La sindrome delle apnee notturne: quale impatto nel paziente anziano?

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Outline

- Definizione
- Cenni di epidemiologia
- Significato clinico
- Peculiarità nell’anziano
- Alcuni aspetti terapeutici
- Una revisione (iper)critica

Criteri diagnostici (ICSD-2014)

NELL' ADULTO

1.Apnea-hypopnea index (AHI) di almeno 5 eventi/ora associato a:

- segni/sintomi (eccessiva sonnolenza diurna, fatica, insonnia, russamento, disturbi respiratori notturni soggettivi, apnee osservate)
- quadri medici e/o psichiatrici (ipertensione arteriosa, patologia coronarica, fibrillazione atriale, insufficienza cardiaca cronica, ictus, diabete, disfunzioni cognitive o disturbi dell' umore)

OPPURE

2.AHI di almeno 15 eventi/ora, indipendentemente da altri segni/sintomi o quadri medici o psichiatrici.

SULLA BASE DELL' AHI L' OSAS È DEFINITA:

•di grado lieve (AHI compreso tra 5 e 14)
•moderato (AHI compreso tra 15 e 29)
•grave (AHI pari o superiore a 30).

Table 1. Obstructive Sleep Apnea–Related Terms and Definitions

Term	Definition
Apnea	Cessation of airflow for at least 10 s[1,2]
Hypopnea	Reduction in airflow by at least 30% for at least 10 s with decrease in oxygen saturation
AHI[a,b,c]	Number of apneas and hypopneas per h of sleep
OSA[d]	
Mild[1,3]	AHI ≥5 to <15
Moderate[1,3]	AHI ≥15 to <30
Severe[1,3]	AHI ≥30
Obstructive sleep apnea syndrome	AHI ≥5 with evidence of daytime sleepiness[1,4,5]

Quadro sinottico

	Riduz. flusso	Desaturaz.	Arousal EEG	Sforzo inspirat. (EMG intercost., sensori toraco-addominali)
Apnea ostruttiva	>90% per >10 sec	>4%	si	Si
Ipopnea ostruttiva	>30% per >10 sec >50% per >10 sec	>4% >3%	si	Si
Apnea centrale	>90% per >10 sec	Lieve/assente	No	No
Ipopnea centrale	>30% per >10 sec	Lieve/assente	No	No

OSAS: ignorata nell'anziano

(Braley TJ et al. J Am Geriatr Soc 2018; 66:1296–1302)

- OBJECTIVES: To estimate the proportion of older Americans at risk for obstructive sleep apnea (OSA) who receive OSA evaluations, diagnosis, and treatment. DESIGN: Cross sectional study.
- SETTING: National Health and Aging Trends Study (NHATS), Round 3 survey. PARTICIPANTS: Community-dwelling Medicare beneficiaries age 65 and older (N51,052).
- RESULTS: Of 1,052 participants who completed the sleep module, 56% (95% confidence interval (CI)553–59%) were estimated to be at high risk of OSA. Only 8% (95% CI55–11%) of the high-risk individuals had been tested for it. Of those tested, 94% (95% CI587–100%) were diagnosed with OSA. Treatment with positive airway pres-sure was prescribed for 82% (95% CI565–99%) of participants with an OSA diagnosis

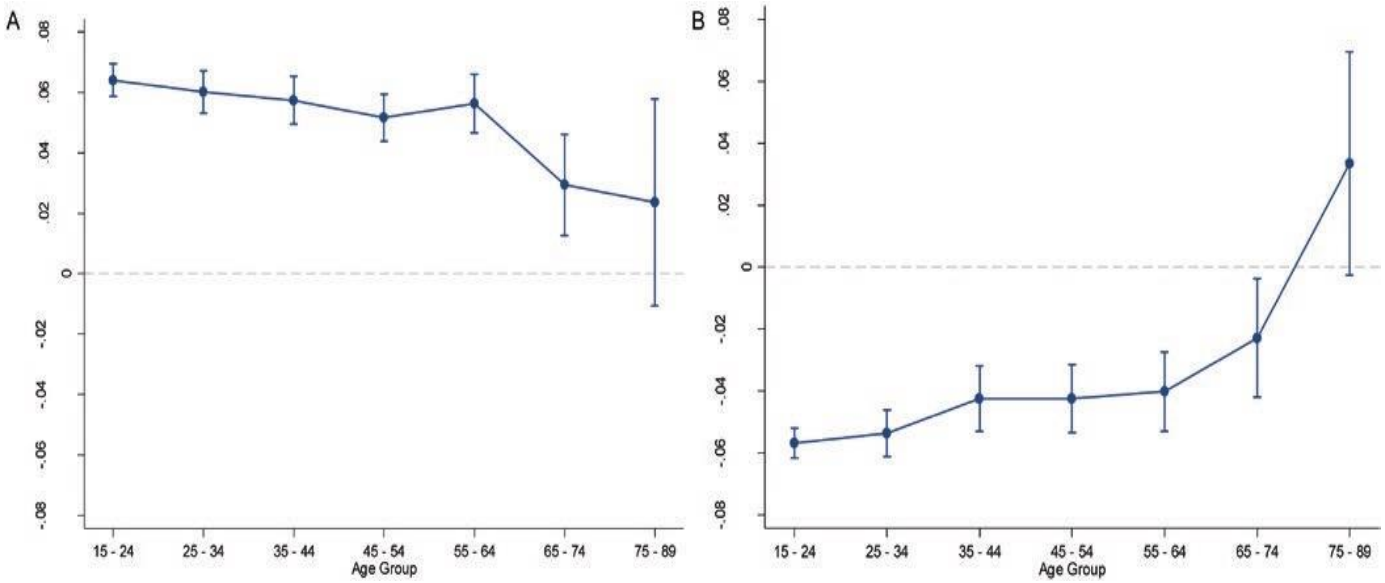
- CONCLUSIONS: Evidence from this nationally representative sample of community-dwelling Medicare beneficiaries suggests that high OSA risk is common but seldom investigated. When investigated, OSA is almost always confirmed and usually treated. These findings suggest a significant gap in OSA assessment for older Americans that could have public health implications.

La sonnolenza, non l'insonnia, è marker di fragilità (Vaz Fragoso C et al. J Am Geriatr Soc 2009; 57:2094–2100)

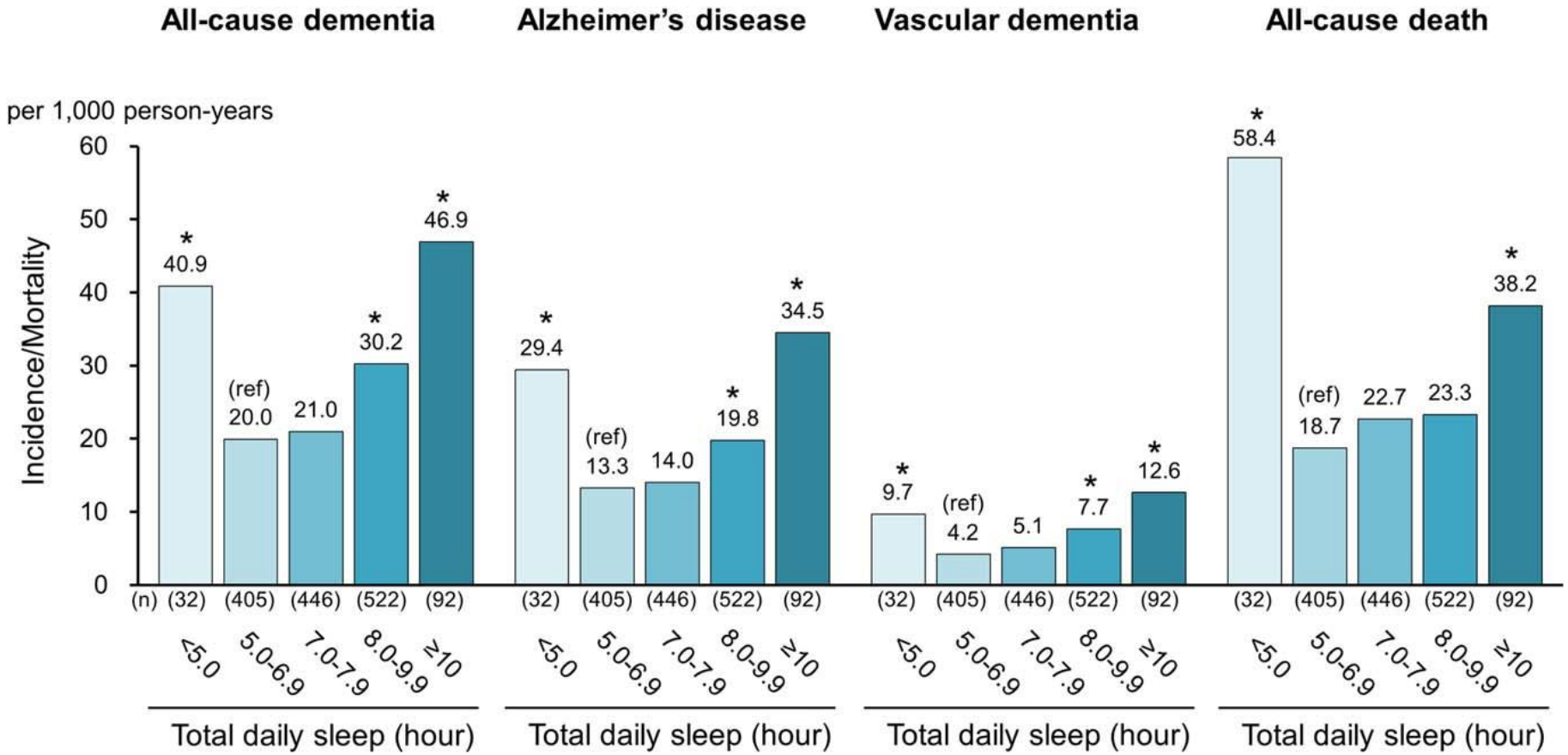
Table 3. Slow Gait Speed According to the Epworth Sleepiness Scale (ESS) and Insomnia Severity Index (ISI)

		Odds Ratio (95% Confidence Interval)	
Sleep Questionnaire	**n/N (%)**	**Unadjusted**	**Adjusted***
ESS score			
<10 (no drowsiness)	126/284 (44.4)	1.00	
≥10 (daytime drowsiness)	61/87 (70.1)	2.94 (1.76–4.92)	3.12 (1.72–5.65)†
ISI score			
<8 (no insomnia)	112/216 (51.9)	1.00	
8–14 (subthreshold insomnia)	57/122 (46.7)	0.81 (0.52–1.27)	0.68 (0.39–1.17)‡
>14 (clinical insomnia)	25/39 (64.1)	1.66 (0.82–3.36)	1.01 (0.42–2.44)‡

Sette ore di sonno si associano con la migliore performance cognitiva, ma nell'anziano…. (Richards A et al. Sleep 2016; 40:1)



Ore di sonno riferite a 60 anni e rischio di demenza e morte a 70 anni (Ohara T et al. **J** Am Ger Soc 2018; **66:1911– 1918)**

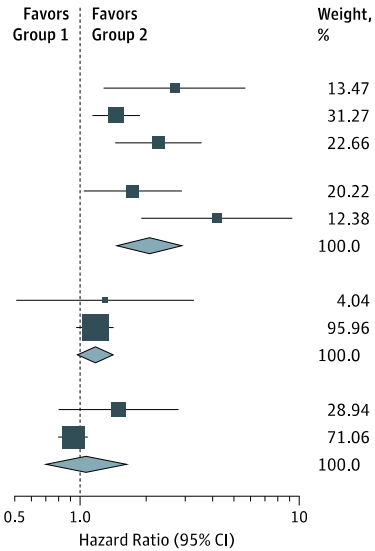


OSA e mortalità

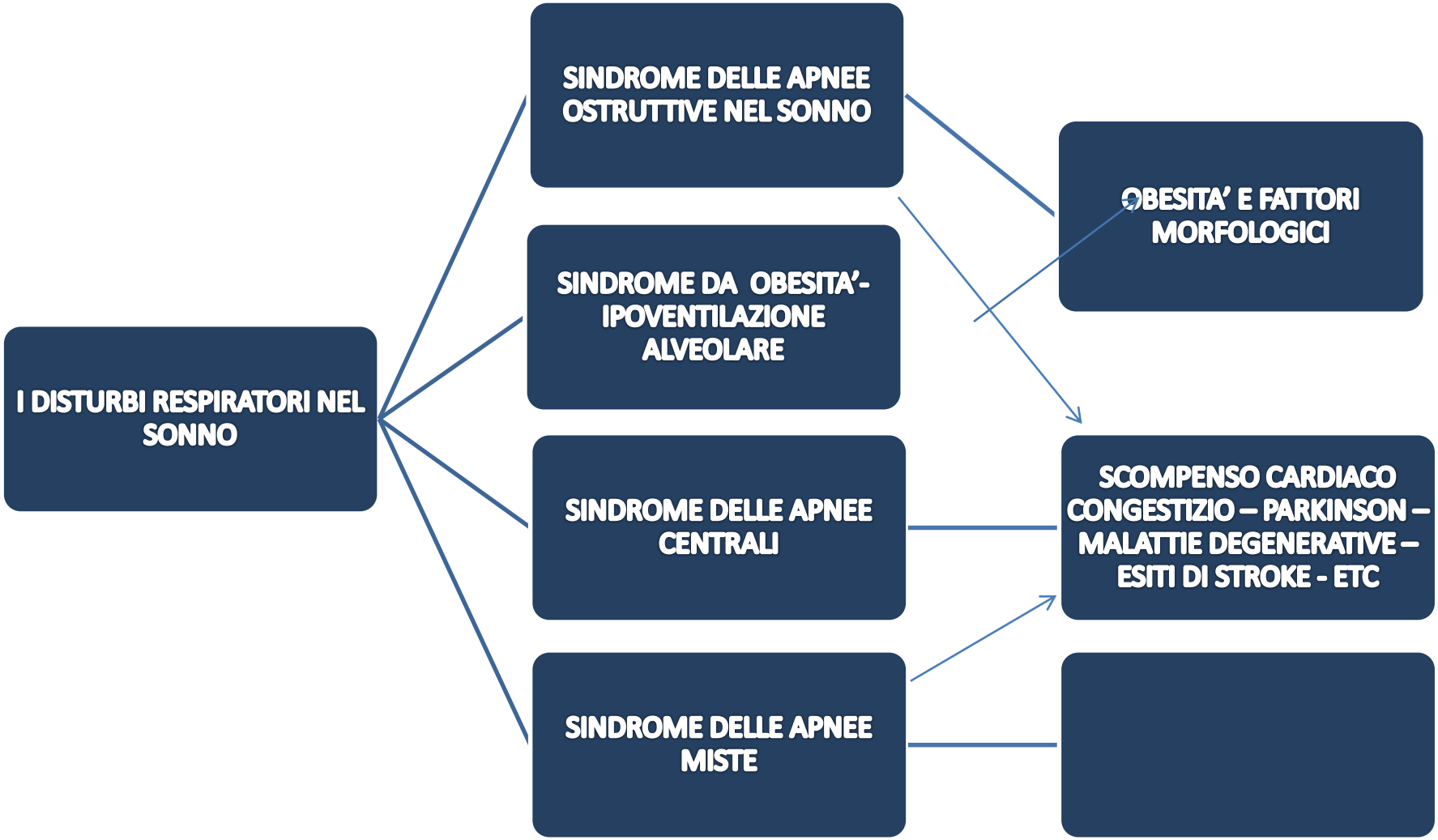
(Jonas DE et al. *JAMA*. 2017; 317: 415-433)

Figure 3. Association Between Apnea-Hypopnea Index and All-Cause Mortality, by OSA Severity

Source	No. of Deaths/ Total No. (%) Group 1	No. of Deaths/ Total No. (%) Group 2	Follow-up, y	Apnea-Hypopnea Index Comparison, Group 1 vs Group 2	Hazard Ratio (95% CI)	Weight, %
Severe OSA						
Young et al,[150] 2008	12/63 (19.0)	46/1157 (4.0)	13.8	≥30 vs <5	2.70 (1.29-5.65)	13.47
Punjabi et al,[151] 2009	86/341 (25.2)	477/3429 (13.9)	8.2	≥30 vs <5	1.46 (1.14-1.86)	31.27
Gooneratne et al,[147] 2011	35/42 (83.3)	59/119 (49.6)	13.8	≥20 and EDS vs <20 and no EDS	2.28 (1.46-3.57)	22.66
Ensrud et al,[144] 2012	25/209 (12.0)	155/2296 (6.8)	3.4	≥30 vs <30	1.74 (1.04-2.90)	20.22
Marshall et al,[153] 2014	10/18 (55.6)	54/294 (18.4)	20	≥15 vs <5	4.20 (1.91-9.24)	12.38
Subtotal (I^2 = 57.8%, P = .05)					2.07 (1.48-2.91)	100.0
Moderate OSA						
Young et al,[150] 2008	6/82 (7.3)	46/1157 (4.0)	13.8	15 to <30 vs <5	1.30 (0.51-3.29)	4.04
Punjabi et al,[151] 2009	165/727 (22.7)	477/3429 (13.9)	8.2	15 to <30 vs <5	1.17 (0.97-1.42)	95.96
Subtotal (I^2 = 0.0%, P = .83)					1.17 (0.97-1.42)	100.0
Mild OSA						
Young et al,[150] 2008	16/220 (7.3)	46/1157 (4.0)	13.8	5 to <15 vs <5	1.50 (0.80-2.81)	28.94
Punjabi et al,[151] 2009	319/1797 (17.8)	477/3429 (13.9)	8.2	5 to <15 vs <5	0.93 (0.80-1.08)	71.06
Subtotal (I^2 = 52.7%, P = .15)					1.07 (0.70-1.63)	100.0



