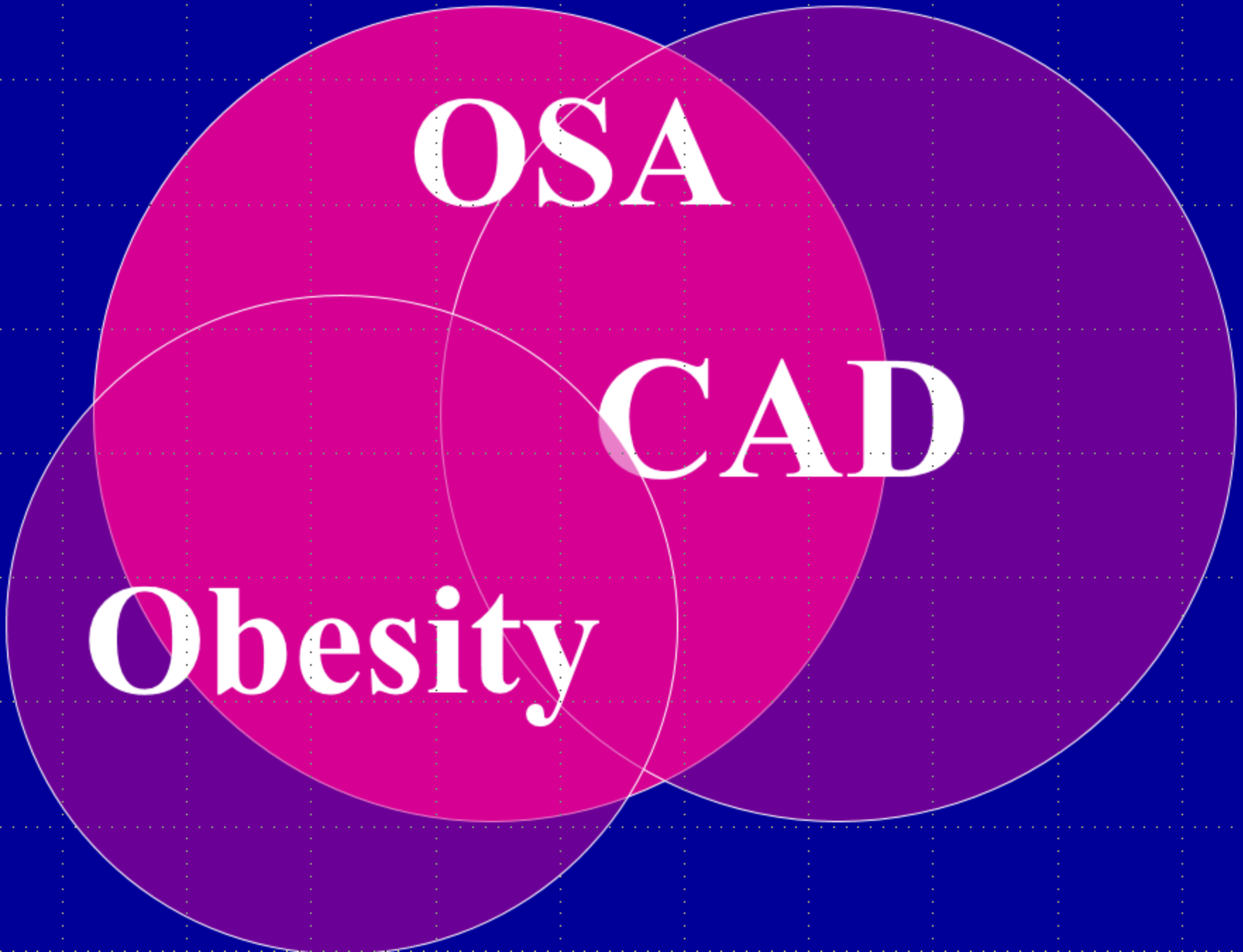
Prevalence of OSA in CAD clinic cohorts

FIRST AUTHOR REF (YEAR)	PATIENTS (NO.)	SEX	PREVALENCE (%)	DIAGNOSTIC CRITERIA (EVENTS/H)	CONTROLLED
Hung 13 (1990)	101	Male	36	AI >5	Yes
Andreas 19 (1996)	50	Male, female	50	AI >10	No
Mooe 17 (1996)	142	Male	37	AHI ≥10	Yes
Mooe 18 (1996)	102	Female	30	AHI ≥10	Yes
Koehler 20 (1996)	74	Male	35	AHI ≥10	No
Peker 15 (1999)	62	Male, female	31	AHI ≥10	Yes
Schafer 14 (1999)	223	Male	31	AHI ≥10	Yes
Skinner 36 (2005)	26	Male, female	50	AHI ≥15	No
Mehra 22 (2006)	104	Male, female	66	AHI ≥10	No
Nakashima 23 (2006)	86	Male, female	43	AHI ≥15	No
Yumino 21 (2007)	89	Male, female	57	AHI ≥10	No
Lee 24 (2009)	105	Male, female	66	AHI ≥15	No
Konecny 25 (2010)	74	Male, female	41	AHI ≥15	No
Schiza 37 (2012)	52	Male, female	54	AHI ≥10	No
Garcia-Rio 16 (2013)	192	Male, female	35	AHI ≥15	Yes
Glantz 26 (2013)	662	Male, female	64	AHI ≥15	No
Aronson 27 (2014)	180	Male, female	64	ODI >5	No
Total or mean	2324	—	47	—	—

Peker Y, Franklin K, Hedner J;
in Principles and Practice of Sleep Medicine (March 2016)




OSA
Obesity


OSA
CAD
Obesity

An independent association between obstructive sleep apnoea and coronary artery disease

Y. Peker*+, H. Kraiczi*, J. Hedner*, S. Löth+, Å. Johansson+, M. Bende+

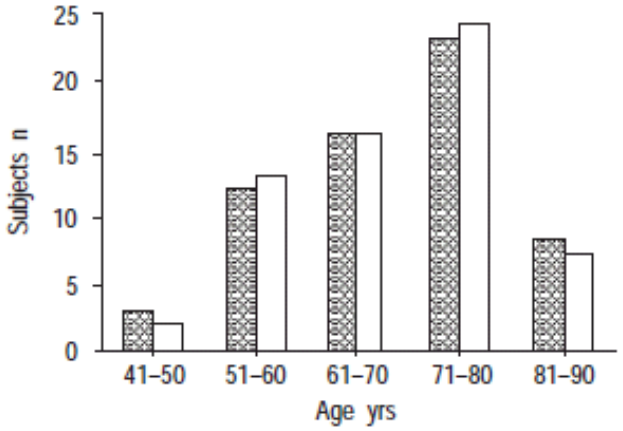


Fig. 1. – Age distribution in patients with coronary artery disease (▩) and control subjects (□) at the time of the overnight sleep study.

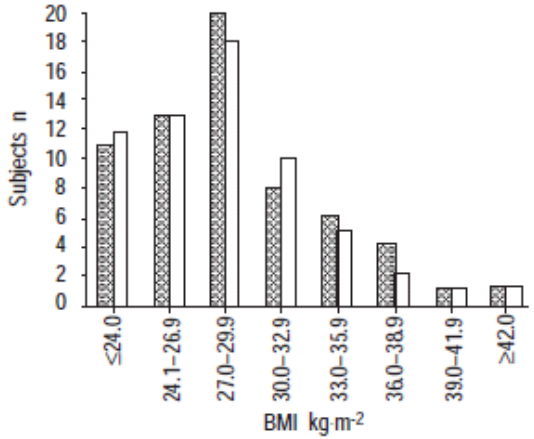


Fig. 2. – Body mass index (BMI) distribution in patients with coronary artery disease (▩) and control subjects (□) at the time of the overnight sleep study.

Table 4. – Explanatory variables associated with coronary artery disease (multiple regression analysis)

Variable	Odds ratio	95% CI	p-value
Current smoking	9.8	2.6–36.5	0.001
Diabetes mellitus	4.2	1.1–17.1	0.045
Obstructive sleep apnoea	3.1	1.2–8.3	0.025

Eur Respir J 1999; 14: 179–184.