I DISTURBI RESPIRATORI NEL SONNO



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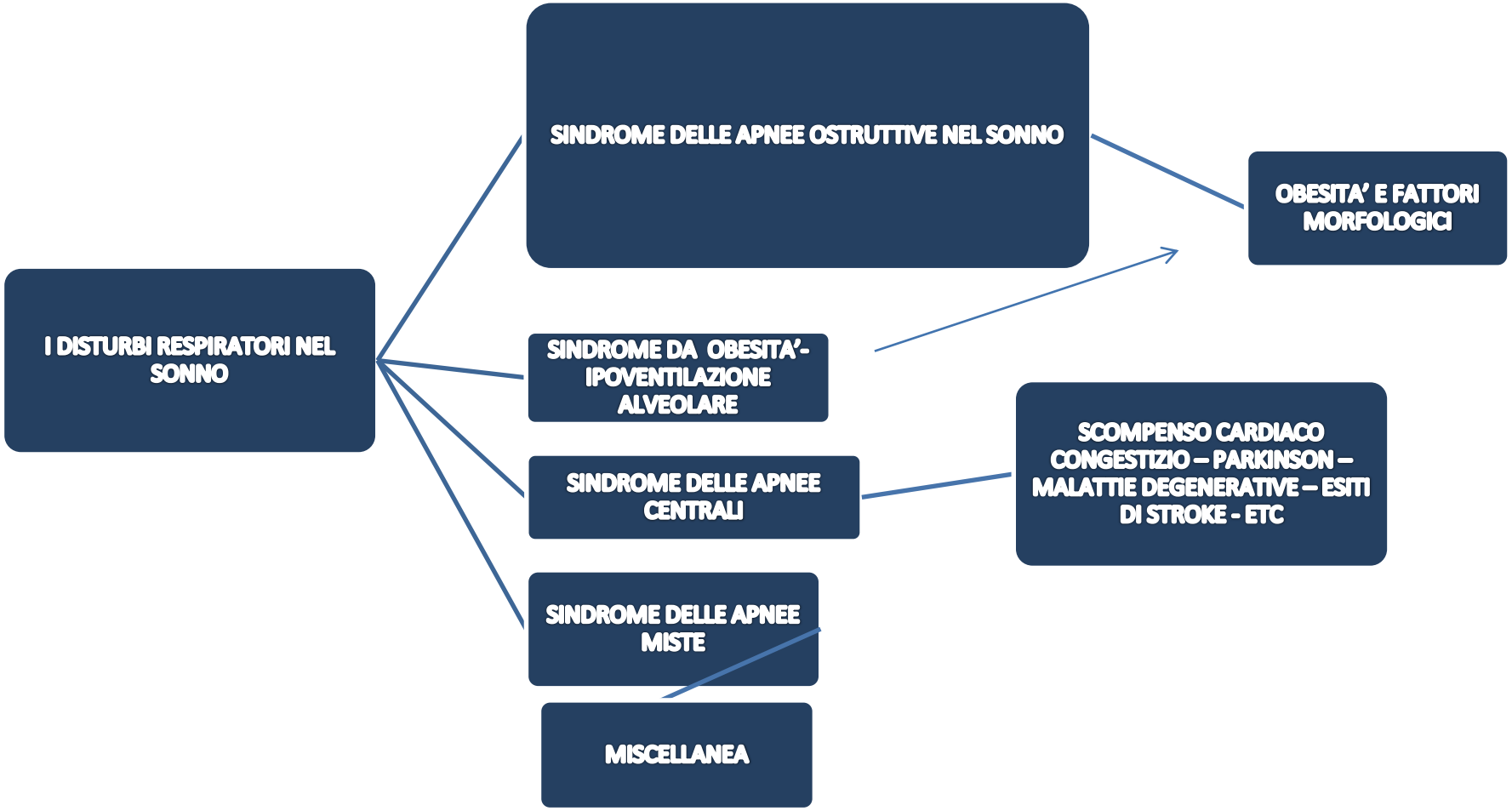
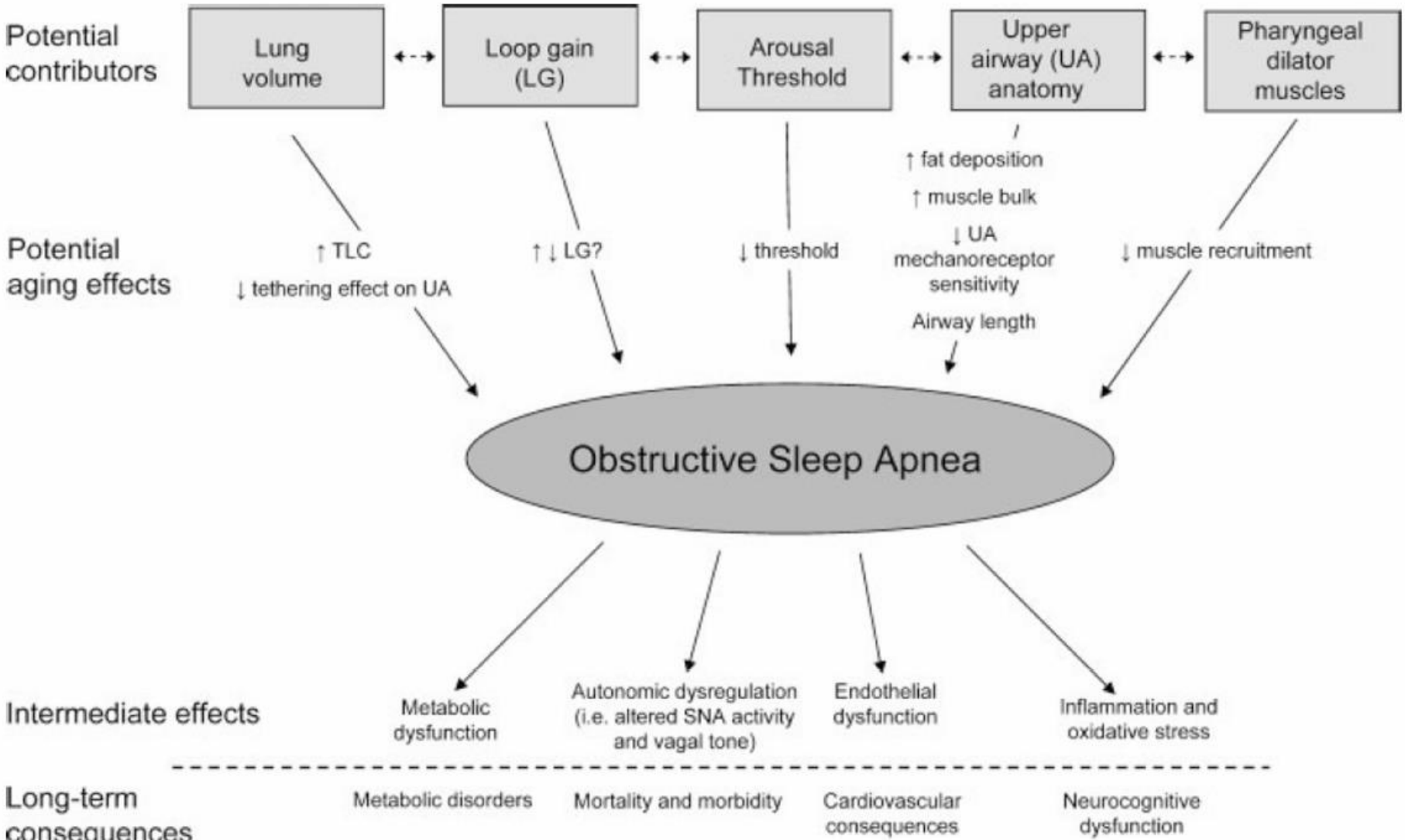


Il rapporto Età-OSA

(Edwards BA et al. Semin Respir Crit Care Med. 2010; 31: 618)



Apnee e CHF stabile

(Ferreira et al. BMC Pulmonary Medicine 2010, 10:9)

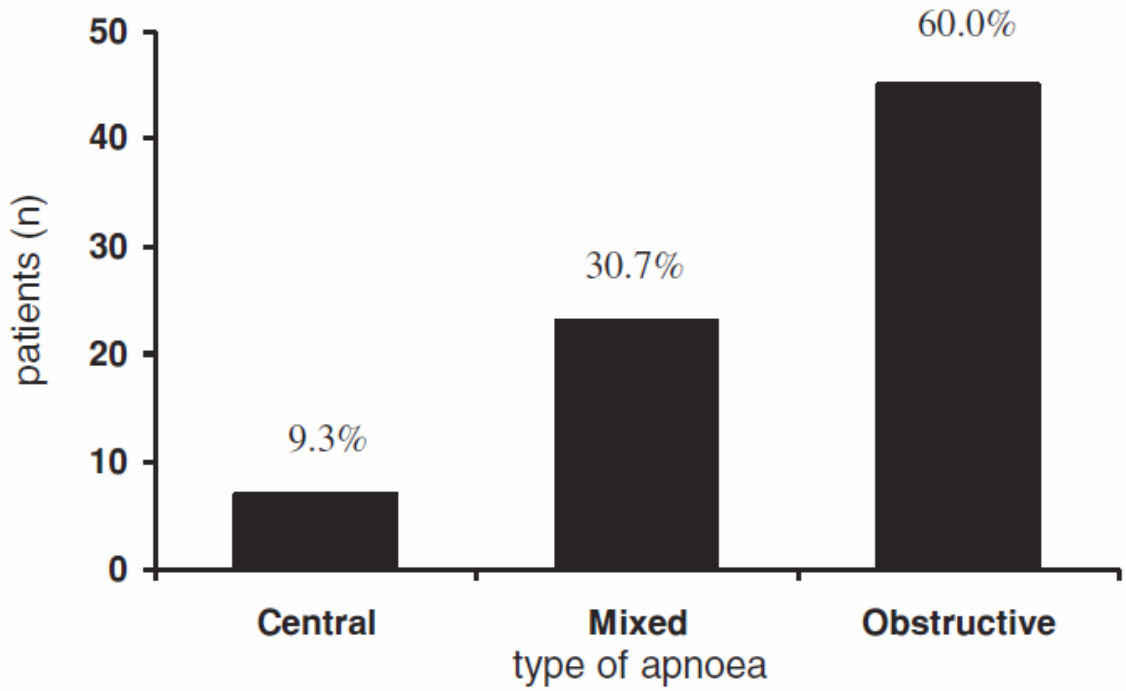
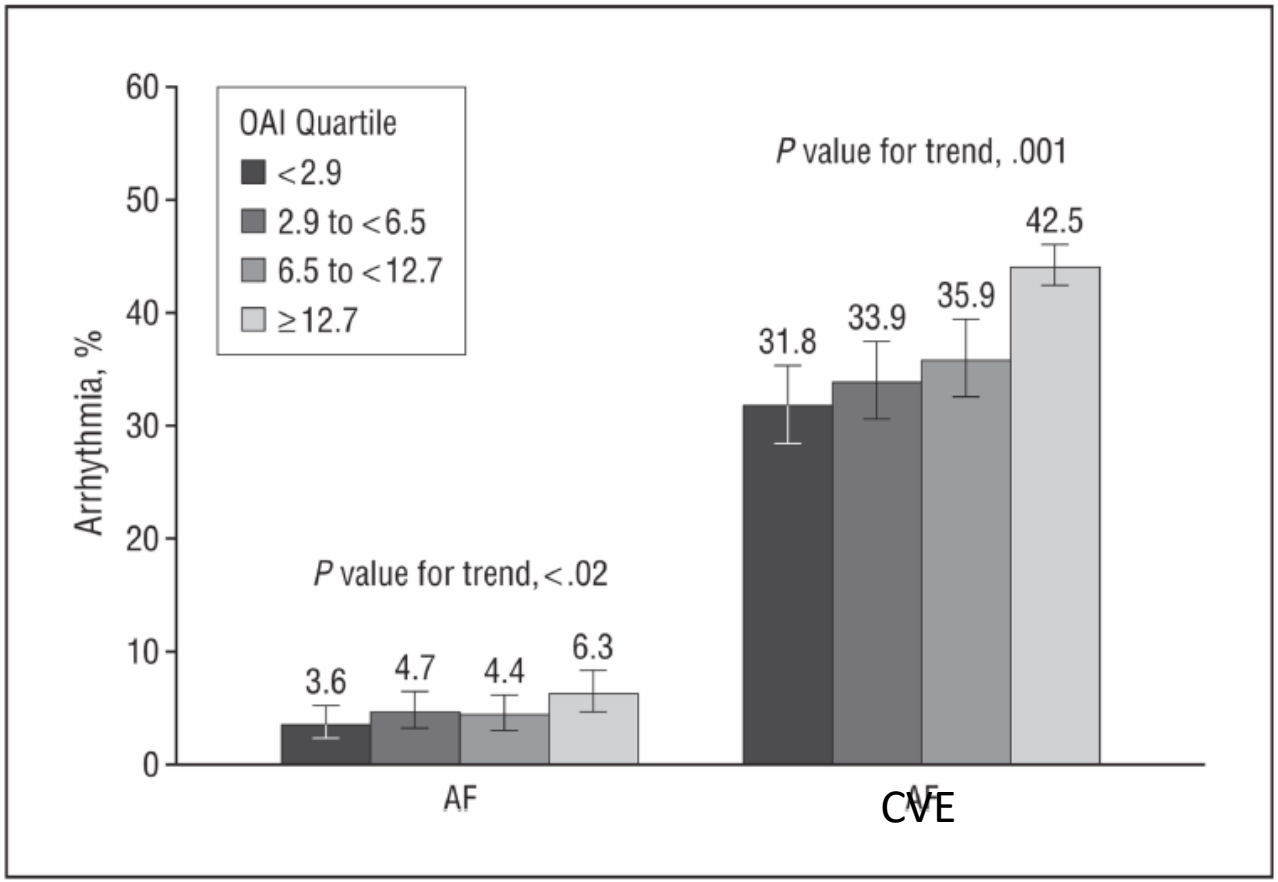


Figure 2 Type of sleep apnoea in heart failure.

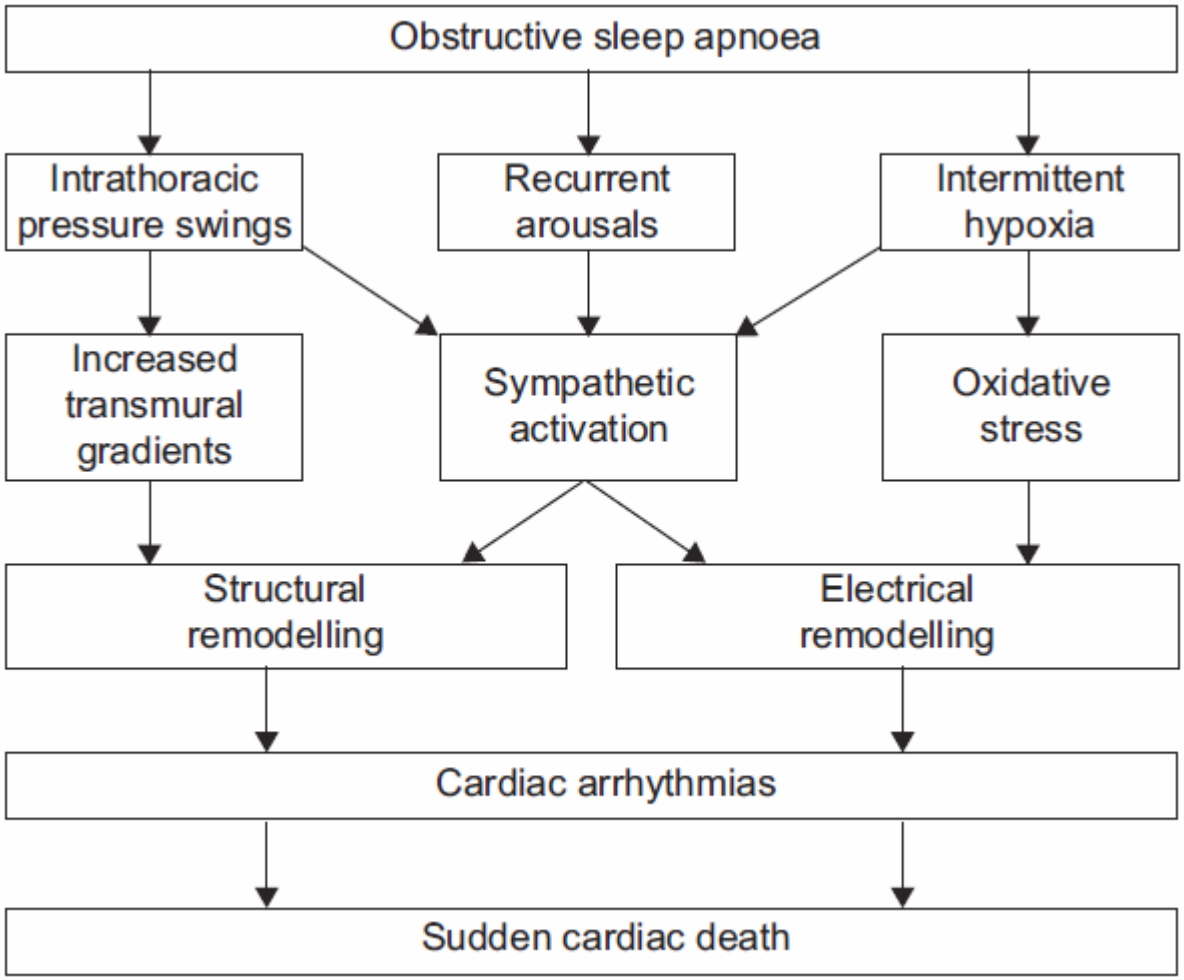
Most patients were non-sleepy
(Epworth < 10- 66%)

OSA e aritmie (Mehra R et al. *Arch Intern Med*. 2009; 169: 1147)

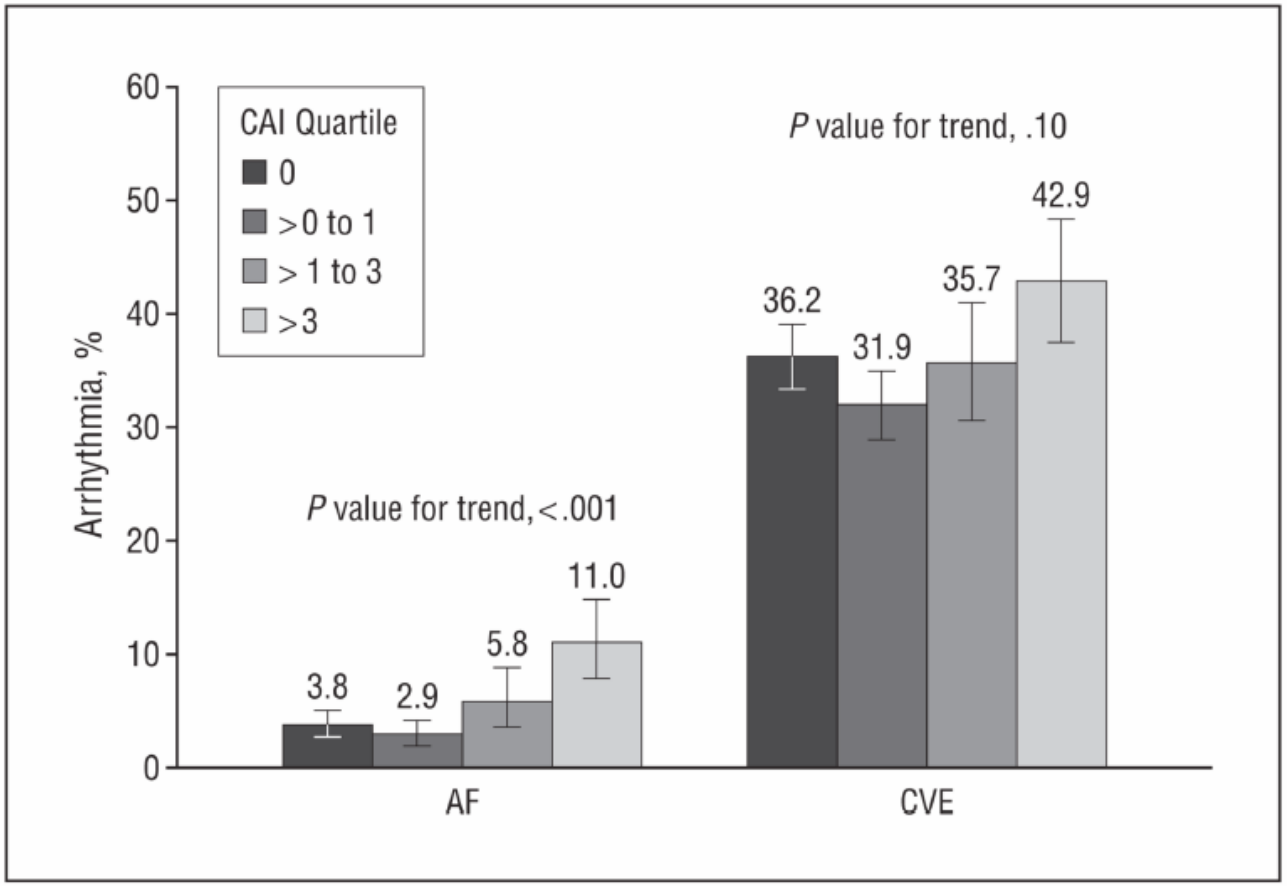


OSA e aritmogenesi

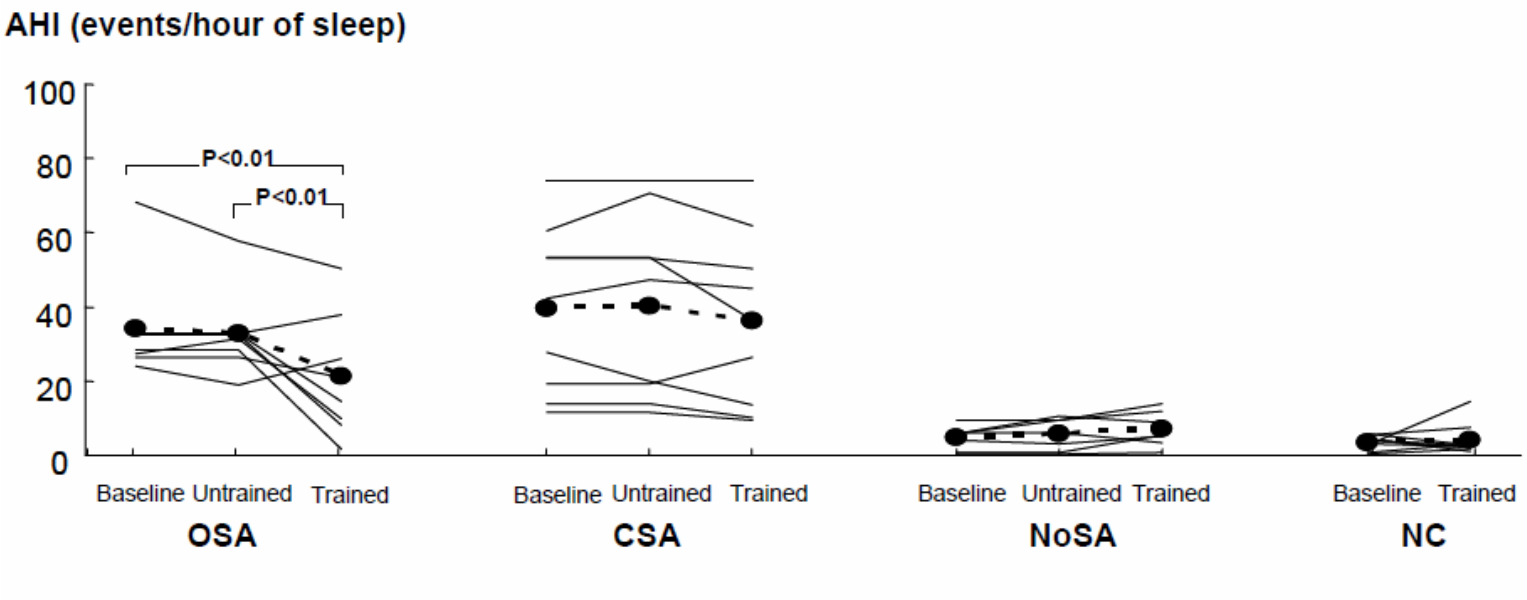
(Rossi VA et al. Eur Respir J 2013; 41: 1439–1451)



CSA e aritmie (Mehra R et al. *Arch Intern Med*. 2009; 169: 1147)



L'esercizio può ridurre le OSA, non le CSA (Ueno LM et al. *SLEEP* 2009;32:637)



Contrariamente all'atteso, OSA predomina anche nei malati neurologici (Johnson KJ et al. *J Clin Sleep Med* 2010;6:131)

Table 3—Percentage of stroke or TIA patients with SDB stratified by AHI

Cutpoint	# Studies (# patients)	% (95% CI)
AHI > 5	9 (908)	72 (60–81)
AHI > 10	24 (1980)	63 (58–68)
AHI > 20	15 (1405)	38 (31–46)
AHI > 30	10 (865)	29 (21–37)
AHI > 40	3 (318)	14 (7–25)
Central*	17 (1286)	7 (5–12)

*Percentage of patients who had primarily central apnea

ODI e Sleep time with SpO2<90%, non AHI predicono declino cognitivo accelerato… (Blackwell T et al. *J Am Geriatr Soc*. 2015 March ; 63(3): 453–461)

Adjusted[a] Annualized Mean Cognitive Decline by Sleep Disordered Breathing Parameter

	Trails B (sec)		3MS Score	
Predictor	**Change per year**	***P*-value**	**Change per year**	***P*-value**
Apnea-hypopnea index, events/h				
<15 (n = 1,504, reference)	2.09	Ref	−0.30	Ref
≥15 (n = 1,132)	2.03	.91	−0.39	.16
Continuous, per 5-unit increase	2.03	.67	−0.35	.18
Oxygen desaturation index, events/h				
<15 (n = 1,219, reference)	2.07	Ref	−0.29	Ref
≥15 (n = 1,417)	2.01	.93	−0.38	.17
Continuous, per 5-unit increase	2.17	.31	−0.36	.01
Sleep time with SaO_2 <90%, %				
<1 (n = 1,284, reference)	1.92	Ref	−0.25	Ref
≥1 (n = 1,352)	2.22	.59	−0.43	.004
Continuous, per SD increase (9.45)	2.27	.53	−0.40	.07
Sleep time in apnea or hypopnea, %				
Quartile 1: <4.6 (n = 659, reference)	2.11	Ref	−0.40	Ref
Quartile 2: 4.6 to <9.7 (n = 659)	2.51	.61	−0.25	.09
Quartile 3: 9.7 to <18.4 (n = 659)	1.70	.60	−0.29	.20
Quartile 4: ≥18.4 (n = 659)	1.93	.82	−0.42	.81
Continuous, per SD increase (13.31)	2.05	.64	−0.34	.08

…ma non clinicamente significativo (Blackwell T et al. *J Am Geriatr Soc*. 2015 March ; 63(3): 453–461)

Predictor	Trails B (sec) Odds Ratio (95% CI)	3MS Score Odds Ratio (95% CI)
Apnea-hypopnea index, events/h		
<15 (n = 1,504, reference)	1.00	1.00
≥15 (n = 1,132)	1.14 (0.84, 1.54)	0.99 (0.79, 1.24)
Continuous, per 5-unit increase	1.01 (0.96, 1.07)	1.01 (0.97, 1.05)
Oxygen desaturation index, events/h		
<15 (n = 1,219, reference)	1.00	1.00
≥15 (n = 1,417)	1.05 (0.78, 1.43)	0.95 (0.75, 1.19)
Continuous, per 5-unit increase	1.02 (0.97, 1.06)	1.01 (0.98, 1.04)
Sleep time with SaO_2 <90%, %		
<1 (n = 1,284, reference)	1.00	1.00
≥1 (n = 1,352)	0.93 (0.68, 1.27)	1.13 (0.90, 1.43)
Continuous, per SD increase (9.45)	0.91 (0.76, 1.10)	1.06 (0.95, 1.18)
Sleep time in apnea or hypopnea, %		
Quartile 1: <4.6 (n = 659, reference)	1.00	1.00
Quartile 2: 4.6 to <9.7 (n = 659)	0.88 (0.58, 1.33)	0.90 (0.66, 1.22)
Quartile 3: 9.7 to <18.4 (n = 659)	1.15 (0.77, 1.73)	0.85 (0.62, 1.17)
Quartile 4: ≥18.4 (n = 659)	0.96 (0.63, 1.46)	0.90 (0.65, 1.23)
Continuous, per SD increase (13.31)	1.05 (0.91, 1.22)	1.01 (0.91, 1.13)

Abbreviations: SD, standard deviation. SaO_2, oxygen saturation.

Le stigmate classiche dell'OSA spesso mancano nell'anziano… (Endeshaw YW . JAGS 2006; 54:1740)

Table 2. Traditional Risk Factors of Obstructive Sleep Apnea According to Obstructive Sleep Apnea Status

Characteristic	AHI <15 (n = 67)	AHI ≥15 (n = 27)	*P*-value
Age, mean ± SD	77.3 ± 6.1	76.9 ± 7.4	.74
Snoring, n (%) (N = 89)			
<1 time a week	16 (26)	5 (19)	
≥1 times a week	9 (14)	7 (27)	.25
Don't know, n (%)	38 (60)	14 (54)	
Told to be snoring, %	41	56	.22
Body mass index, kg/m^2, mean ± SD	25.1 ± 3.6	26.7 ± 4.6	.08
AHI/hour of sleep	7 ± 4	32 ± 16	.001

AHI = apnea-hypopnea index; SD = standard deviation.

..e la presentazione dell'OSA può sfuggire

Table 3. Subjective Sleep Characteristics According to Obstructive Sleep Apnea* (OSA) Status

Self-Reported Symptoms	Female (n = 67)		Male (n = 27)		Total (N = 94)	
	OSA –	OSA+	OSA –	OSA+	OSA –	OSA+
Problem falling asleep, %	22	17	17	7	21	11
Time to fall asleep, minutes, mean ± SD	27.5 ± 27.1	26.4 ± 19.9	23.0 ± 28.8	29.1 ± 32.4	26.8 ± 27.2	27.1 ± 28.0
Number of times you wake up, n, mean ± SD	2.3 ± 1.4	2.5 ± 1.3	2.3 ± 0.5	2.8 ± 1.3	2.3 ± 1.3	2.7 ± 1.3
Problem getting back to sleep, %	21	21	0	40†	17	31
Do not feel well rested in the morning, %	27	75‡	18	39	25	56‡
Number of naps/day, n, mean ± SD	0.8 ± 0.6	1.0 ± 0.5	1.1 ± 0.3	1.4 ± 0.9	0.8 ± 0.6	1.2 ± 0.8†
Epworth Sleepiness Scale, mean ± SD	5.1 ± 2.6	9.2 ± 4.8‡	7.7 ± 2.5	7.3 ± 3.8	5.6 ± 2.8	8.3 ± 4.4‡
Nocturia frequency per night, n, mean ± SD	1.7 ± 0.9	2.1 ± 1.4	1.1 ± 1.0	2.1 ± .7‡	1.6 ± 1.0	2.1 ± 1.1†

*Apnea-hypopnea index ≥15 per hour of sleep.
$P <$ †.05, ‡.01.

L'OSA è causa importante di nicturia

(Endeshaw YW et al. JAGS 2004; 52:957)

Table 2. Selected Demographic and Clinical Findings by Sleep-Disordered Breathing Category

Finding	A AHI 0–9 (n = 26)	B AHI 10–24 (n = 21)	C AHI ≥25 (n = 11)	*P*-value*
	Mean ± Standard Deviation			
Age	76.9 ± 6.0	79.7 ± 6.9	76.5 ± 7.3	.260
Body mass index, kg/m^2	24.5 ± 3.8	23.4 ± 3.0	28.0 ± 5.7	.010†
Epworth Sleepiness Scale	5.5 ± 3.8	6.6 ± 2.4	8.4 ± 5.4	.100
Geriatric Depression Scale	1.8 ± 1.4	1.8 ± 1.8	2.6 ± 1.9	.380
Mean arterial blood pressure, mmHg	99.9 ± 11.5	91.9 ± 11.3	105.2 ± 14.7	.015‡
Nocturia episodes	1.7 ± 1.1	1.6 ± 0.9	2.6 ± 1.4	.028§

* Analysis of variance.
† C > A (P = .040); C > B (P = .008); (Tukey honestly significant difference (HSD)).
‡ C > B (P = .021); (Tukey HSD).
§ C > A (P = .050); C > B (P = .021); (Tukey HSD).
AHI = Apnea Hypopnea Index.

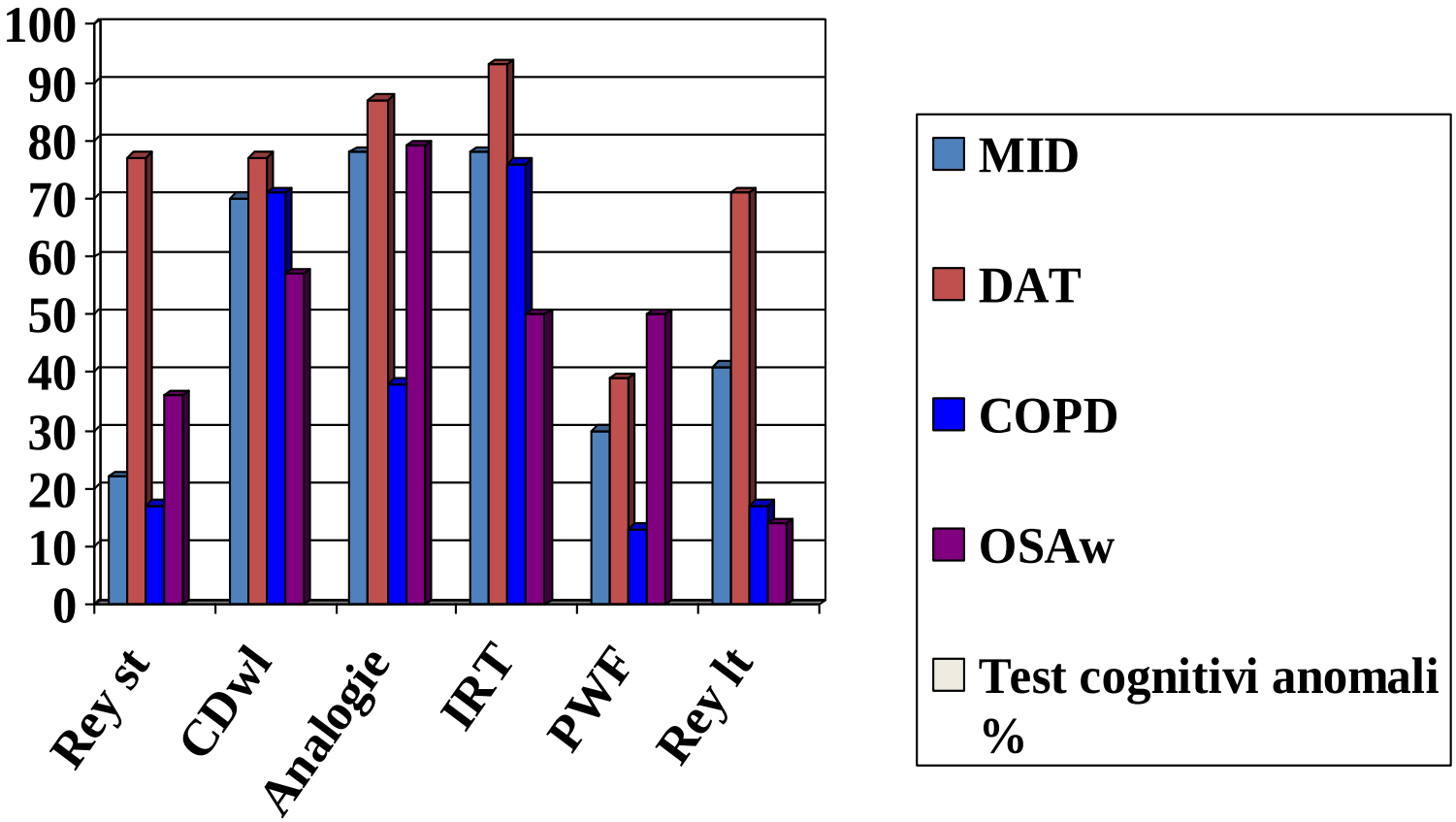
Correlati della nicturia (prevalenza: 23%) nell'OSAS

(Finamore P et al Sleep Med 2018; 45: 69)

Results of the multivariable logistic regression model (Odds Ratios, OR, and 95% confidence intervals, CI) for the occurrence of nocturia in the study population of 275 participants. All the covariates were entered simultaneously into the model.