Prognosis of CAD with concomitant OSA is WORSE than the prognosis for CAD patients without OSA

- ***Peker et al, AJRCCM 2000***
- ***Mooe et al, AJRCCM 2001***
- ***Yumino et al, Am J Cardiol 2007***

Respiratory Disturbance Index

An Independent Predictor of Mortality in Coronary Artery Disease

YÜKSEL PEKER, JAN HEDNER, HOLGER KRAICZI, and STEEN LÖTH

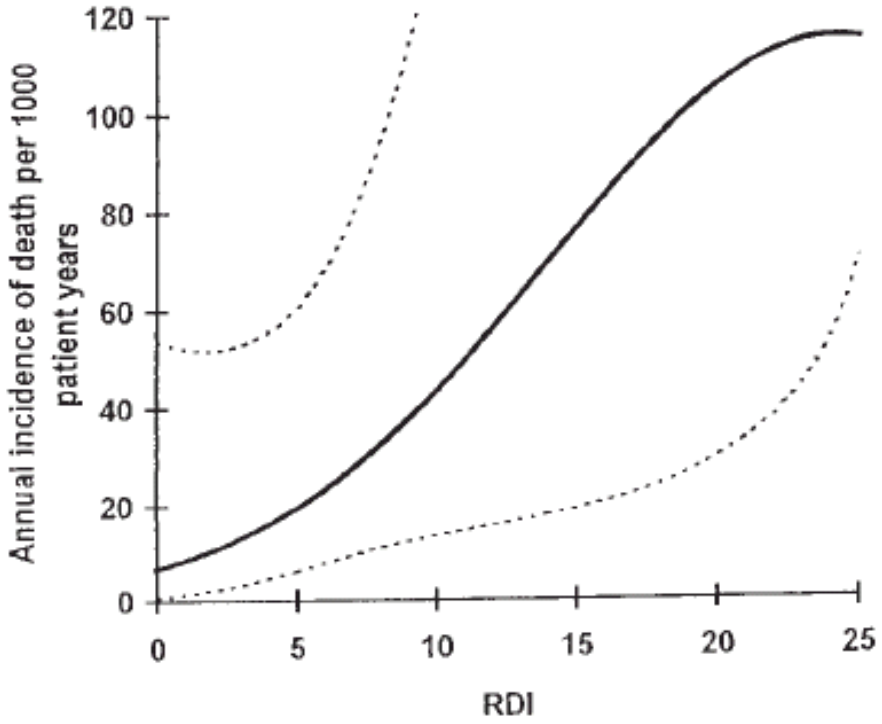


Figure 1. By use of a Poisson model the death hazard was calculated as a function of RDI, current age, and time elapsed after the intensive care episode for CAD. The *bolded curve* gives the function at the current age 70 yr and 3 yr after intensive care. The *dotted curves* represent 95% CI.

Am J Respir Crit Care Med Vol 162. pp 81–86, 2000

CAUSALITY

- Incident CAD in OSA
- Impact of the treatment of OSA on CAD

Eur Respir J 2006; 28: 596–602
DOI: 10.1183/09031936.06.00107805

Increased incidence of coronary artery disease in sleep apnoea: a long-term follow-up

Y. Peker*,#, J. Carlson* and J. Hedner*

ABSTRACT: An increased incidence of cardiovascular disease has previously been reported in middle-aged males during a follow-up period of 7 yrs. The aim of the present study was to address the incidence of coronary artery disease (CAD) in a larger sample without any heart disease at baseline.

The population comprised 308 snorers (245 males and 63 females) with a mean±SD age of 49.0±9.9 yrs in 1991. Data were collected *via* the Swedish Hospital Discharge Register, National Cause of Death Registry, clinical charts and questionnaires.

Over 7 yrs, CAD was observed in 17 (16.2%) of 105 patients with obstructive sleep apnoea (OSA; overnight (6 h) oxygen desaturations ⩾30 events) compared with 11 (5.4%) of 203 snorers without OSA. OSA diagnosis at baseline was associated with an increased risk of development of CAD in a multivariate model. In the OSA group, CAD was confirmed in 16 (24.6%) of 65 incompletely treated patients compared with one (3.9%) of 26 efficiently treated subjects. Efficient treatment of OSA reduced this risk.

It is concluded that middle-aged sleep apnoeics are at high risk of developing coronary artery disease if they are not treated efficiently, which should be considered in cardiovascular disease