	OR	95% CI	P
Age (each year)	1.01	0.97–1.03	0.904
Sex (female)	1.11	0.52–2.36	0.781
Coronary disease	2.02	0.83–4.80	0.120
Dyslipidemia	1.34	0.60–2.98	0.478
Dry mouth	2.92	1.37–6.25	0.006
Snoring	0.18	0.04–0.72	0.016
Severe obstructive sleep apnea syndrome	0.52	0.14–2.28	0.347
Oxygen desaturation index	1.03	1.01–1.06	0.042

OSA non è solo un disturbo del sonno (Antonelli Incalzi et al J Sleep Res 2004 13:79-86)



Sintesi degli effetti cognitivi dell' OSA

(Lal C et al. *CHEST 2012; 141: 1601)*

Table 2—*Terminology and Definitions*

Terminology	Definition	Degree Affected by OSAS	Reference
Intelligence	Ability for abstract thought, reasoning, and comprehension	No effect	44
Executive functioning	Working memory, planning, problem solving, inductive reasoning (moving from a specific observation to a broad generalization), deductive reasoning (moving from generalizations to specific outcomes)	+++	12, 45, 46
Motor functioning	A learned sequence of movements required to perform a task	++	47, 48, 49
Vigilance (sustained attention)	Ability to maintain alertness for a prolonged period of time	++++	50, 51

+ = mild impairment; ++ = moderate impairment; +++ = severe impairment; ++++ = very severe impairment. See Table 1 legend for expansion of abbreviation.

OSA e SDAT: un rapporto solido? (Kadotani H et al. Jama 2001; 285: 2888)

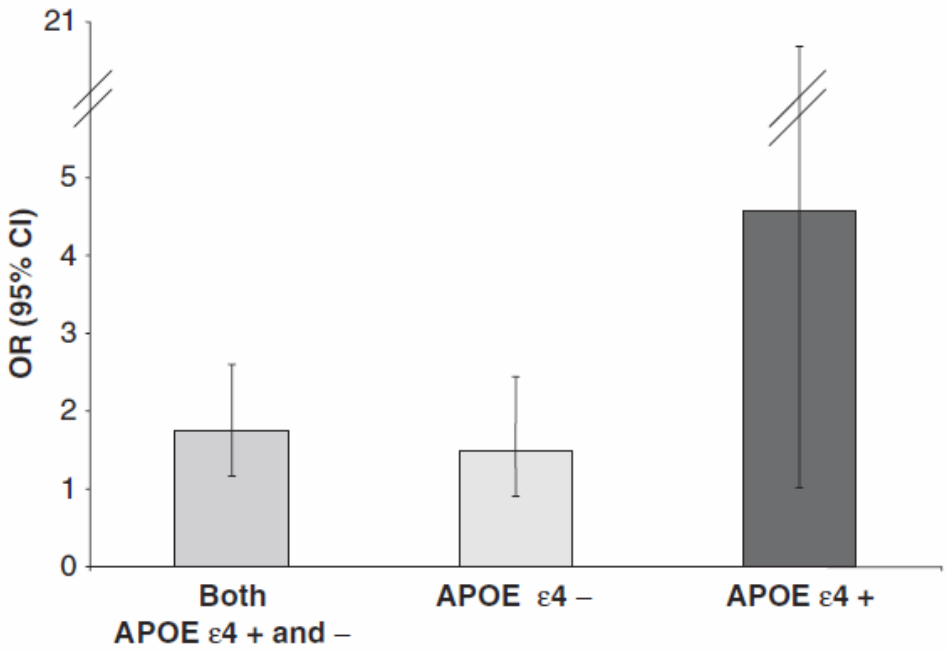
Table 2. Effects of the *ApoE* ϵ*4* Genotype on Sleep-Disordered Breathing*

	ApoE ϵ*4*–Negative (n = 569)	*ApoE* ϵ*4*–Positive (n = 222)	*P* Value†	No. of ϵ*4* Alleles 0 (n = 569)	1 (n = 208)	2 (n = 14)	*P* for Trend†
Sleep studies, No.‡	960	384		960	360	24	
AHI index							
Mean (SEM)	4.8 (0.3)	6.5 (0.6)	.01§	4.8 (0.3)	6.2 (0.6)	10.5 (3.5)	.003§
Median (range)	1.3 (0-121)	2.0 (0-81)		1.3 (0-121)	2.0 (0-81)	3.6 (0-54)	
Adjusted mean (SEM)‖	5.2 (0.6)	6.7 (0.9)	.01§	5.2 (0.6)	6.4 (0.8)	10.9 (4.5)	.03
OR (95% CI) for AHI ≥15		2.0 (1.2-3.5)	.01		2.1 (1.2-3.2)	3.9 (1.5-9.9)	.005

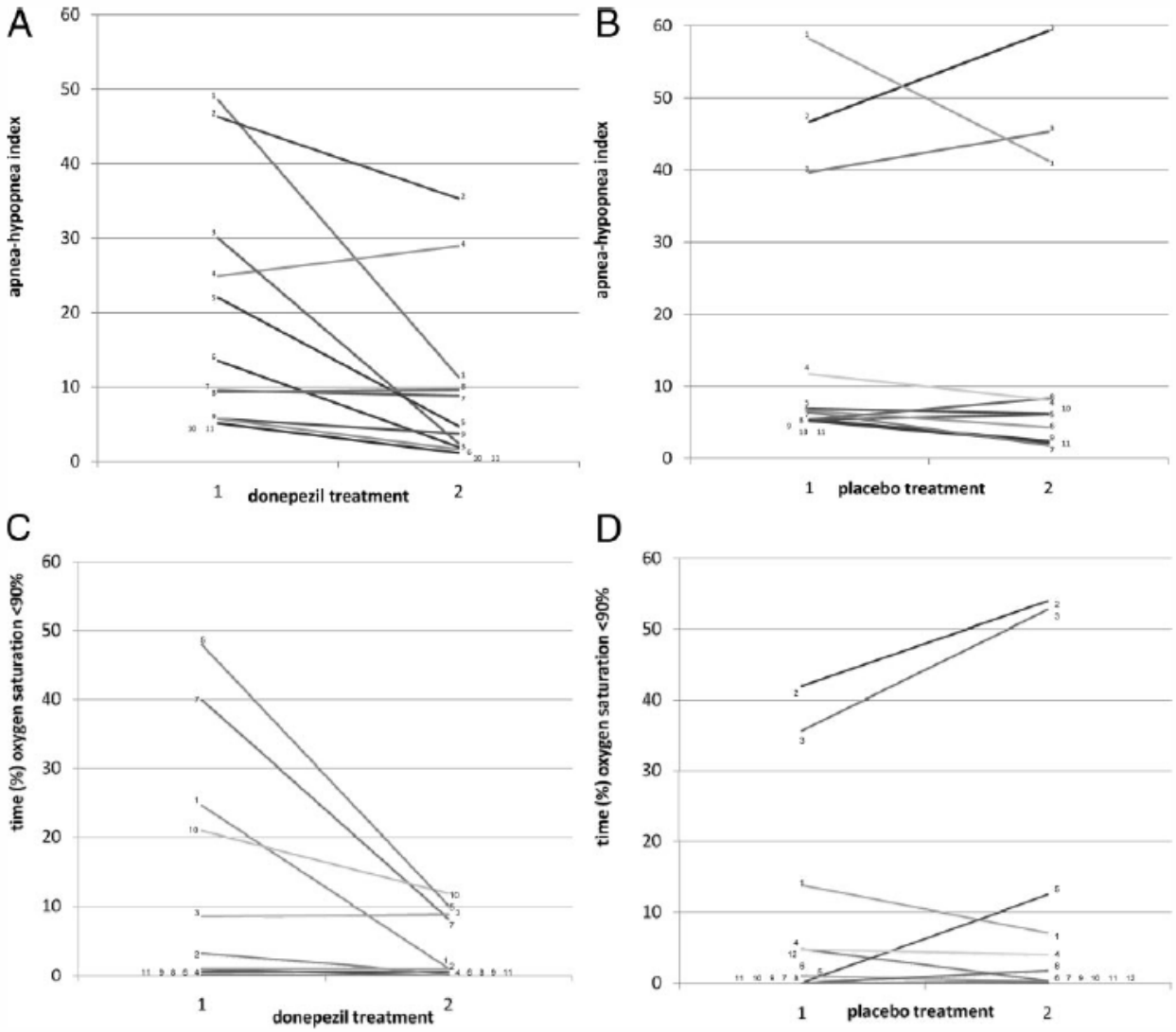
*ApoE indicates apolipoprotein E; AHI, apnea-hypopnea index; OR, odds ratio; and CI, confidence interval.
†Corrected for multiple measurements for some participants.
‡Participants had 1, 2, or 3 studies.
§Calculated for log (AHI + 1).
‖Adjusted for ϵ2, age, sex, body mass index, smoking, hypertension, and ethnicity.

Associazione AHI-deficit cognitivo nelle donne

(Spira AP et al. J Am Geriatr Soc 2008; 56:45)



Effetti del donezepil su AHI e SpO2 in malati SDAT con OSA (scarsa correlazione con i benefici effetti cognitivi!)(Moraes W et al. CHEST 2008; 133:677)



Possibili meccanismi d'azione del donezepil contro l 'OSA

- Non legato alla struttura del sonno: aumenta il REM.
- Stimolazione motoneuroni respiratori
- Potenziamento chemiosensibilità centrale e chemioriflesso
- Potenziamento attività dell' ipoglosso nel modello sperimentale (iniezione intrabulbare di carbacolo)
- Allungamento dell' intervallo di contrazione ipoglosso-diaframma>migliore ossigenazione
- Aumento della salivazione: ridotta tensione superficiale aumenta la stabilità delle alte vie aeree

Effetti dell' OSA in ambito affettivo e comportamentale: forse il russamento di per sé si associa con problemi (Ekici A et al. Sleep Breath 2013; 17: 305)

MMPI clinical scale	Snorers (n=30)		OSA (n=46)		P values[a]
	Mean+SD	% elevated	Mn+SD	% elevated	
Hypochondriasis	58.4±7.9	3.3	65.0±12.0*	26.1	0.01
Depression	57.9±10.0	10.0	58.5±10.2	8.6	0.8
Hysteria	60.7±10.8	23.3	62.6±12.3	23.9	0.9
Psychopathic deviate	52.1±10.0	0	54.6±12.9	13.0	0.03
Masculinity/femininity	51.9±9.7	0	48.6±9.8	0	
Paranoia	53.3±9.0	6.7	54.6±11.7	13.0	0.3
Psychasthenia	58.2±9.2	6.7	56.7±9.1	6.5	0.9
Schizophrenia	54.2±9.3	6.7	53.6±10.1	8.7	0.7
Hypomania	55.1±10.2	3.3	53.5±11.1	10.9	0.2
Social introversion	58.1±11.5	10.0	57.6±9.4	6.5	0.5
MMPI mean t score	56.0±6.0	56.5±7.3	0.7		
Number of elevations	0.7±1.1	1.1±1.6	0.1		

Ma sul versante cognitivo l'ipossia ha un peso rilevante tranne che per forme molto gravi di psicopatologia (Ekici A et al. Sleep Breath 2013; 17: 305)

Table 4 The clinical features and MMPI profiles

	Normal profile *n*:41	Second profile[a] *n*:15		Third profile[b] *n*:9		Disability profile[c] *n*:8	
SF-36 Physical health summary score	77.4±16.8	62.1±18.2	0.007	60.5±12.5	0.01	48.6±28.0	0.0001
SF-36 Mental health summary score	72.9±18.4	65.2±14.4	0.1	58.7±12.9	0.04	27.4±28.8	0.0001
Epworth sleepiness scale	8.4±6.5	10.0±4.0	0.4	9.5±5.0	0.6	17.2±7.2	0.003
Attention deficit score	6.7±4.2	7.4±3.0	0.5	9.1±3.5	0.1	13.3±6.9	0.0001
Fatigue score	2.6±1.7	2.8±1.3	0.7	3.4±1.4	0.1	4.8±1.2	0.001
Arousal index	22.1±15.3	19.0±13.8	0.5	29.7±12.3	0.1	22.1±19.2	0.9
AHI index	21.9±22.8	25.8±32.0	0.6	47.9±37.2	0.01	28.1±21.5	0.6

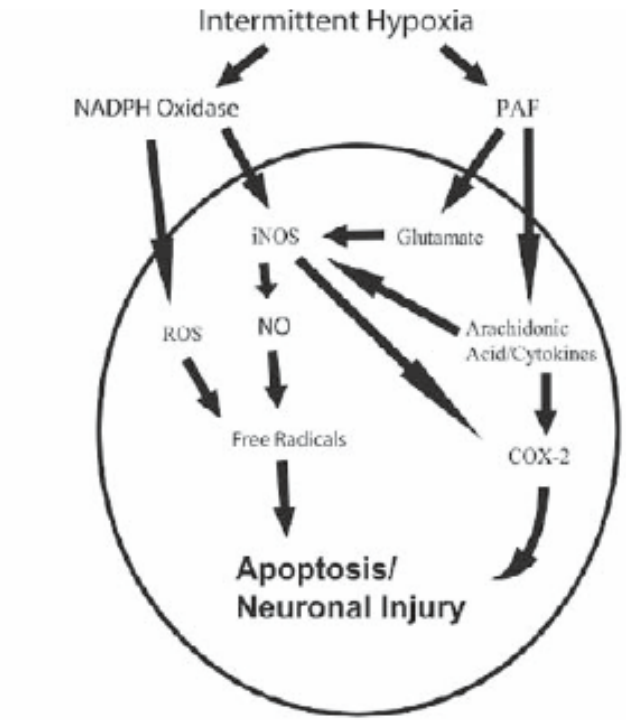
[a]Second profile consists of one clinical elevations

[b]Third profile consists of two or three clinical elevations

[c]Disability profile consists of more or four clinical elevations

Danno cerebrale da ipossia intermittente(Row

BW: Chapter 5 in *Hypoxia and the Circulation,* edited by R.C. Roach *et al.*
Springer, New York, 2007)



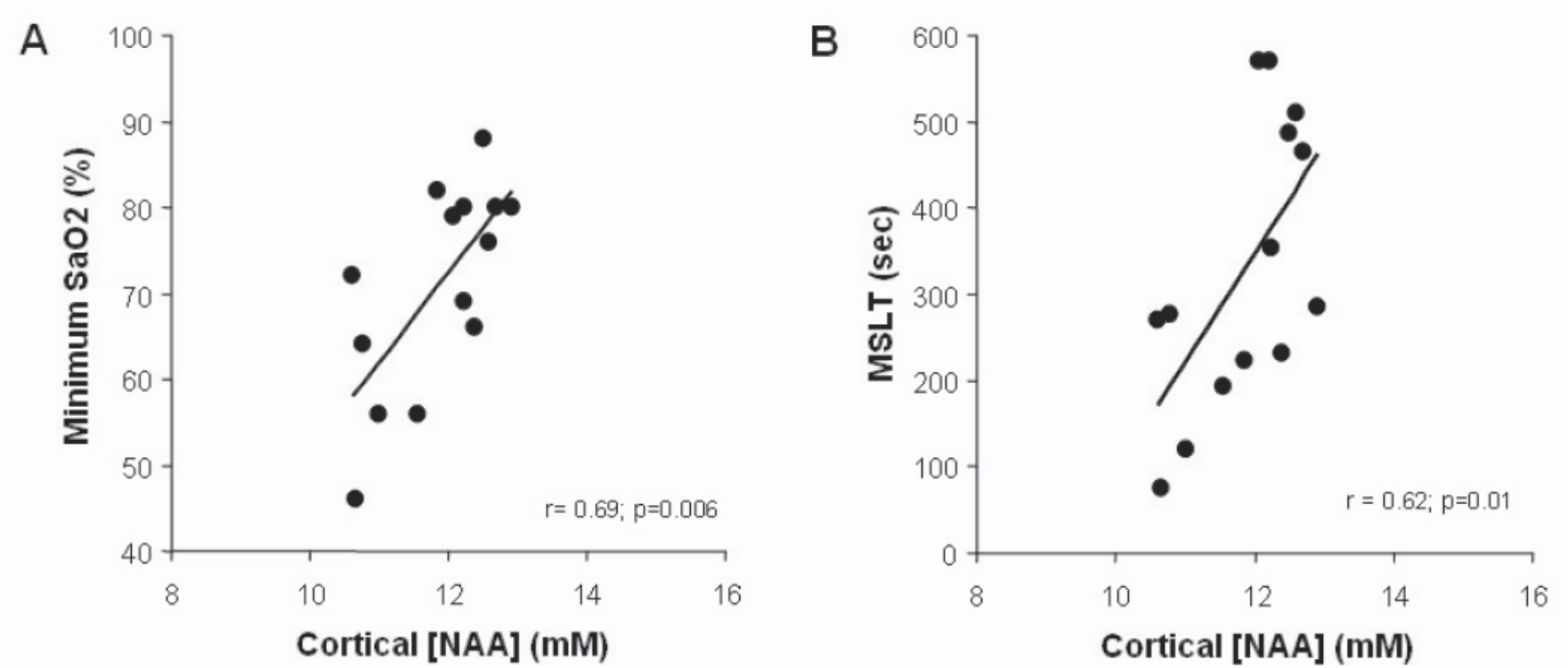
Anche nel bambino con OSA il deficit esecutivo correla con l'ipossia notturna

(Esposito M et al. Neuropsych Dis Treat 2013; 9:1087)

Table 3 Correlation between nocturnal respiratory indexes and MCST scores in our study sample

	AHI	ODI	Mean SpO_2 (%)	Mean SpO_2 desaturation (%)
CAT	**−0.3528**	**−0.1850**	**0.2122**	**−0.2828**
CS	0.0753	0.0339	−0.0193	**0.2039**
CE	0.0325	0.1230	−0.0620	0.1249
TE	**0.4745**	0.1374	**−0.2602**	**0.5000**
% TE	**0.5167**	**0.2517**	**−0.2485**	**0.5314**
PE	**0.4183**	**0.2100**	**−0.3603**	**0.4114**
% PE	**0.3787**	**0.1880**	**−0.3123**	**0.3660**
NPE	**0.3529**	**0.1910**	−0.0176	**0.4220**
% NPE	**0.4199**	**0.2198**	**−0.1636**	**0.4643**
FMS	**0.2086**	0.0353	**−0.1620**	0.0346

Anche nell'adulto l'ipossiemia correla con il danno neuronale (Tonon C et al *SLEEP* 2007;30:305)



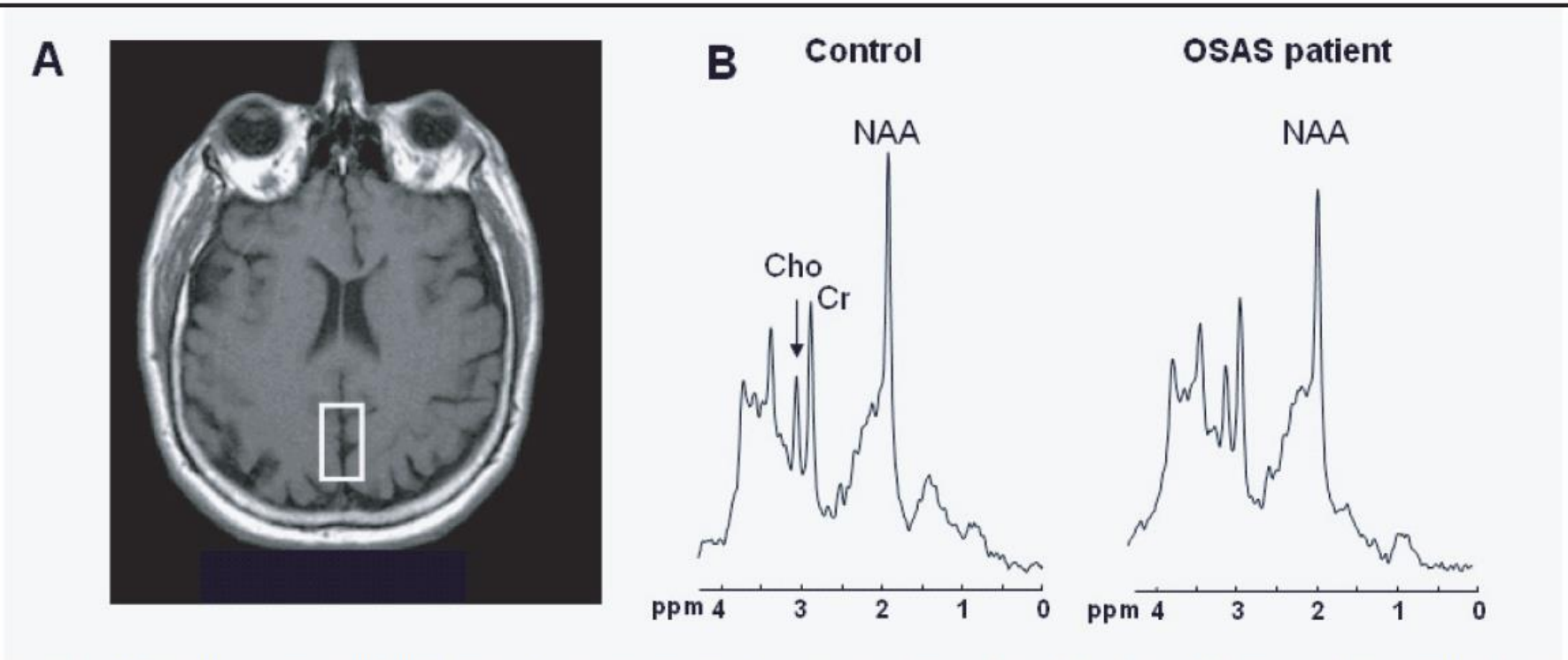
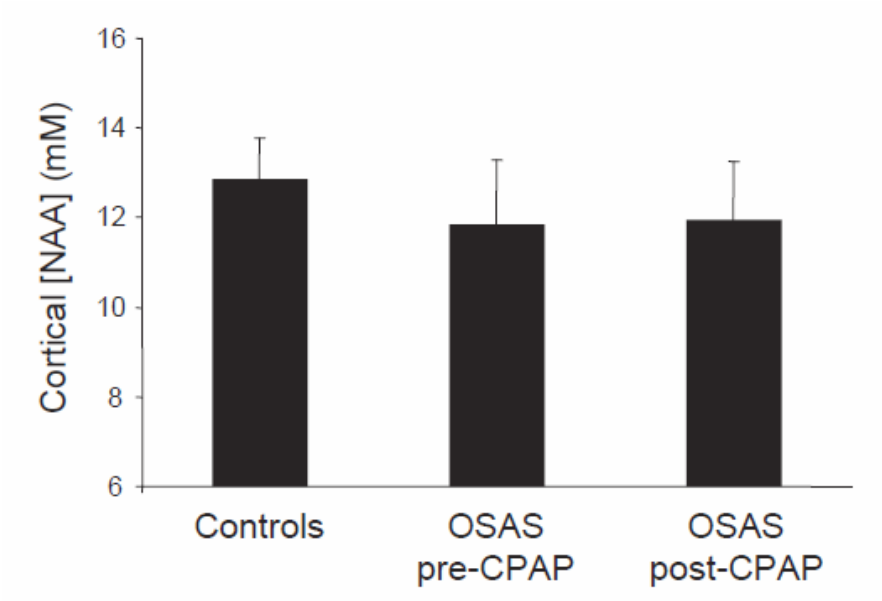


Figure 1—A) Localization of medial brain parietal-occipital grey matter volume of interest (VOI). B) Proton MR spectra from an OSAS patient (case no. 4) compared to a sex- and age-matched control (TE= 35ms; TR= 4000ms). The NAA (N-acetyl-aspartate) peak is lower in the patient.

Il danno neuronale è in parte irreversibile… (Tonon C et al *SLEEP* 2007;30:305)



…così come il deficit cognitivo (Tonon C et al *SLEEP* 2007;30:305)

	Total PNT N (%)	Case number with n ≥1 PNT (%)	Number of pts. with 3 PNT	Number of pts. with 2 PNT	Number of pts. with 1 PNT	Type of task (number of patients)
Baseline	7/350 (2.0%)	4, 3,9, 10 (28.5%)	1	1	2	CRT (2), DSB (1), SS (1), Barr S (1), CVART (1), CVARTe (1)
After CPAP	4/350 (1.1%)	4,3,11,12 (28.5%)	0	0	4	CRT (1), SRTe (1), DSB (1), Barr S (1), SVARTe (1)

CRT: complex reaction times; DSB: digit span backwards; SS: spatial span; Barr S: barrage score; CVART: complex visual reaction times; CVARTe: complex visual reaction times errors; SRTe: simple reaction time errors; SVARTe: simple visual attention reaction times errors.

L'evidenza morfometrica è chiara (Cross NE et al. Eur Respir J 2018; 52: 1800740)…

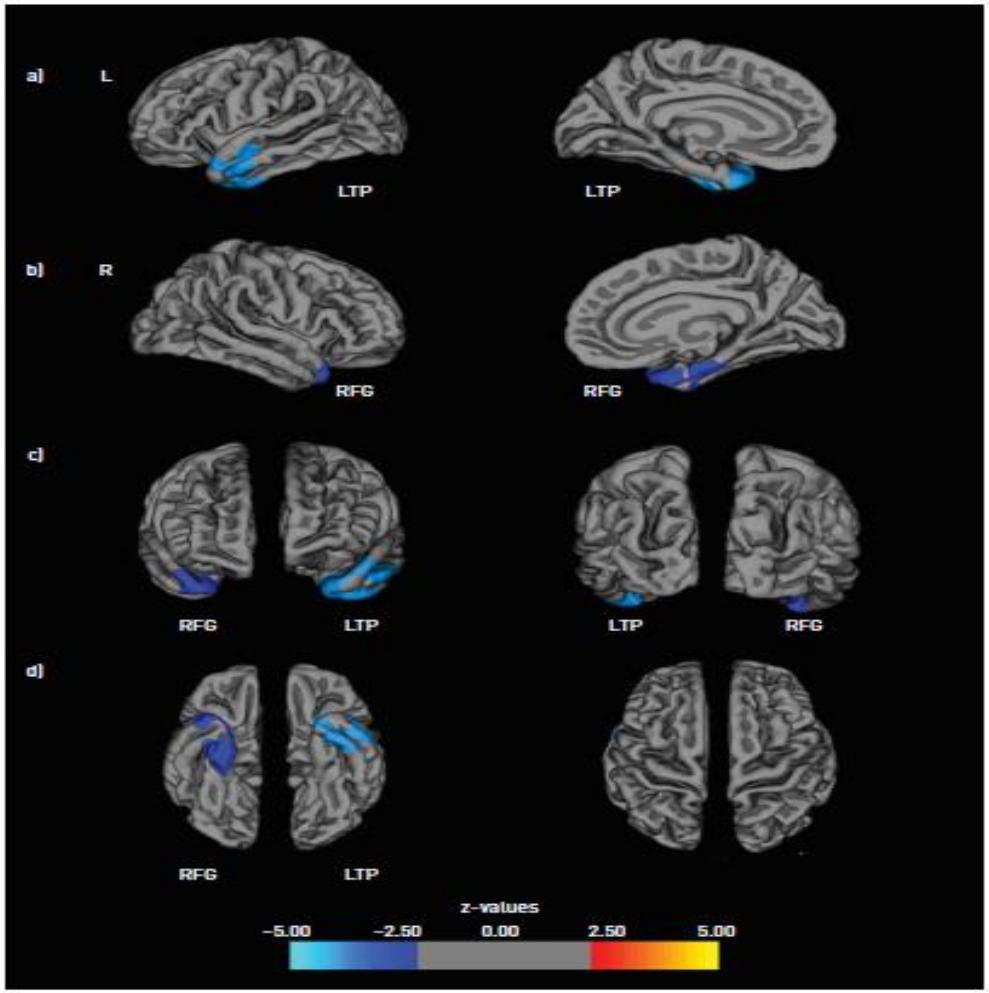
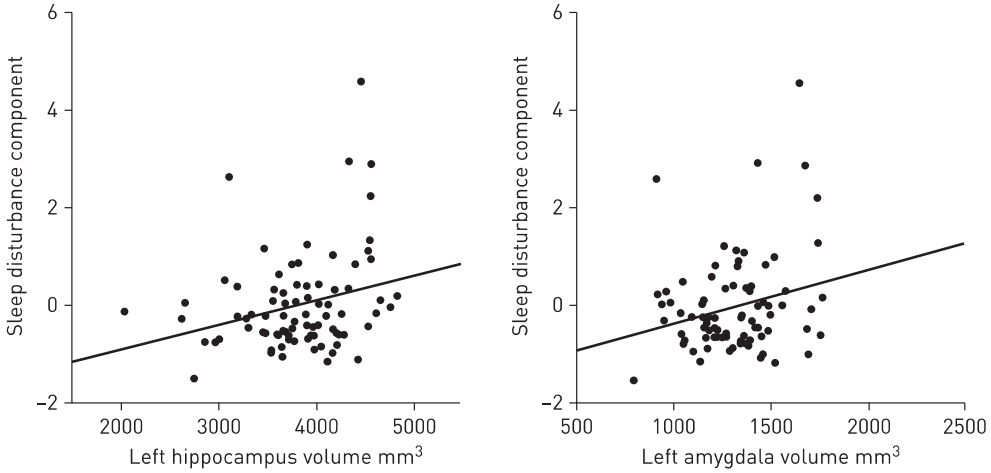


FIGURE 1 Significant atrophy in the left temporal pole (LTP) and right fusiform gyrus (RFG) related to "oxygen desaturation" in older "at-risk" patients; displayed on Qdec's (query, design, estimate, contrast) semi-inflated cortical surfaces. a) Left lateral and left medial; b) right lateral and right medial; c) anterior and posterior; d) inferior and superior views. Results were obtained using Monte Carlo simulation, with a threshold of $p<0.05$, to provide cluster-wise correction for multiple comparisons. Clusters are labelled based on the location of the vertex with the greatest association as defined by Qdec.

…ancorchè eterogenea (Cross NE et al. Eur Respir J 2018; 52: 1800740)



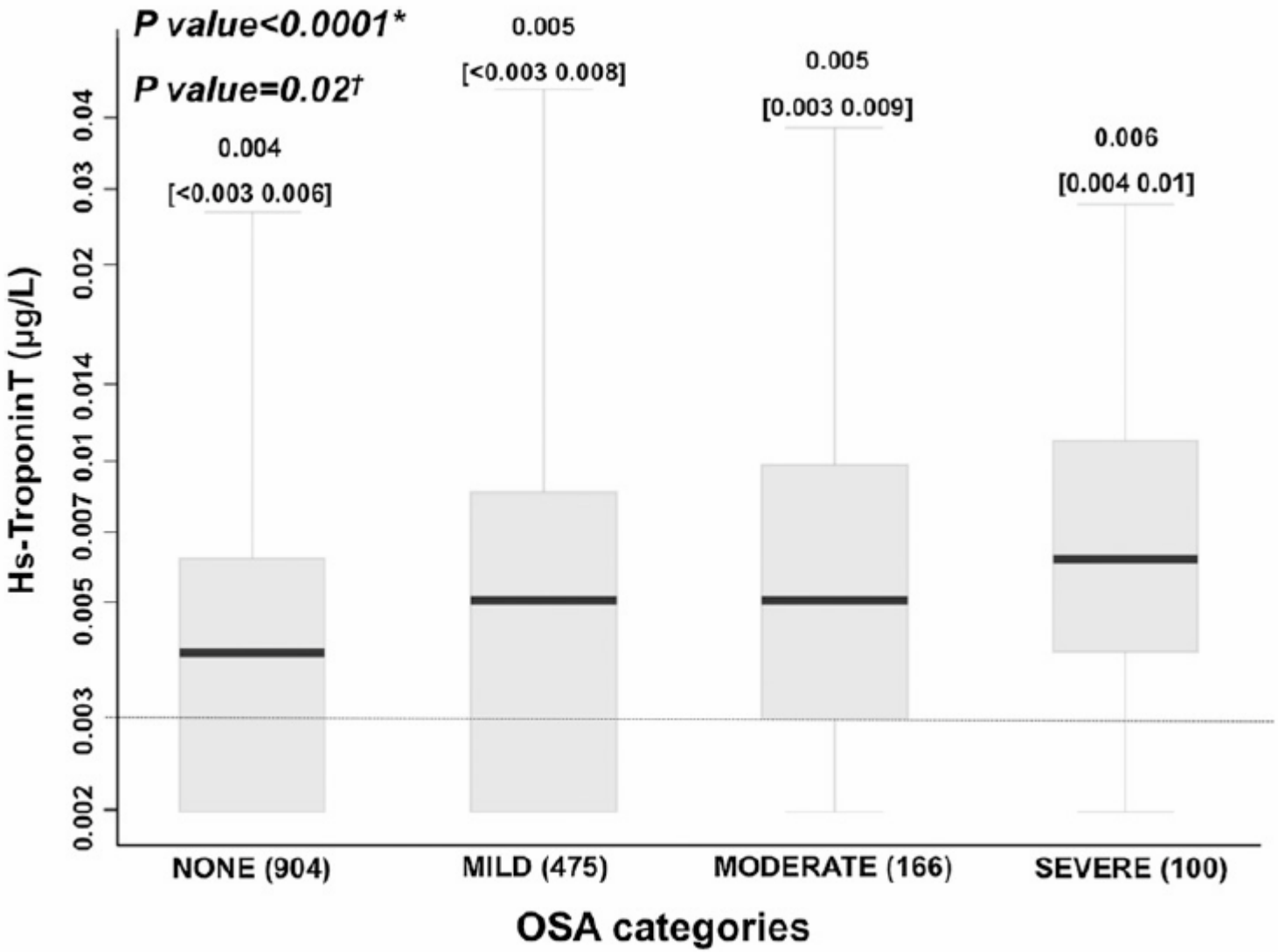
OSA e danno cardiovascolare: review sistematica (26 studi)

(Kendzerska T et al. Sleep Medicine Reviews 2014; 18: 49-59)

- A systematic review of the prognostic value of risk factors for adverse long-term outcomes of untreated obstructive sleep apnea (OSA) revealed the following:
- 1. Evidence exists in men for a relationship between OSA and both all-cause mortality and a composite cardiovascular outcome (composite of cardio-vascular events, e.g., myocardial infarction, stroke, hospitalization due to revascularization procedures and heart failure).
- 2. Associations between OSA and other clinically important outcomes (diabetes and depression, separate components of composite cardio-vascular outcome) remain uncertain.
- 3. Among OSA-specific markers, only the apnea-hypopnea index was a consistent predictor. Other consistent predictors were traditional cardio-vascular risk factors (age, sex, blood pressure, history of cardio-vascular comorbidities and diabetes at baseline).