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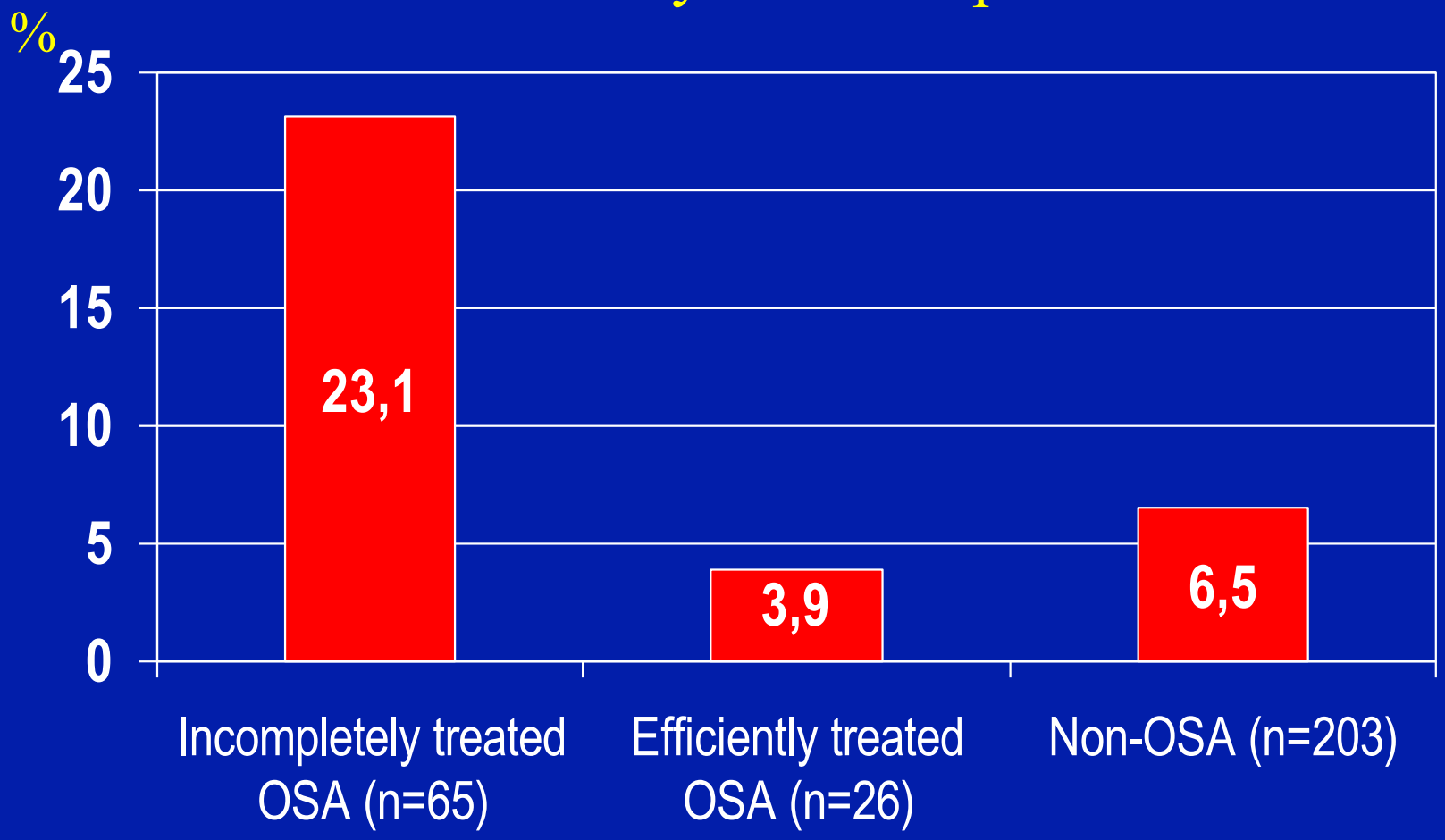
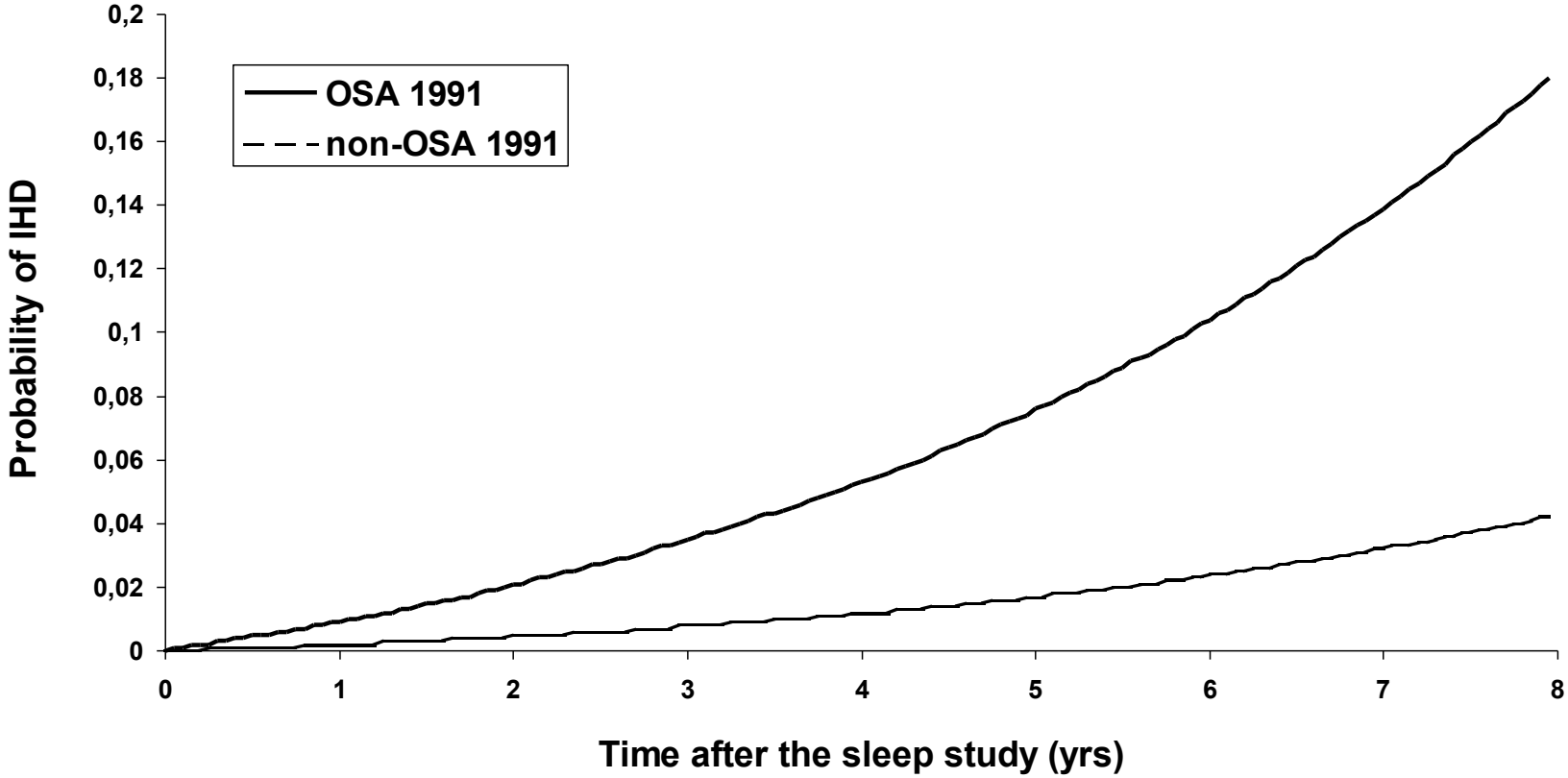
Received:

CAD incidence in a sleep-clinic cohort at a 7-yr follow-up



Peker et al, ERJ 2006

Probability of IHD incidence estimated by Poisson model Start age 49 yrs, Systolic BP 133 mmHg and Sat. min 86%



Peker et al, ERJ 2006

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Sleep-Disordered Breathing and Mortality: A Prospective Cohort Study

Naresh M. Punjabi[1]*, Brian S. Caffo[1], James L. Goodwin[2], Daniel J. Gottlieb[3], Anne B. Newman[4], George T. O'Connor[5], David M. Rapoport[6], Susan Redline[7], Helaine E. Resnick[8], John A. Robbins[9], Eyal Shahar[2], Mark L. Unruh[4], Jonathan M. Samet[10]

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Abstract

Background: Sleep-disordered breathing is a common condition associated with adverse health outcomes including hypertension and cardiovascular disease. The overall objective of this study was to determine whether sleep-disordered breathing and its sequelae of intermittent hypoxemia and recurrent arousals are associated with mortality in a community sample of adults aged 40 years or older.

Methods and Findings: We prospectively examined whether sleep-disordered breathing was associated with an increased risk of death from any cause in 6,441 men and women participating in the Sleep Heart Health Study. Sleep-disordered breathing was assessed with the apnea–hypopnea index (AHI) based on an in-home polysomnogram. Survival analysis and proportional hazards regression models were used to calculate hazard ratios for mortality after adjusting for age, sex, race, smoking status, body mass index, and prevalent medical conditions. The average follow-up period for the cohort was 8.2 y during which 1,047 participants (587 men and 460 women) died. Compared to those without sleep-disordered breathing (AHI: <5 events/h), the fully adjusted hazard ratios for all-cause mortality in those with mild (AHI: 5.0–14.9 events/h), moderate (AHI: 15.0–29.9 events/h), and severe (AHI: ≥30.0 events/h) sleep-disordered breathing were 0.93 (95% CI: 0.80–1.08), 1.17 (95% CI: 0.97–1.42), and 1.46 (95% CI: 1.14–1.86), respectively. Stratified analyses by sex and age showed that the increased risk of death associated with severe sleep-disordered breathing was statistically significant in men aged 40–70 y (hazard ratio: 2.09; 95% CI: 1.31–3.33). Measures of sleep-related intermittent hypoxemia, but not sleep fragmentation, were independently associated with all-cause mortality. Coronary artery disease–related mortality associated with sleep-disordered breathing showed a pattern of association similar to all-cause mortality.

Conclusions: Sleep-disordered breathing is associated with all-cause mortality and specifically that due to coronary artery disease, particularly in men aged 40–70 y with severe sleep-disordered breathing.

Please see later in the article for the Editors' Summary.

Table 3. Adjusted hazard ratios (95% confidence intervals) for all-cause mortality associated with sleep-disordered breathing,stratified by sex and age in the Sleep Heart Health Study.