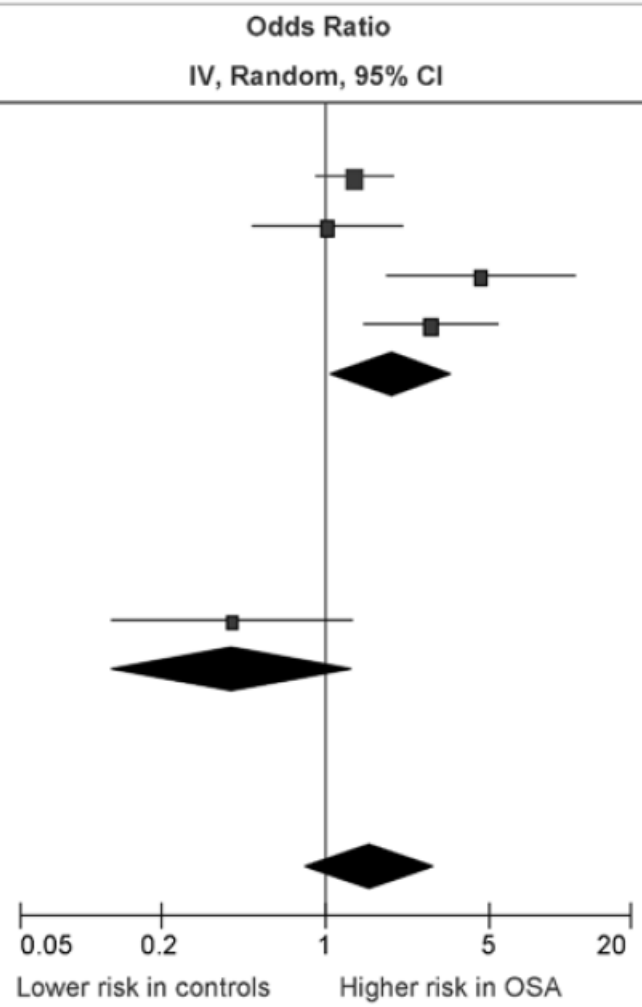
OSA e danno miocardico subclinico

(Querejeta Roca G et al. Am J Respir Crit Care Med 2013; 188: 1460–1465)



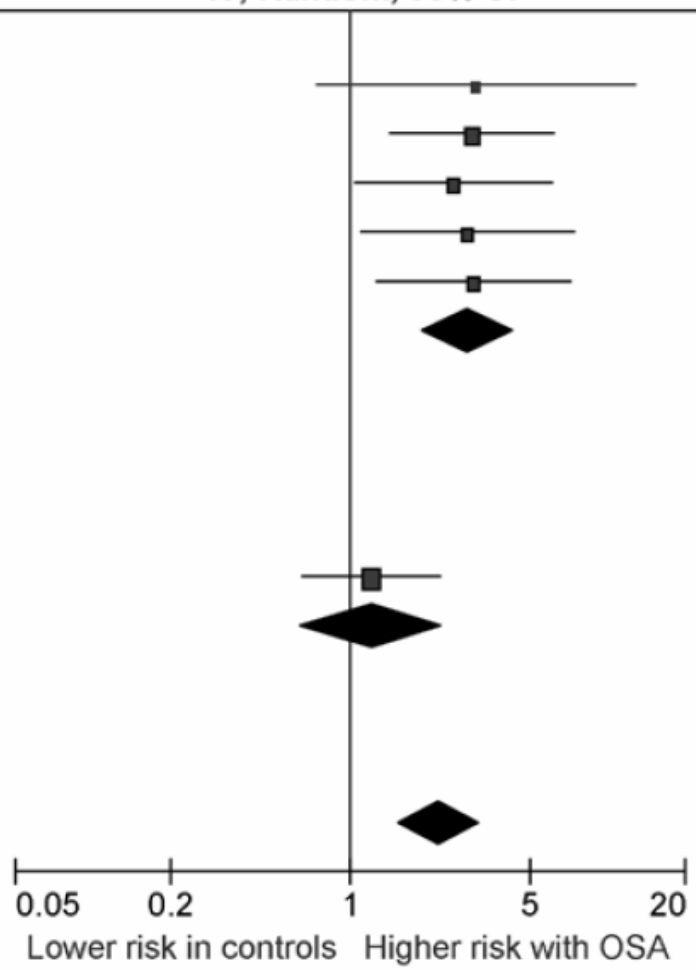
OSA e rischio di CAD: metanalisi (9 studi) (Loke Y et al. *Circ Cardiovasc Qual Outcomes.* 2012;5:720-728.)

Study or Subgroup	Weight	Odds Ratio IV, Random, 95% CI
Predominantly Male		
Gottlieb 2010a	25.9%	1.33 [0.91, 1.95]
Mooe (Unadjusted) 2001	20.5%	1.02 [0.49, 2.13]
Peker 2006	17.6%	4.60 [1.83, 11.58]
Shah 2010	21.8%	2.82 [1.46, 5.45]
Subtotal (95% CI)	**85.8%**	**1.92 [1.06, 3.48]**
Heterogeneity: Tau² = 0.25; Chi² = 10.14, df = 3 (P = 0.02); I² = 70%		
Test for overall effect: Z = 2.16 (P = 0.03)		
Predominantly Female		
Gottlieb 2010b	14.2%	0.40 [0.12, 1.30]
Subtotal (95% CI)	**14.2%**	**0.40 [0.12, 1.30]**
Heterogeneity: Not applicable		
Test for overall effect: Z = 1.52 (P = 0.13)		
Total (95% CI)	**100.0%**	**1.56 [0.83, 2.91]**
Heterogeneity: Tau² = 0.35; Chi² = 15.42, df = 4 (P = 0.004); I² = 74%		
Test for overall effect: Z = 1.39 (P = 0.16)		
Test for subgroup differences: Chi² = 5.44, df = 1 (P = 0.02), I² = 81.6%		

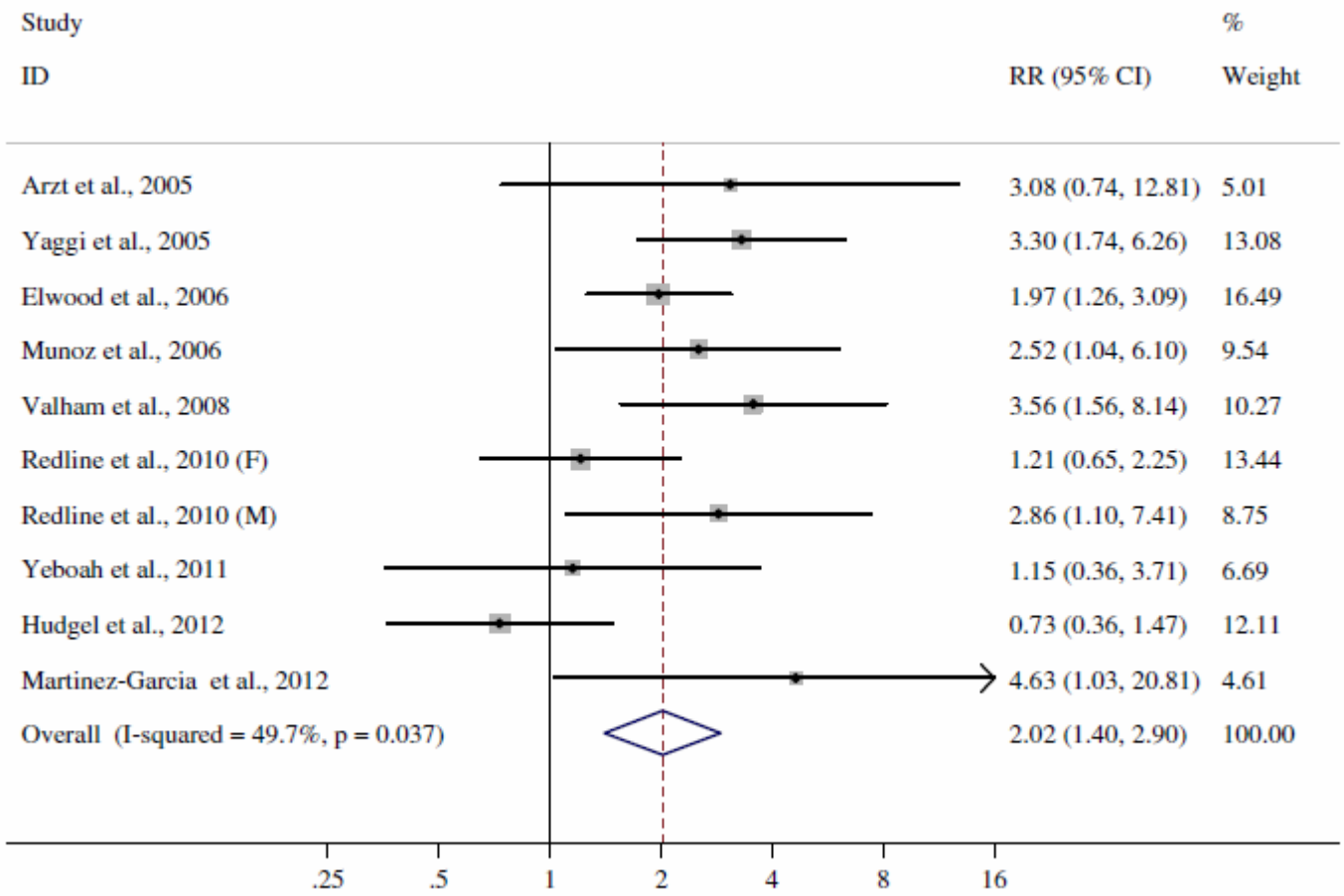


OSA e rischio di stroke: metanalisi (9 studi) (Loke Y et al. *Circ Cardiovasc Qual Outcomes.* 2012;5:720-728.)

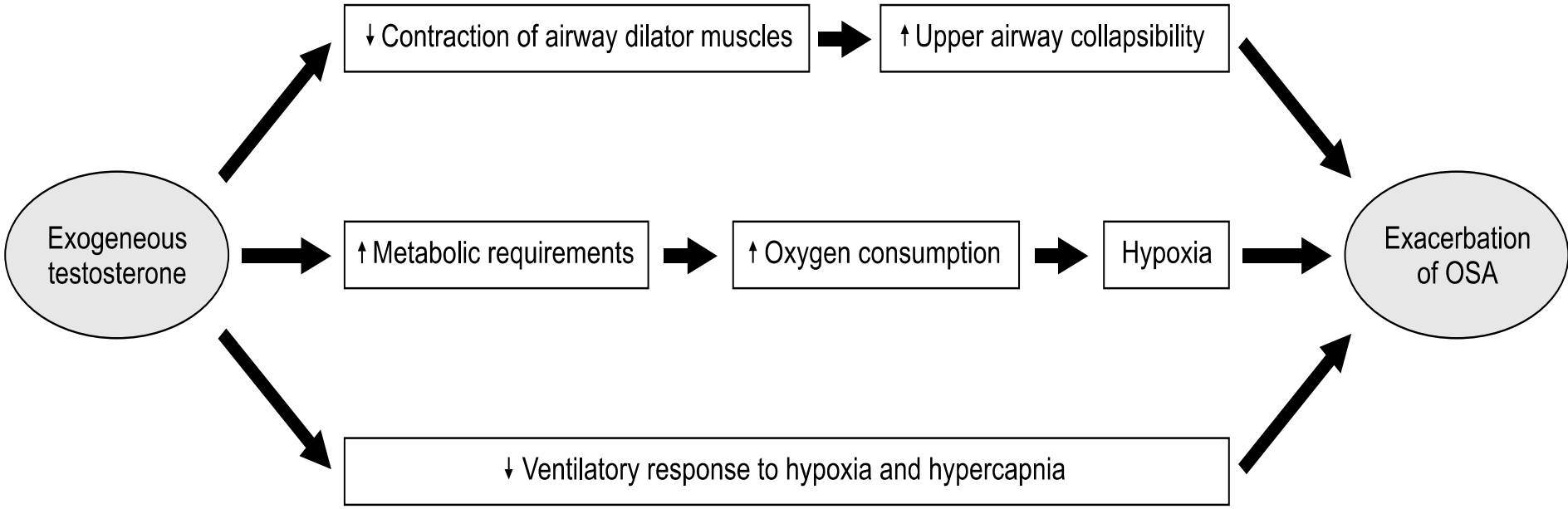
Study or Subgroup	Weight	Odds Ratio IV, Random, 95% CI
Predominantly Male		
Arzt 2005	6.0%	3.08 [0.74, 12.81]
Mooe (Adjusted) 2001	21.3%	2.98 [1.43, 6.20]
Munoz 2006	15.1%	2.52 [1.04, 6.10]
Redline 2010a	13.1%	2.86 [1.10, 7.41]
Yaggi (Unadjusted) 2005	15.6%	3.03 [1.27, 7.21]
Subtotal (95% CI)	**71.1%**	**2.87 [1.91, 4.31]**
Heterogeneity: Tau² = 0.00; Chi² = 0.12, df = 4 (P = 1.00); I² = 0%		
Test for overall effect: Z = 5.09 (P < 0.00001)		
Predominantly Female		
Redline 2010b	28.9%	1.21 [0.65, 2.25]
Subtotal (95% CI)	**28.9%**	**1.21 [0.65, 2.25]**
Heterogeneity: Not applicable		
Test for overall effect: Z = 0.60 (P = 0.55)		
Total (95% CI)	**100.0%**	**2.24 [1.57, 3.19]**
Heterogeneity: Tau² = 0.01; Chi² = 5.36, df = 5 (P = 0.37); I² = 7%		
Test for overall effect: Z = 4.45 (P < 0.00001)		
Test for subgroup differences: Chi² = 5.24, df = 1 (P = 0.02), I² = 80.9%		



OSA e rischio di stroke: una conferma (Dong Y et al. Atherosclerosis 2013; 229: 489-495)



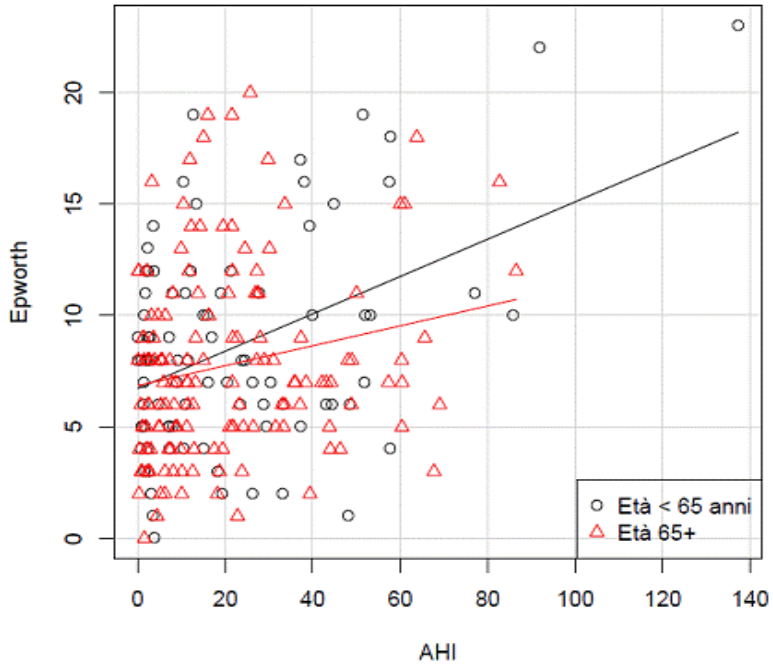
Il deficit di testosterone spesso coesiste con OSAS, ma la sua correzione peggiora l'OSAS (Kim S et al. World J Mens Health Published online May 16, 2018)