Apnea–Hypopnea Index (Events/h)	*N*	Person–Years	Deaths	Mortality Rate[a]	Model 1[b]	Model 2[c]	Model 3[d]
Men ≤70 y							
<5.0	985	8,220	91	11.1	1.00	1.00	1.00
5.0–14.9	694	5,697	82	14.4	1.10 (0.81–1.48)	1.16 (0.85–1.58)	1.24 (0.90–1.71)
15.0–29.9	322	2,623	47	17.9	1.37 (0.96–1.95)	1.44 (1.00–2.08)	1.45 (0.98–2.14)
≥30.0	168	1,355	28	20.7	1.67 (1.09–2.55)	1.88 (1.19–2.95)	2.09 (1.31–3.33)
Men >70 y							
<5.0	277	2,055	125	60.8	1.00	1.00	1.00
5.0–14.9	282	2,176	111	51.0	0.86 (0.67–1.11)	0.89 (0.69–1.16)	0.92 (0.70–1.20)
15.0–29.9	140	1,029	67	65.1	1.18 (0.87–1.58)	1.25 (0.92–1.70)	1.23 (0.90–1.68)
≥30.0	74	517	36	69.6	1.16 (0.80–1.69)	1.25 (0.85–1.83)	1.27 (0.86–1.86)
Women ≤70 y							
<5.0	1641	13,902	90	6.5	1.00	1.00	1.00
5.0–14.9	527	4,448	40	9.0	1.00 (0.68–1.45)	0.99 (0.66–1.47)	0.97 (0.64–1.48)
15.0–29.9	161	1,350	14	10.4	1.11 (0.63–1.96)	1.12 (0.62–2.02)	1.15 (0.63–2.11)
≥30.0	63	537	8	14.9	1.73 (0.84–3.58)	1.75 (0.82–3.74)	1.76 (0.77–3.95)
Women >70 y							
<5.0	526	4,149	171	41.2	1.00	1.00	1.00
5.0–14.9	294	2,382	86	36.1	0.77 (0.60–1.00)	0.78 (0.60–1.02)	0.77 (0.58–1.00)
15.0–29.9	104	821	37	45.1	0.98 (0.68–1.40)	0.99 (0.69–1.42)	0.89 (0.61–1.31)
≥30.0	36	261	14	53.6	1.09 (0.62–1.89)	1.10 (0.63–1.92)	1.14 (0.65–2.01)

n.s

n.s

n.s

[a]Crude mortality rate per 1,000 person years.
[b]Model 1: Adjusted for age (continuous) and race.
[c]Model 2: Adjusted for covariates of model 1 and body mass index (continuous).
[d]Model 3: Adjusted for covariates of model 2, smoking status (never, former, current), systolic and diastolic blood pressure, prevalent hypertension, diabetes, and cardiovascular disease.

CAUSALITY

- Incident CAD in OSA
- Impact of the treatment of OSA on CAD

Continuous Positive Airway Pressure (CPAP)

CPAP

- Diminishes snoring
- Improves sleep quality
- Improves quality of life
- Improves daytime sleepiness
- Improves alertness
- Reduces risk för traffic accidents
- Reduces blood pressure
- Improves glycemic control in diabetics
- May reduce cardiovascular risk

in symptomatic OSA patients

CPAP treatment of CAD patients with nonsleepy OSA

Scandinavian Cardiovascular Journal
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713683216

Rationale and design of the Randomized Intervention with CPAP in Coronary Artery Disease and Sleep Apnoea - RICCADSA trial

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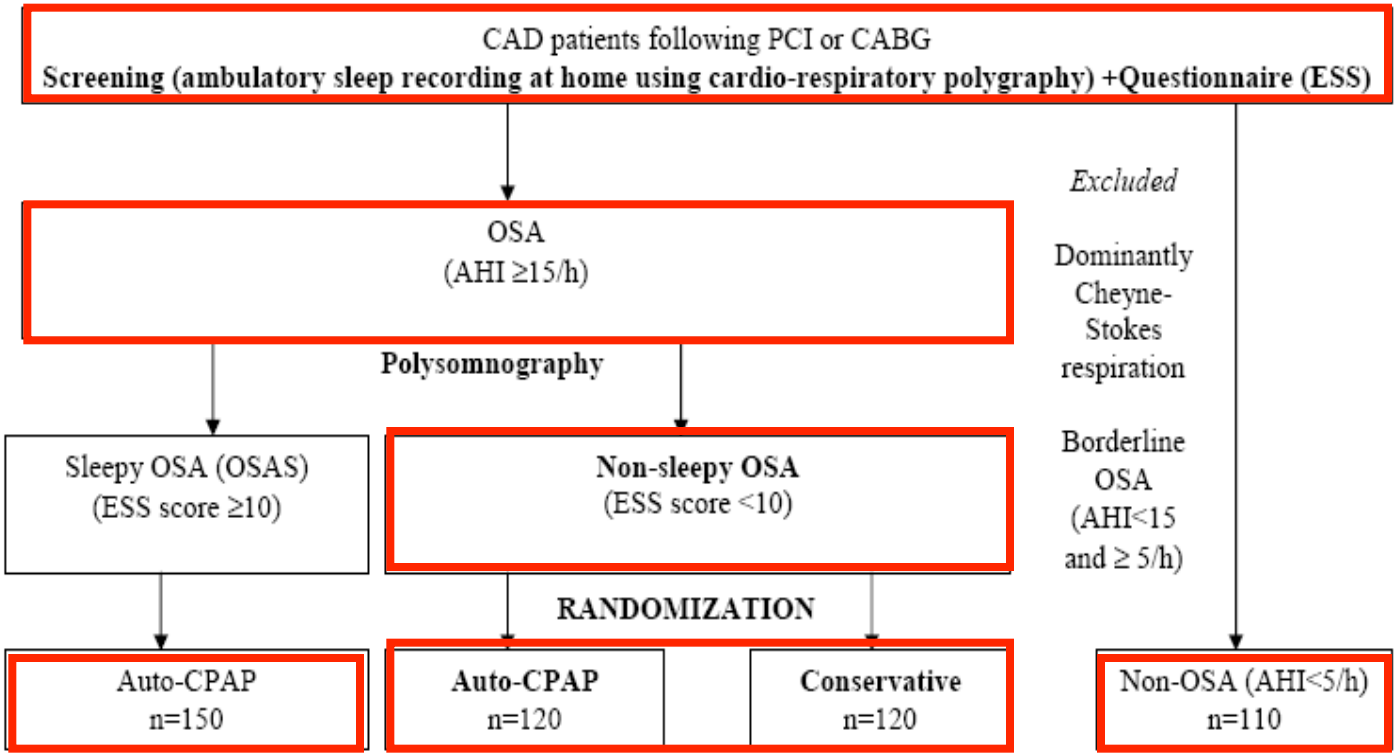
First Published on: 29 July 2008

Abstract

Rationale. Obstructive sleep apnoea (OSA) is common in coronary artery disease (CAD) and a possible cause of increased mortality. To date, there is a lack of randomized controlled trials to draw the conclusion that all CAD patients should be investigated for OSA and subsequently be treated with continuous positive airway pressure (CPAP). *Objective.* The Randomized Intervention with CPAP in CAD and OSA (RICCADSA) trial is designed to address if CPAP treatment reduces the combined rate of new revascularization, myocardial infarction, stroke and cardiovascular mortality over a 3-year period in CAD patients with OSA. Secondary outcomes include cardiovascular biomarkers, cardiac function and maximal exercise capacity at 3-month- and 1-year follow-ups. *Patients and methods.* A sample of 400 CAD patients (100 non-sleepy OSA patients randomized to CPAP, 100 to non-CPAP; 100 sleepy OSA patients on CPAP, and 100 CAD patients without OSA) will be included. So far, 240 patients have been enrolled in the trial since December 31, 2005. *Conclusion.* The RICCADSA trial will contribute to defining the impact of CPAP on prognosis of CAD patients with OSA.

Key words: *Coronary artery disease, sleep apnoe, CPAP, revascularization*

Randomized Intervention with CPAP in Coronary Artery Disease and Sleep Apnea - RICCADSA trial



Primary outcome

Combined rate of new PCI/CABG, myocardial infarction, stroke and cardiovascular mortality over a mean follow-up period of 3 years

Secondary outcomes

- Left ventricular function, maximal exercise capacity, quality of life, anxiety and depression state, cardiovascular biomarkers at baseline, 3-month- and 1-year follow-up
- Polysomnographic findings at baseline (OSA *vs* OSAS)
- Adherence to CPAP therapy during the follow-up period

Occurrence and Predictors of Obstructive Sleep Apnea in a Revascularized Coronary Artery Disease Cohort

Helena Glantz[1,2], Erik Thunström[2], Johan Herlitz[3], Björn Cederin[4], Salmir Nasic[5], Jan Ejdebäck[6], and Yüksel Peker[2,5,7]

[1]Department of Internal Medicine, Skaraborg Hospital, Lidköping, Sweden; [2]Department of Molecular and Clinical Medicine/Cardiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [3]Center of Prehospital Care in Western Sweden, University College of Borås and Sahlgrenska University Hospital, Gothenburg, Sweden; and [4]Department of Internal Medicine, [5]Center for Research, Development, and Education, [6]Department of Cardiology, and [7]Sleep Medicine Unit, Skaraborg Hospital, Skövde, Sweden

Abstract

Background: Knowledge about the prevalence of obstructive sleep apnea (OSA) in coronary artery disease (CAD) is insufficient. The aim of the current report was to evaluate the occurrence and predictors of OSA among revascularized patients with CAD within the framework of a randomized controlled trial (Randomized Intervention with CPAP in Coronary Artery Disease and Sleep Apnea [RICCADSA]), evaluating the impact of continuous positive airway pressure on cardiovascular outcomes in CAD patients with OSA.