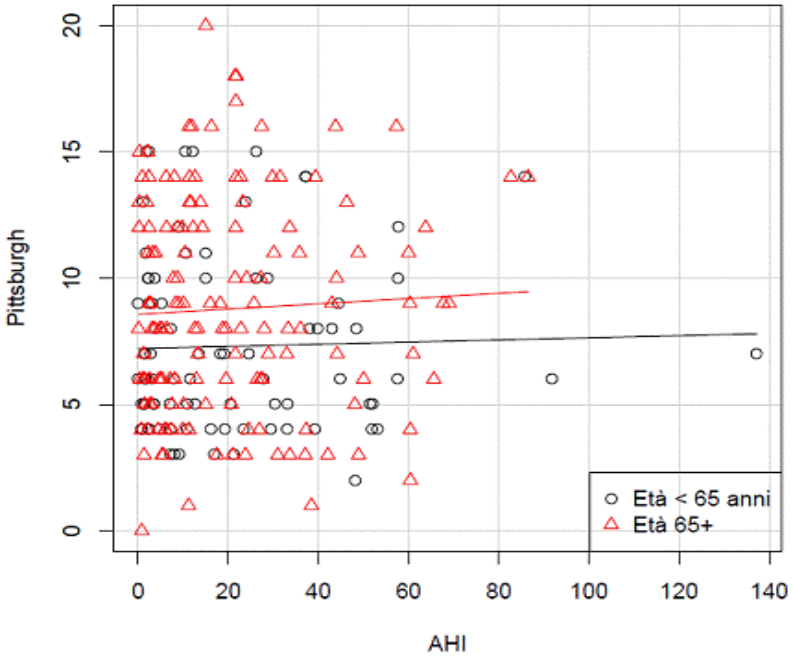


Screening

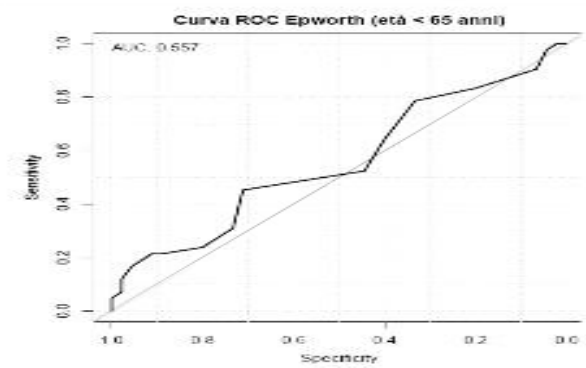
Screening tramite Pittsburgh ed Epworth: inefficace

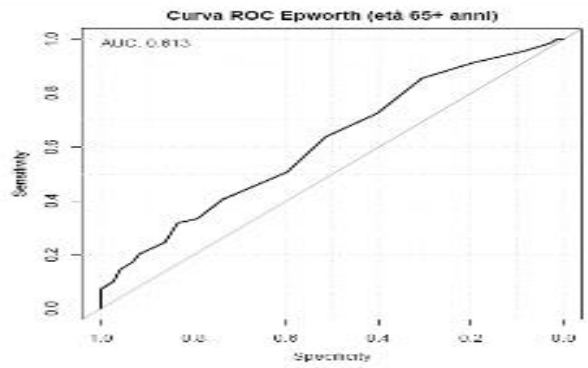
	Età < 65	Età 65+	Tutti
Correlazione AHI vs Epworth R (p-value)	0.429 (<0.001)	0.202 (0.016)	0.308 (<0.001)
Correlazione AHI vs Pittsburgh R (p-value)	0.029 (0.791)	0.047 (0.581)	0.037 (0.581)

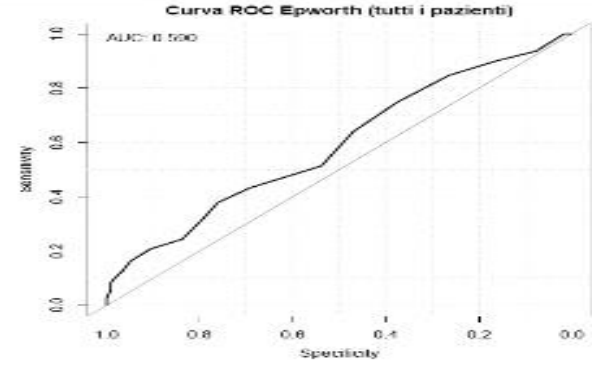


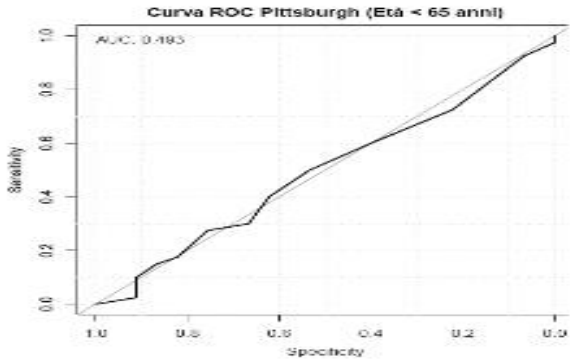


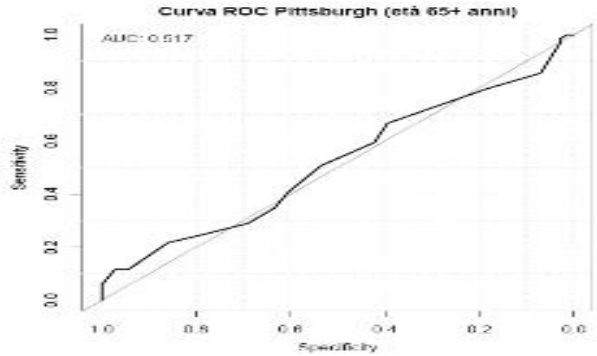
	Età <65	Età 65+	Tutti
EPWORTH			
Sensibilità	45.2 %	33.3 %	36.8 %
Specificità	71.1 %	79.2 %	76.1 %
PPV	59.4 %	60.5 %	60 %
NPV	58.2 %	55.3 %	56.3 %
PITTSBURGH			
Sensibilità	60 %	75.4 %	69.7 %
Specificità	40 %	25.3 %	31.0 %
PPV	47.1 %	49.5 %	48.7 %
NPV	52.9 %	51.4 %	52.2 %

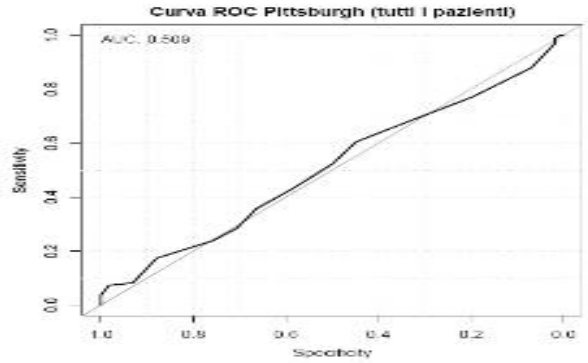






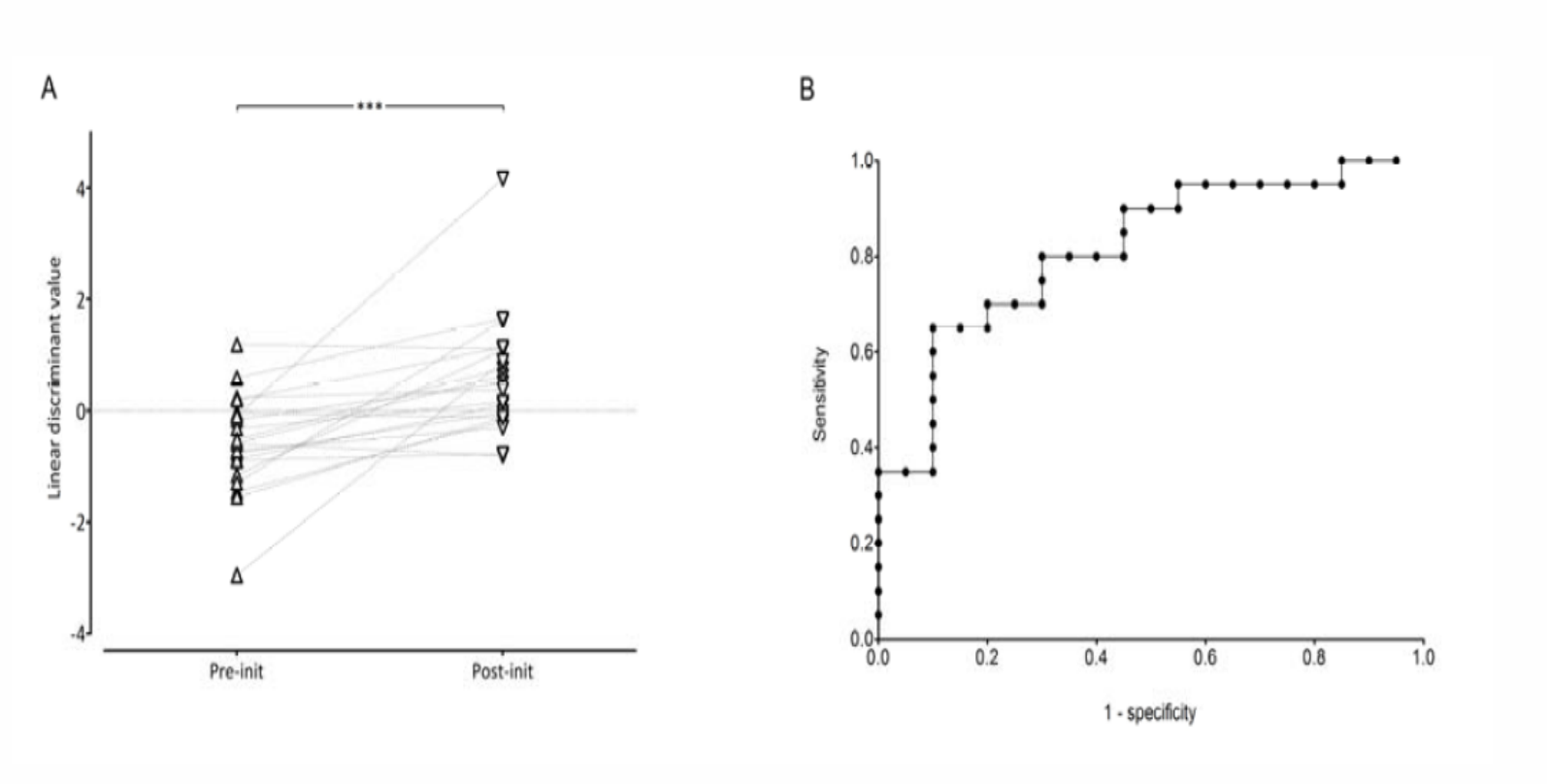






Effects of 3 month C-PAP ventilation on BP of OSAS

(Greulich T et al. Eur Respir J. 2013; 42: 145)



One night ventilation changes the BP of OSAS, but in two alternative ways ... (Antonelli Incalzi R et al. Sleep Breath 2015; 19: 623-30)

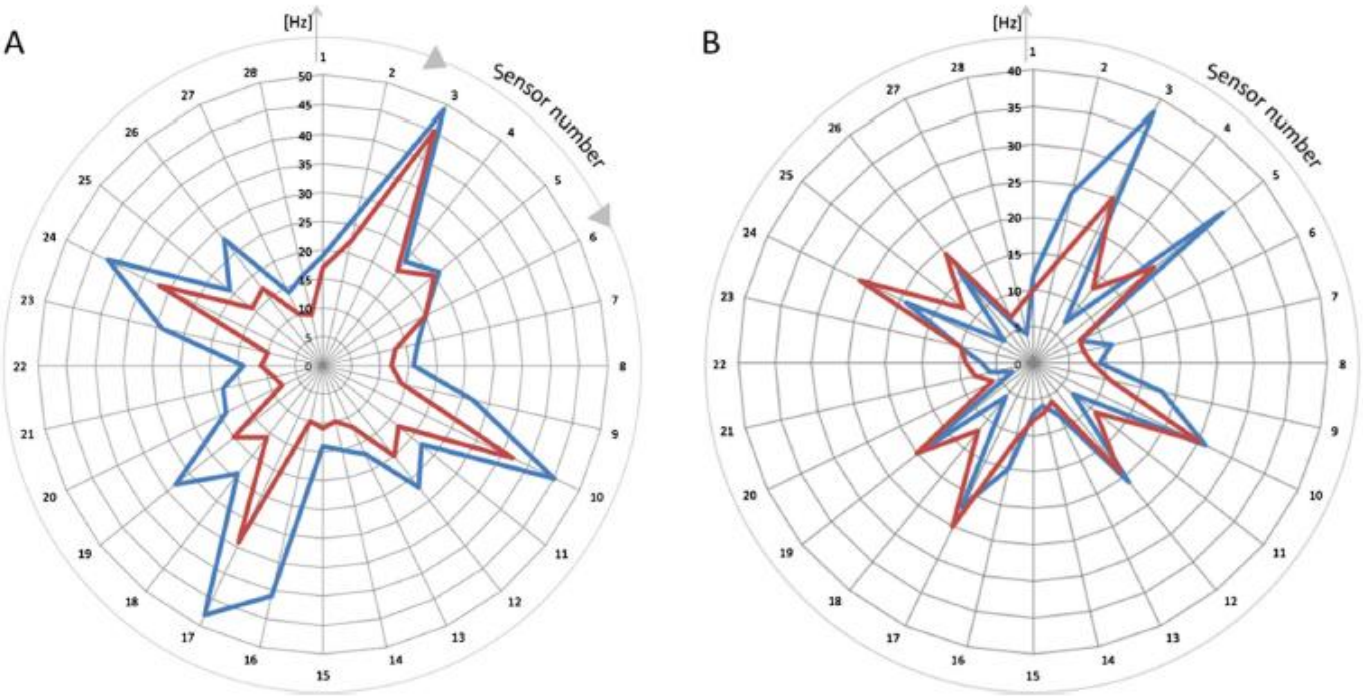


Fig. 2 **a** BP of a patient belonging to group C before (*blue*) and after (*red*) CPAP. CPAP effect graphically emerges by a common mode reduction of sensor response magnitude (*from blue to red curve*). **b** In group D, various BP changes coexist and all differ from that typical of group C. The one reported here is characterized by a BP increase in magnitude after CPAP (*from blue to red curve*)

…depending upon the pattern of comorbidity of OSAS…

	C	D	p
Diabetes mellitus n° (%)	5 (17.2)	9 (28)	p<0.06*
Metabolic Syndrome n° (%)	8 (27.6)	14 (66.6)	p<0.01*
Chronic Heart Failure n° (%)	2 (6.9)	6 (28.6)	p<0.05*
Atrial Fibrillation n° (%)	2 (6.9)	6 (28.6)	p<0.05*
Number of comorbidities (mean/standard deviation)	1.55 (1.0)	3.14 (1.8)	p<0.01**

C-PAP: efficace sul profilo di rischio cardiovascolare

(Litvin AY et al.
Vascular Health and Risk Management 2013:9 229–235)

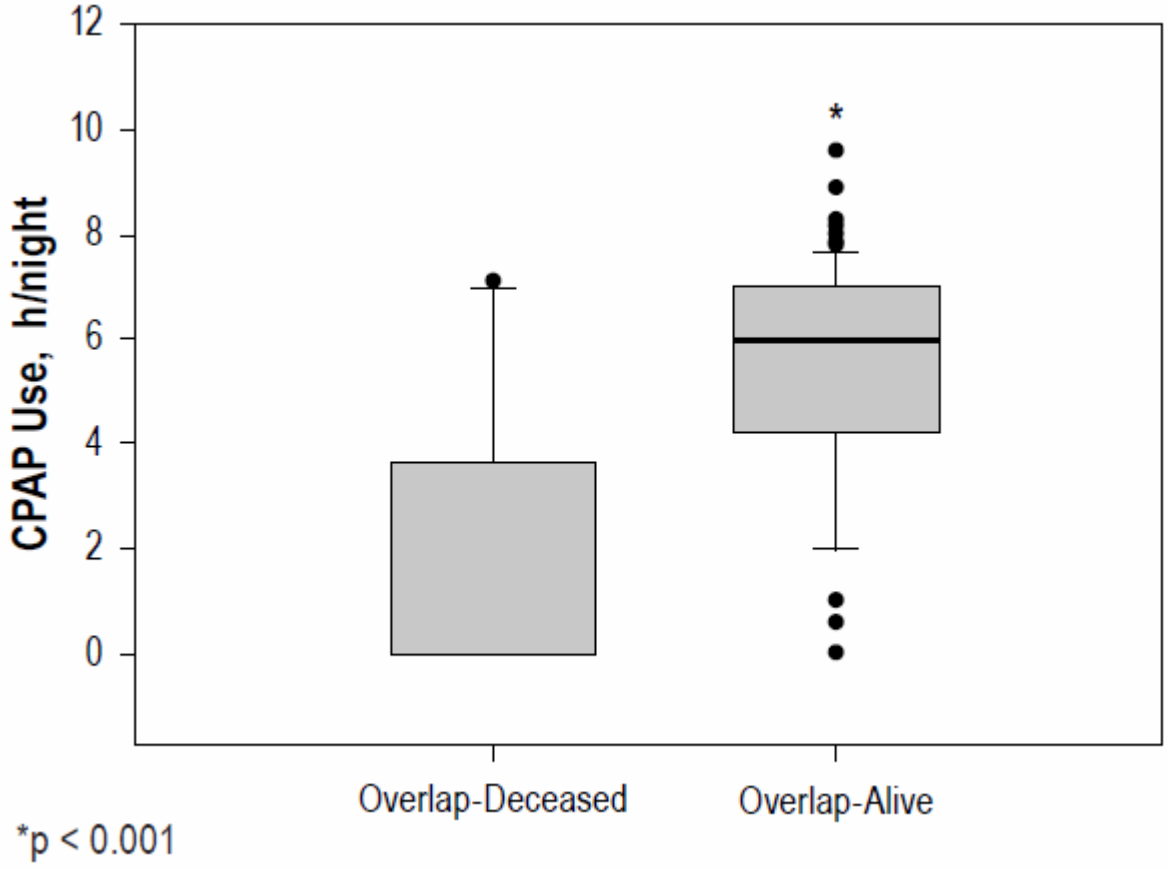
Table 2 Blood pressure values according to treatment regimen

Mean ± SD	Baseline	AT	pCPAP	eCPAP
Office systolic BP (mmHg)	166 ± 11	141 ± 11*	140 ± 9	135 ± 10#
Office diastolic BP (mmHg)	96 ± 11	85 ± 8*	86 ± 9	80 ± 8#
Central systolic BP (mmHg)	155 ± 11	129 ± 11*	126 ± 8	122 ± 10#
Central diastolic BP (mmHg)	97 ± 13	86 ± 10*	85 ± 10	81 ± 9#
PWV (m/sec)	13.9 ± 2.8	12.0 ± 2.5*	12.0 ± 2.7	11.3 ± 2.7*,#
AASI	0.55 ± 0.17	0.48 ± 0.39	0.54 ± 0.28	0.41 ± 0.18*
AIx75**	25.6 ± 11.1	21.6 ± 12.0	21.7 ± 15.1	19.7 ± 14.3*

Notes: *$P < 0.05$ versus baseline; #$P < 0.05$ versus antihypertensive therapy; **AIx values were normalized to a standard heart rate of 75 per minutes.