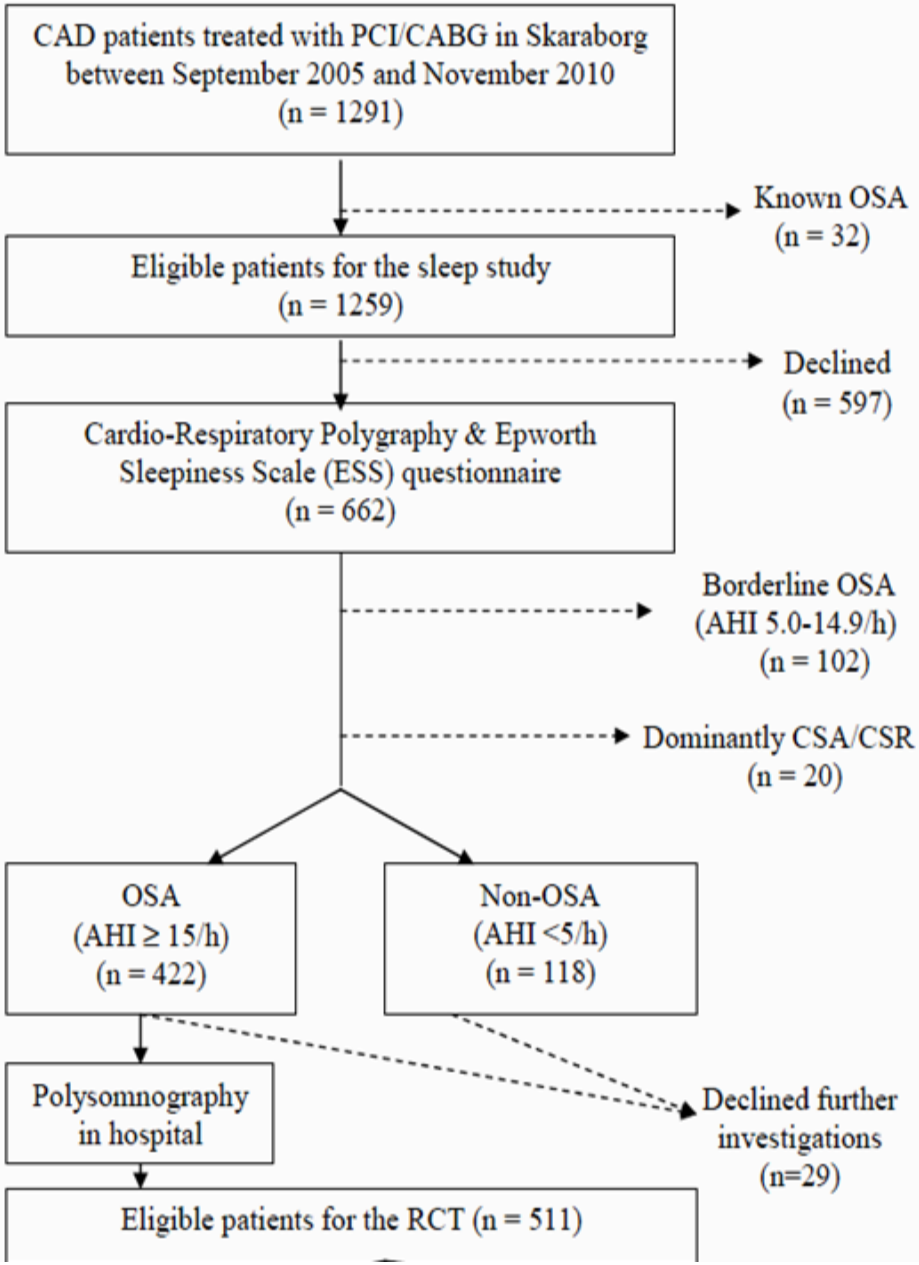
Material and Methods: All patients undergoing percutaneous coronary intervention or coronary artery bypass grafting between September 2005 and November 2010 (n = 1,291) were invited to participate. Anthropometrics and medical history were obtained, ambulatory sleep recording was performed, and all subjects completed the Epworth Sleepiness Scale (ESS) questionnaire.

Results: In total, 662 patients participated in the sleep study. OSA, defined as an apnea–hypopnea index equal to or greater than 15/hour, was found among 422 (63.7%). The prevalence of hypertension was 55.9%; obesity (body mass index $\geq$ 30 kg/m^2), 25.2%; diabetes mellitus, 22.1%; and current smoking, 18.9%. The patients with CAD who did not participate in the study demonstrated an almost similar anthropometric and clinical profile compared with the studied group. The majority (61.8%) of the patients with OSA were nonsleepy (ESS score $<$ 10). Patients with OSA had a higher prevalence of obesity, hypertension, diabetes mellitus, and history of atrial fibrillation, whereas current smoking was more common in the non-OSA group. Age, male sex, body mass index, and ESS score, but not comorbidities, were independent predictors of OSA.

Conclusions: The occurrence of unrecognized OSA in this revascularized CAD cohort was higher than previously reported. We suggest that OSA should be considered in the secondary prevention protocols in CAD.

Keywords: angioplasty; bypass; coronary disease; risk factors; sleep apnea

STUDY POPULATION



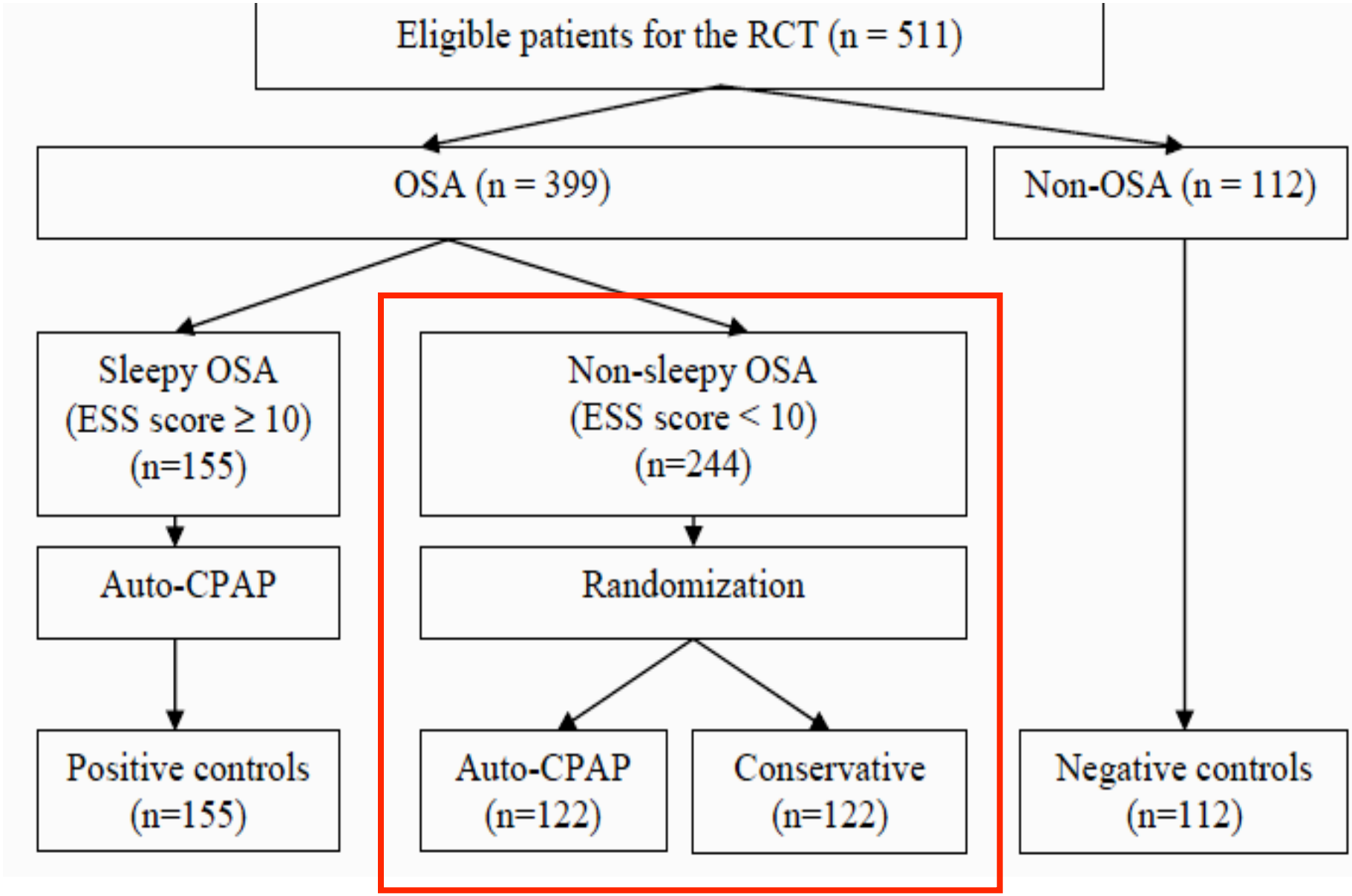
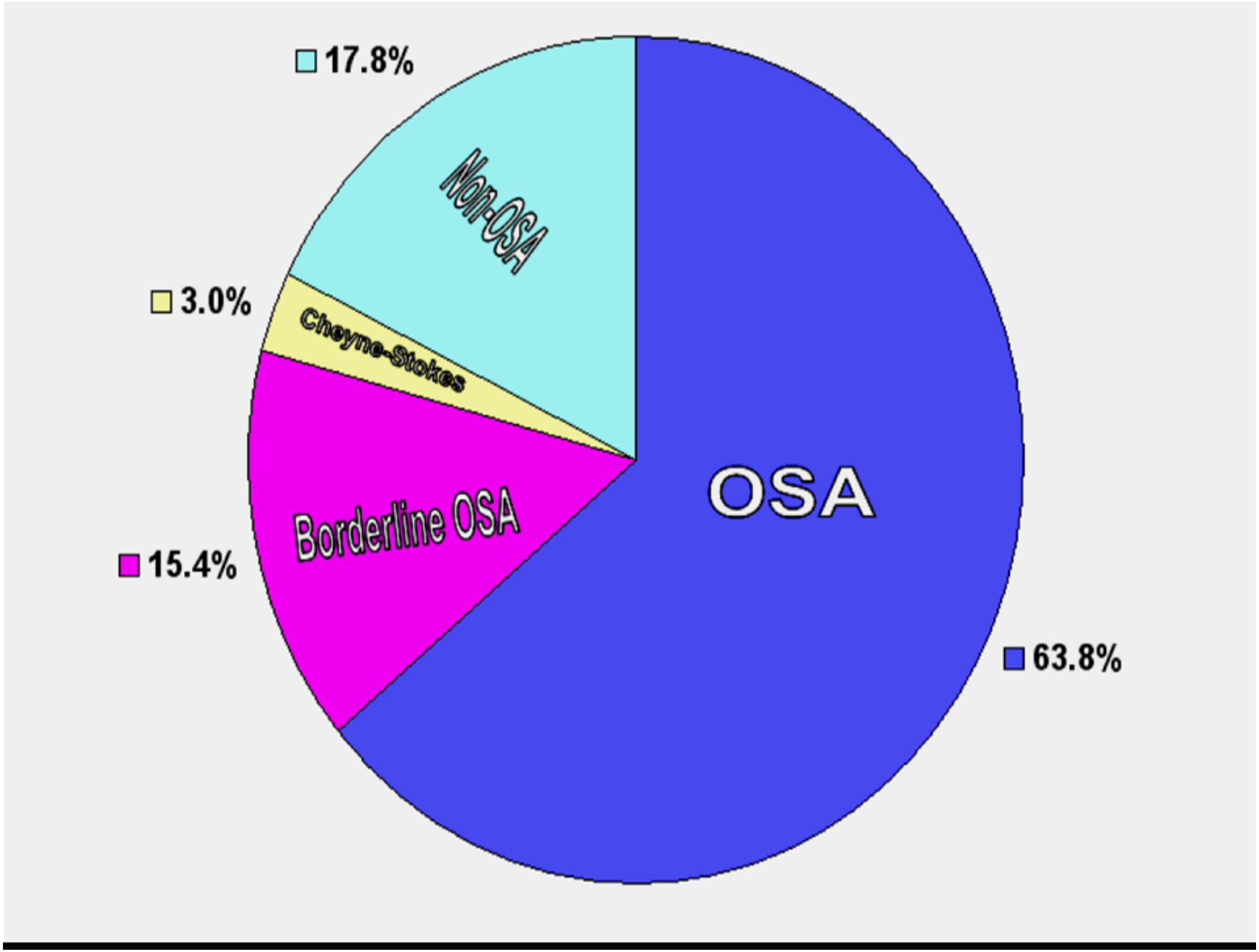

Eligible patients for the RCT (n = 511)
OSA (n = 399)
Non-OSA (n = 112)
Sleepy OSA
(ESS score ≥ 10)
(n=155)
Non-sleepy OSA
(ESS score < 10)
(n=244)
Auto-CPAP
Randomization
Positive controls
(n=155)
Auto-CPAP
(n=122)
Conservative
(n=122)
Negative controls
(n=112)

Table 1. Demographic and clinical characteristics of entire study population

Variable	Sleep Study Performed (*n* = 662)	No Sleep Study (*n* = 597)	*P* Value*
Age, yr	64.1 ± 8.7	66.8 ± 9.2	<0.001
BMI, kg/m^2	28.0 ± 4.0	27.5 ± 4.2	0.061
Obesity, %	25.2	22.1	0.198
Male sex, %	84.3	76.9	<0.001
Current smokers, %	20.1	23.9	0.117
Lung disease, %	9.1	5.8	0.024
CABG at inclusion, %	24.0	30.8	0.007
Hypertension, %	56.7	55.2	0.592
Atrial fibrillation, %	17.9	18.8	0.679
Diabetes mellitus, %	22.2	24.4	0.362
Stroke, %	7.2	7.3	0.951
Depression, %	4.9	3.9	0.420

Ann Am Thorac Soc Vol 10, No 4, pp 350–356, Aug 2013

Sleep Study Results based on Polygraphy (n=662)