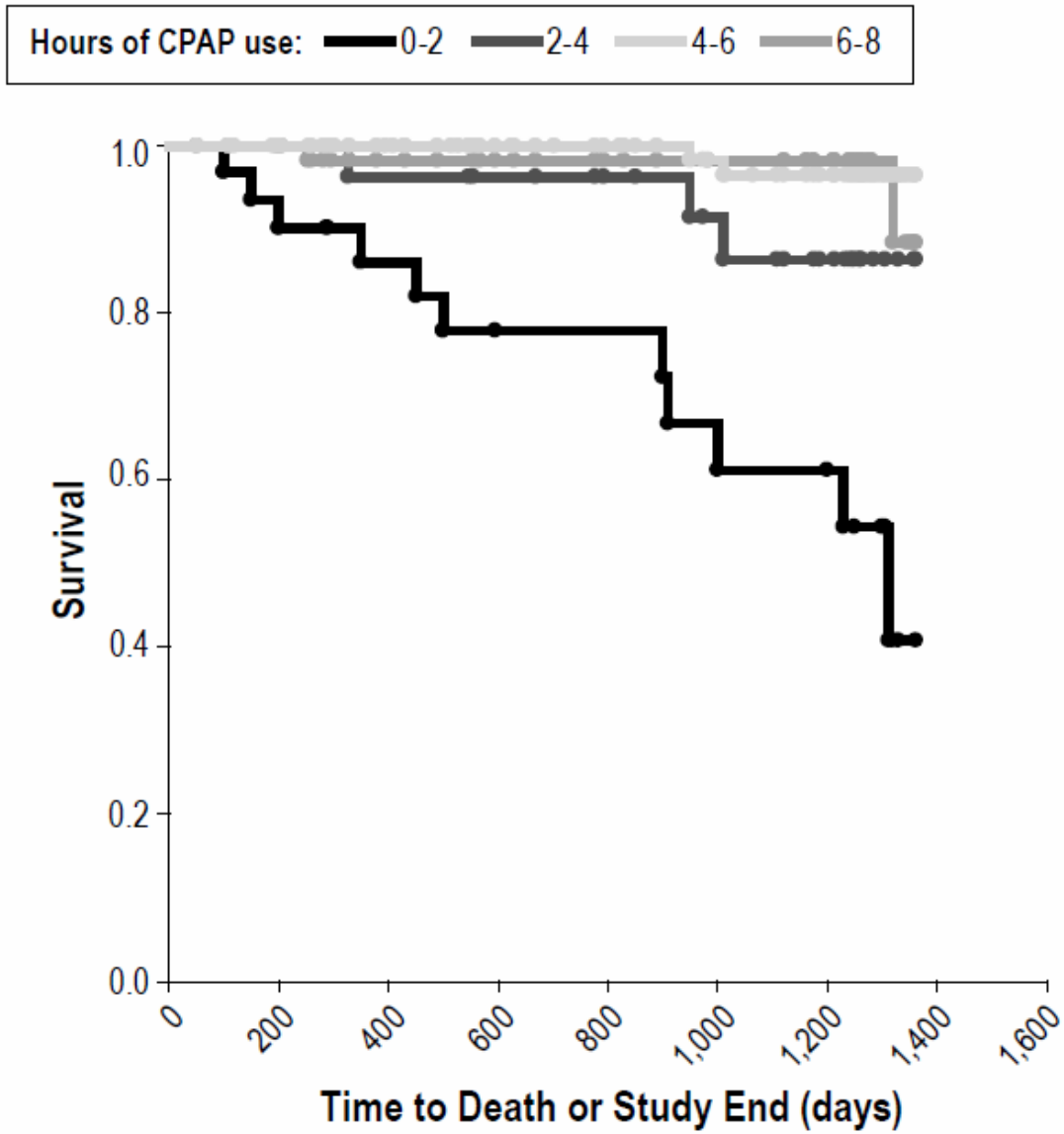
Abbreviations: AASI, ambulatory arterial stiffness index; AIx, augmentation index; AT, antihypertensive therapy; BP, blood pressure; CPAP, continuous positive airways pressure; eCPAP, effective CPAP; SD, standard deviation; pCPAP, placebo CPAP; PWV, pulse wave velocity.

C-PAP: sembra ridurre la mortalità nell'overlap syndrome

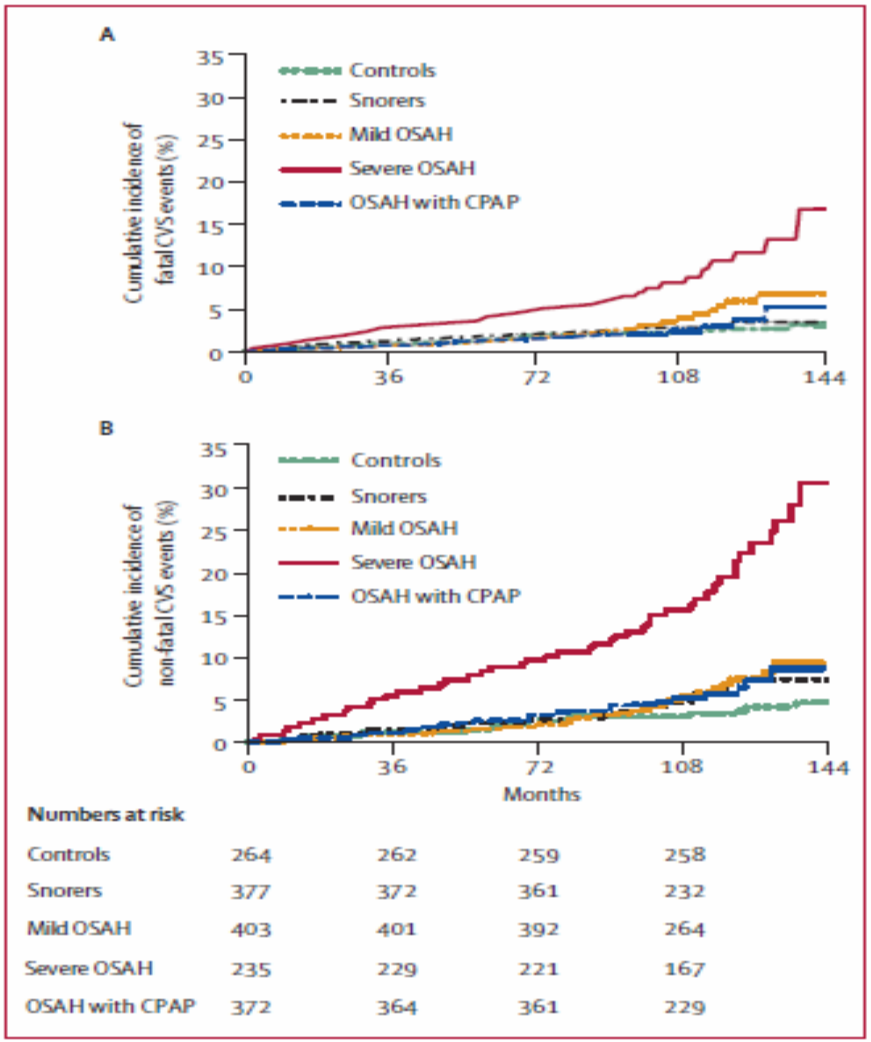


..già per poche ore per notte

(Stanchina ML et al. *J Clin Sleep Med* 2013; 9: 767-772)



C-PAP: conferme di possibile efficacia da uno studio osservazionale (Marin JM et al. *Lancet* 2005; 365: 1046–53)



Se persiste sonnolenza malgrado la CPAP

(Santamaria J et al. Sleep Medicine Reviews 2007; 11:195)

- Primary failure
- incorrect diagnosis of OSAS;
- inadequate CPAP treatment;
- undiagnosed associated conditions (poor sleep
- hygiene, depression, other sleep disorders,
- secondary gain);
- other unknown causes.

- Secondary failure

- loss of previously good compliance (development of rhinitis, new bed partner with poor tolerance to the machine); increase in weight;
- development of a new associated condition (poor sleep hygiene, depression, other sleep disorders, secondary gain);
- loss of ‘‘honeymoon’’/placebo effect revealing associated conditions not previously diagnosed.

In caso di intolleranza alla C-PAP

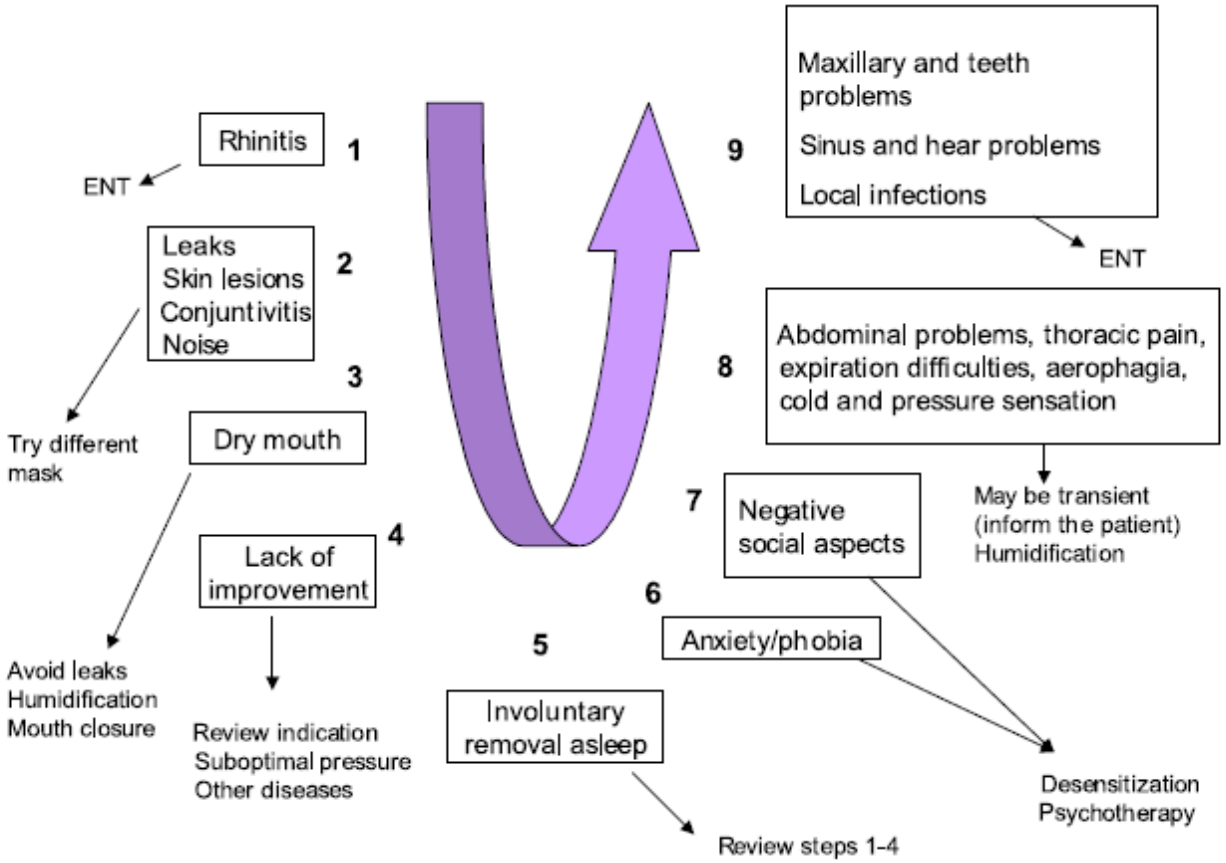


Table 3 Conditions associated with EDS that may be present in CPAP-treated subjects with residual EDS.

Depression
Narcolepsy with cataplexy
Narcolepsy without cataplexy
Idiopathic hypersomnia
Behaviorally induced insufficient sleep syndrome
Hypersomnia due to a medical or neurological disorder including stroke, neurodegenerative diseases, brain tumors, myotonic dystrophy, head trauma and limbic encephalitis
Hypersomnia due to drugs
Circadian rhythm sleep disorders including shift work, delayed sleep phase, advanced sleep phase and irregular sleep–wake patterns
Menstrual related hypersomnia
Kleine–Levin syndrome

Il device vibrotattile: uno strumento potenzialmente efficace (Scarlata S et al. J Thor Dis 2016; 8: 1820)

Night Shift™, Advanced Brain Monitoring, Carlsbad, CA, USA

	Baseline PSG values Mean (SD)	Positional Therapy PSG values Mean (SD)	p-value
AHI events/h	16.8 (9.5)	4.4 (5.5)	<0.001
ODI events/h	13.7 (7.5)	3.8 (5.2)	<0.001
RDI events/h	20.0 (9.5)	5.2 (5.6)	<0.001
% time spent supine	62.1 (22.7)	33.7 (23.9)	<0.001

Abbreviations: PSG= Polisomnography; AHI=Apnea Hypopnea Index; ODI= Oxygen Desaturation Index; RDI=Respiratory Disturbance Index.

Il device vibrotattile: uno strumento potenzialmente efficace (Scarlata S et al. J Thor Dis 2016; 8: 1820)

- **Vibro-tactile Positional Therapy**
- The Night Shift is a clinically proven solution for patients with positional obstructive sleep apnea (POSA) and snorers.
- Worn on the back of the neck, Night Shift begins to vibrate when the users start to back-sleep. The vibration slowly increases in intensity until the user changes positions.
- **Intelligent Interactive Monitoring**
- Night Shift is also an intelligent, interactive monitor that measures sleep quality and the frequency of unhealthy loud snoring.
- The internet-based Report Portal enables users to monitor the effectiveness of the therapy and its improvements in sleep quality.

Ma vale la pena curare l'OSAS? (Jonas DE et al. *JAMA*. 2017; 317: 415-433)

- **OBJECTIVE** To review primary care–relevant evidence on screening adults for OSA, test accuracy, and treatment of OSA, to inform the US Preventive Services Task Force.
- **DATA SOURCES** MEDLINE,Cochrane Library,EMBASE,and trial registries through October 2015, references, and experts, with surveillance of the literature through October 5, 2016.

- **CONCLUSIONS AND RELEVANCE** There is uncertainty about the accuracy or clinical utility of all potential screening tools. Multiple treatments for OSA reduce AHI, ESS (Epworth Sleepiness Scale) scores, and blood pressure. Trials of CPAP and other treatments have not established whether treatment reduces mortality or improves most other health outcomes, except for modest improvement in sleep-related quality of life.

Ma vale la pena curare l'OSAS nell'anziano?

(Celle S et al. Eur Respir J 2018; 51: 1702450)

- ABSTRACT The link between sleep apnoea and brain structure is unclear; although dysfunction of the hippocampus, middle temporal gyrus and brainstem/cerebellum have been observed previously. However, this link has been little explored in elderly subjects. The aim of this study was to explore the link between sleep apnoea and the brain in an elderly population.
- 226 asymptomatic elderly subjects (age mean±SD 75.3±0.9 years, range 72.3–77.8 years) from the PROOF (Evaluation of Ageing, Autonomic Nervous System Activity and Cardiovascular Events) cohort study were explored using linear voxel-based or cortical thickness with apnoea/hypopnoea index (AHI; mean±SD 15.9±11.5 events·h−1, range 6–63.6 events·h−1) as a covariate of main interest. The brain volumes of 20 control subjects, 18 apnoeic (AHI >29 events·h−1) treated patients and 20 apnoeic untreated patients from this population were compared using voxel-based morphometry, cortical thickness or surface-based analyses.
- AHI was not associated with any change in local brain volume, cortical thickness or cortex surface. Control subjects, apnoeic treated and untreated patients were not different in terms of local brain volume, cortical thickness or surface.
- In a specific population of asymptomatic elderly healthy subjects, sleep apnoea does not seem to be associated with a change in local brain volume or in cortical thickness.

OSA nell’anziano: conclusioni

- Prevalenza: certamente elevata
- Diagnosi: molto carente
- Presentazione: spesso atipica
- Correlati clinici: evidenti
- Cura: mediamente efficace
- Cura: costo/efficace? Dipende dall’outcome
- Prospettive: precision medicine and personalized medicine