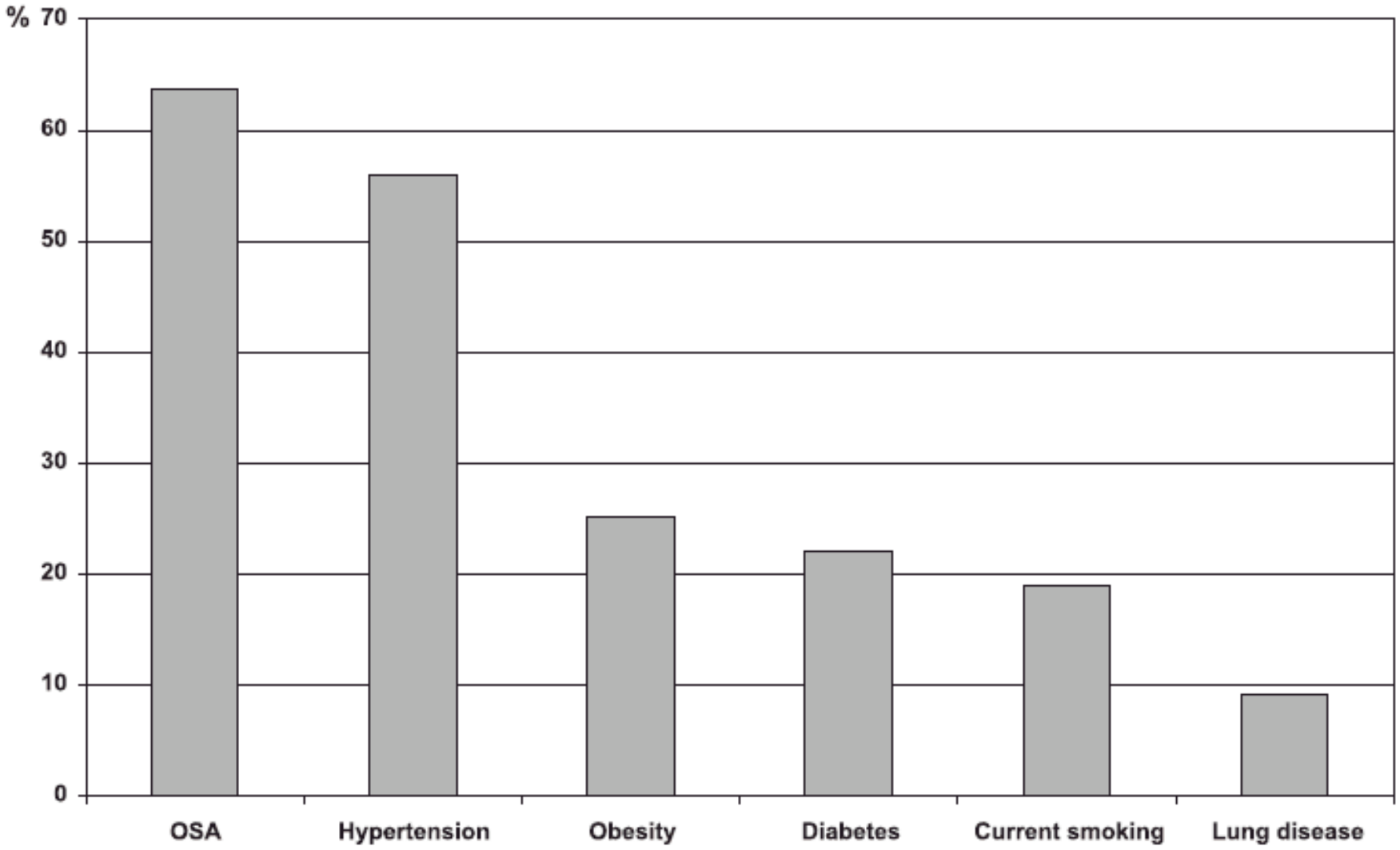


Figure 2. Occurrence of obstructive sleep apnea and the traditionally recognized risk indicators for coronary artery disease. OSA = obstructive sleep apnea.

Ann Am Thorac Soc Vol 10, No 4, pp 350–356, Aug 2013

Baseline characteristics of the RICCADSA cohort

Variable	OSA	non-OSA	p Value
AHI (n/h)	30.1±14.6	3.2±2.5	<0.001
Age (yrs)	64.4±8.4	61.9±9.0	0.011
Male gender (%)	85.4	75.5	0.018
BMI (kg/m^2)	29.4±11.5	25.5±3.0	0.001
Obesity (BMI≥30 kg/ m^2) (%)	33.7	5.9	<0.001
Hypertension (%)	60.6	47.8	0.029
Diabetes mellitus (%)	25.4	12.8	0.013
Atrial fibrillation (%)	19.8	9.1	0.019
Baseline by-pass-surgery (%)	28.1	17.6	0.033
Previous revascularization (%)	20.2	18.9	N S
Current smokers (%)	16.9	26.4	0.044
COPD/Asthma (%)	8.4	15.6	0.043

CONCLUSIONS

- Among revascularized CAD patients, OSA was more prevalent than other traditional risk indicators, suggesting that OSA should be considered as a confounding factor in the secondary prevention protocols

- Whether or not all CAD patients with OSA should be treated by CPAP, regardless of daytime sleepiness, needs to be further clarified

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Effect of Positive Airway Pressure on Cardiovascular Outcomes in Coronary Artery Disease Patients with Non-Sleepy Obstructive Sleep Apnea: The RICCADSA Randomized Controlled Trial

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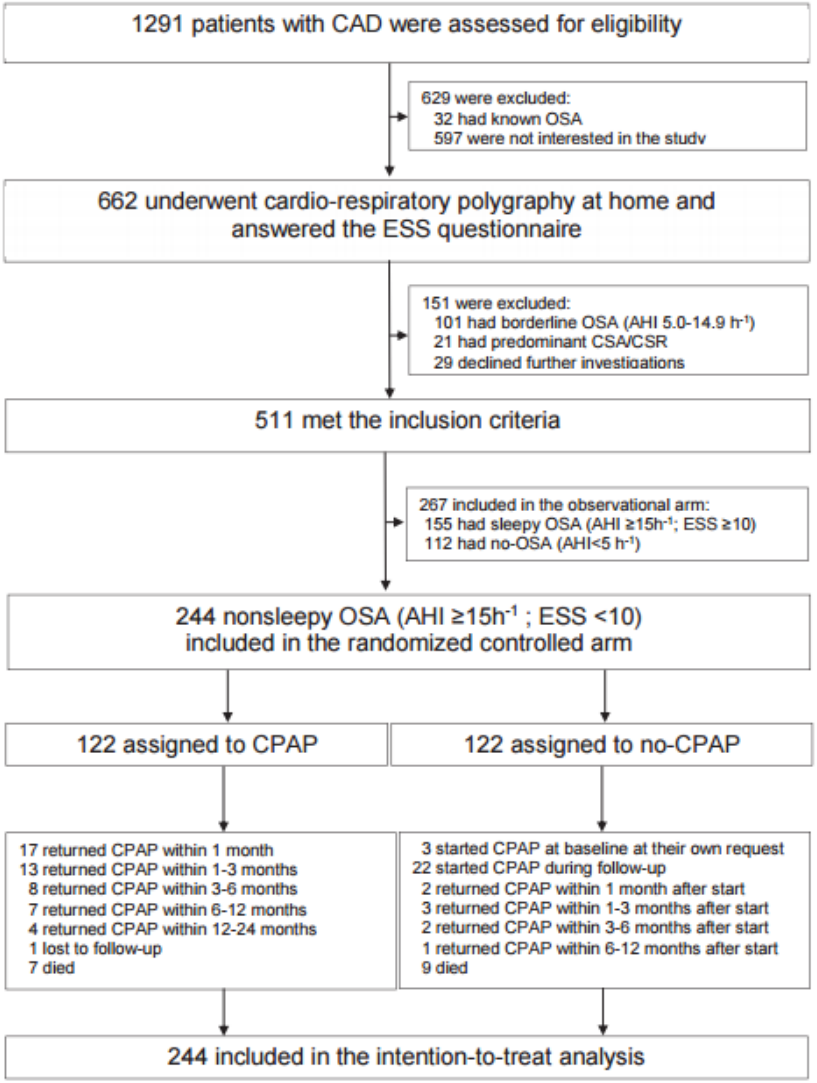

Figure 1. Flow of patients through the study. Definition of abbreviations: AHI, apnea-hypopnea index; CAD; coronary artery disease; CPAP, continuous positive airway pressure; CSA-CSR, central sleep apnea-Cheyne Stokes respiration; ESS, Epworth Sleepiness Scale; OSA, obstructive sleep apnea; RICCADSA, Randomized Intervention with CPAP in Coronary Artery Disease and Sleep Apnea.

Intention-to-treat Population

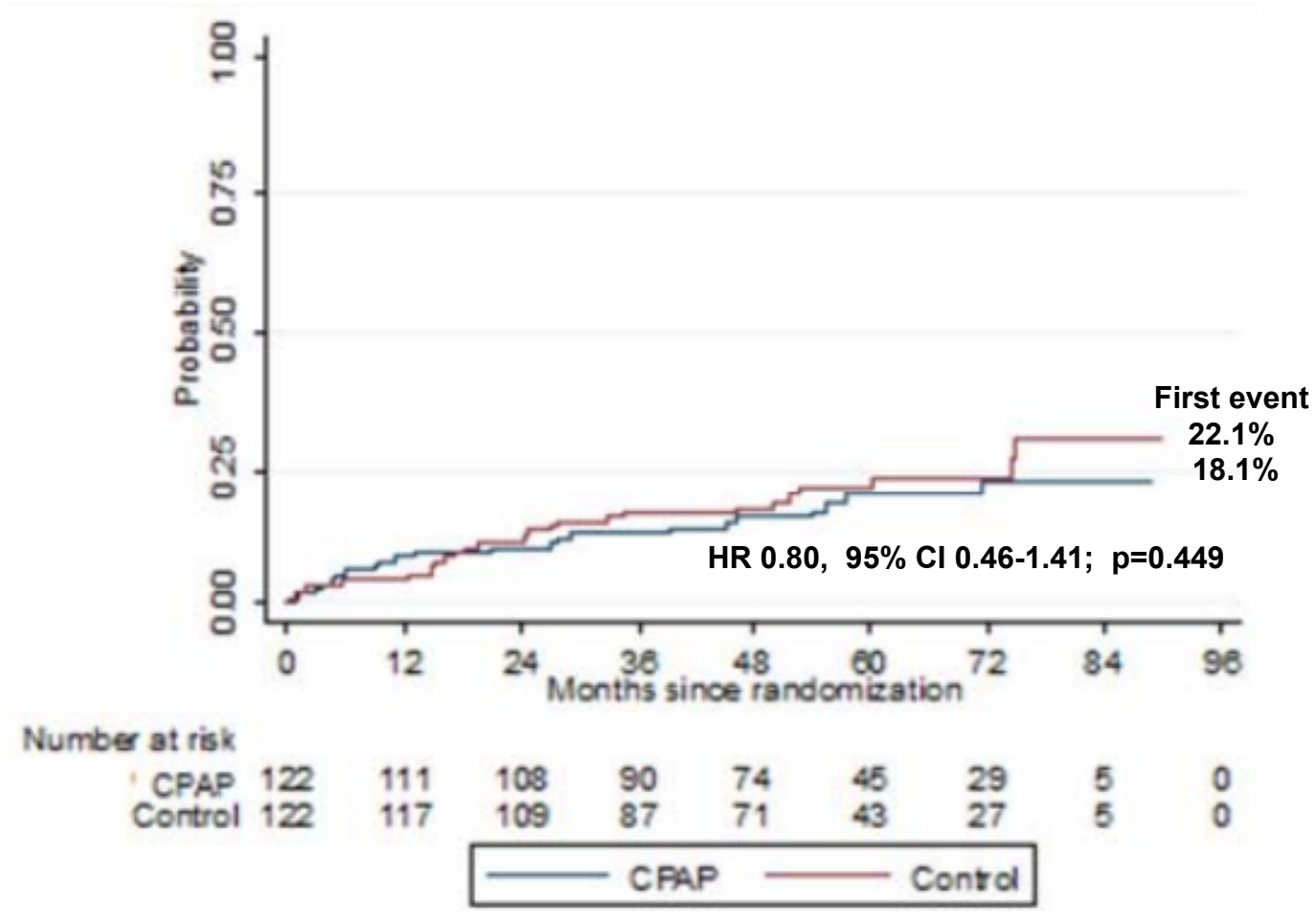

Table 2. Cox regression analysis of baseline covariables associated with risk for adverse cardiovascular outcomes in revascularized patients with coronary artery disease and obstructive sleep apnea without daytime sleepiness in the intention-to-treat analysis (n=244; 49 patients reached the composite endpoint)

	Univariate			Multivariate		
	Hazard Ratio	**95% CI**	***P* Value**	**Hazard Ratio**	**95% CI**	**Value**
CPAP assignment vs. no-CPAP	0.80	0.46–1.41	0.449	0.62	0.34–1.13	0.120
Age	1.02	0.98–1.05	0.372	1.01	0.98–1.05	0.474
Females vs. males	0.48	0.17–1.33	0.155	0.43	0.15–1.23	0.114
Apnea-hypopnea index	1.00	0.98–1.02	0.783	0.99	0.97–1.01	0.363
Body mass index	1.01	0.94–1.09	0.753	0.99	0.91–1.08	0.802
CABG vs. PCI	0.38	0.17–0.84	0.017	0.30	0.12–0.75	0.010
Current smoking	1.29	0.63–2.67	0.485	1.78	0.80–3.96	0.156
Hypertension	1.09	0.60–1.96	0.776	1.59	0.81–3.12	0.176
Diabetes mellitus	1.92	1.06–3.47	0.030	2.05	1.06–3.98	0.034
Acute myocardial infarction	1.02	0.58–1.79	0.947	1.03	0.54–1.94	0.937
Previous PCI or CABG	3.36	1.91–5.93	<0.001	3.29	1.77–6.10	0.001
Pulmonary disease	1.39	0.50–3.85	0.532	0.95	0.33–2.74	0.925
Left ventricular ejection fraction	0.99	0.96–1.02	0.594	0.99	0.96–1.02	0.513

Definition of abbreviations: CABG, coronary artery bypass grafting; CI, confidence interval; CPAP, continuous positive airway pressure; PCI, percutaneous coronary intervention.

Table 3. Cox regression analysis of the association between time-dependent CPAP usage (hours/night) and adverse cardiovascular outcomes in 244 revascularized patients with coronary artery disease and obstructive sleep apnea without daytime sleepiness (49 patients reached the composite endpoint).

	Univariate			Multivariate		
	Hazard Ratio	**95% CI**	***P* Value**	**Hazard Ratio**	**95% CI**	***P* Value**
CPAP usage ≥3 hours/night	0.64	0.31–1.33	0.234	0.91	0.16–5.13	0.911
CPAP usage ≥4 hours/night	0.43	0.18–1.02	0.057	0.29	0.10–0.86	0.026
CPAP usage ≥5 hours/night	0.43	0.17–1.09	0.075	0.34	0.10–1.12	0.075

Definition of abbreviations: CPAP, continuous positive airway pressure, CI, confidence interval.
*Adjusted for age, gender, body mass index, apnea hypopnea index, current smoking, pulmonary disease, hypertension, diabetes mellitus, acute myocardial infarction, revascularization type at baseline, former revascularization, and left ventricular ejection fraction at baseline.

Conclusions

- Routine prescription of CPAP to CAD and nonsleepy OSA did not significantly reduce long-term adverse cardiovascular event rate
- Significant beneficial effect of CPAP was seen after adjusting for baseline comorbities and CPAP adherence
- These findings need to be confirmed in larger clinical cohorts with homogenous phenotypes of CAD and OSA

Short Communication

The sleep apnea cardiovascular endpoints (SAVE) trial: Rationale and start-up phase

R Doug McEvoy [1], Craig S Anderson [2], Nick A Antic [1], Baoyuan Chen [3], Quanying He [4], Emma Heeley [2], Shaoguang Huang [5], Yining Huang [6], Jiguang Wang [7], Nanshan Zhong [8]

J Thorac Dis 2010;2:138-143

Trial Designs

Rationale and Methodology of the Impact of Continuous Positive Airway Pressure on Patients With ACS and Nonsleepy OSA: The ISAACC Trial

Cristina Esquinas, RN, MPH; Manuel Sánchez-de-la Torre, Phd; Albina Aldomá, MD; Marina Florés, MD; Montserrat Martínez, BSc(Stat); Antonia Barceló, MD; Ferran Barbé, MD; on behalf the Spanish Sleep Network

Clin Cardiol 2013;36:495-501