APNEA DEL SON. Afectació cardiovascular. Què en sabem i què ens manca per saber?

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POBLACIÓ GENERAL

CARDIOPATIA ISQUÈMICA

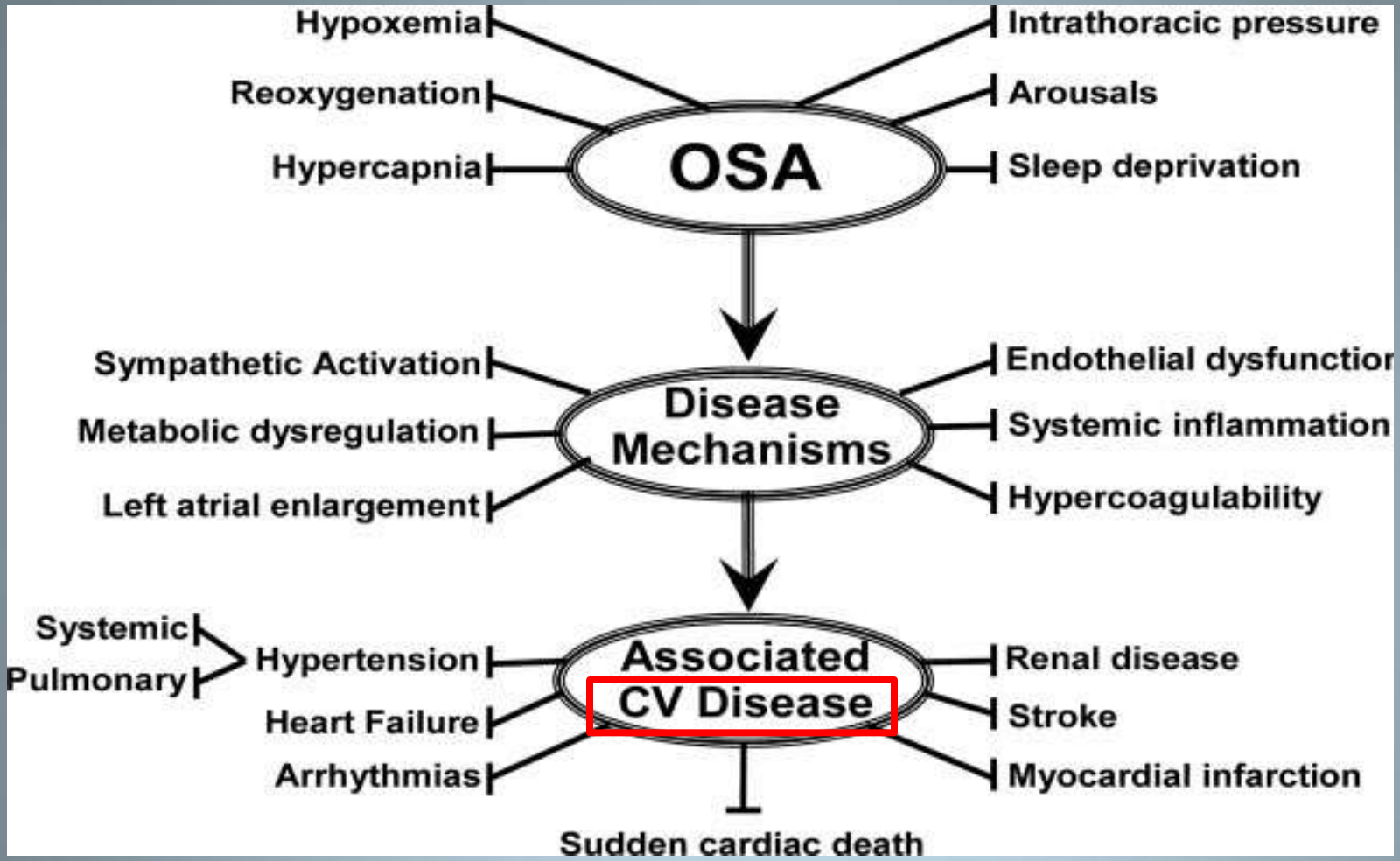
APNEA OBSTRUCTIVA

INSUFICIÈNCIA CARDÍACA

APNEA CENTRAL

APNEA OBSTRUCTIVA

POBLACIÓ GENERAL



Mai?

Sempre?

A vegades?

Somers VK et al. Circulation. 2008;118:1080-1111

TROPONINA

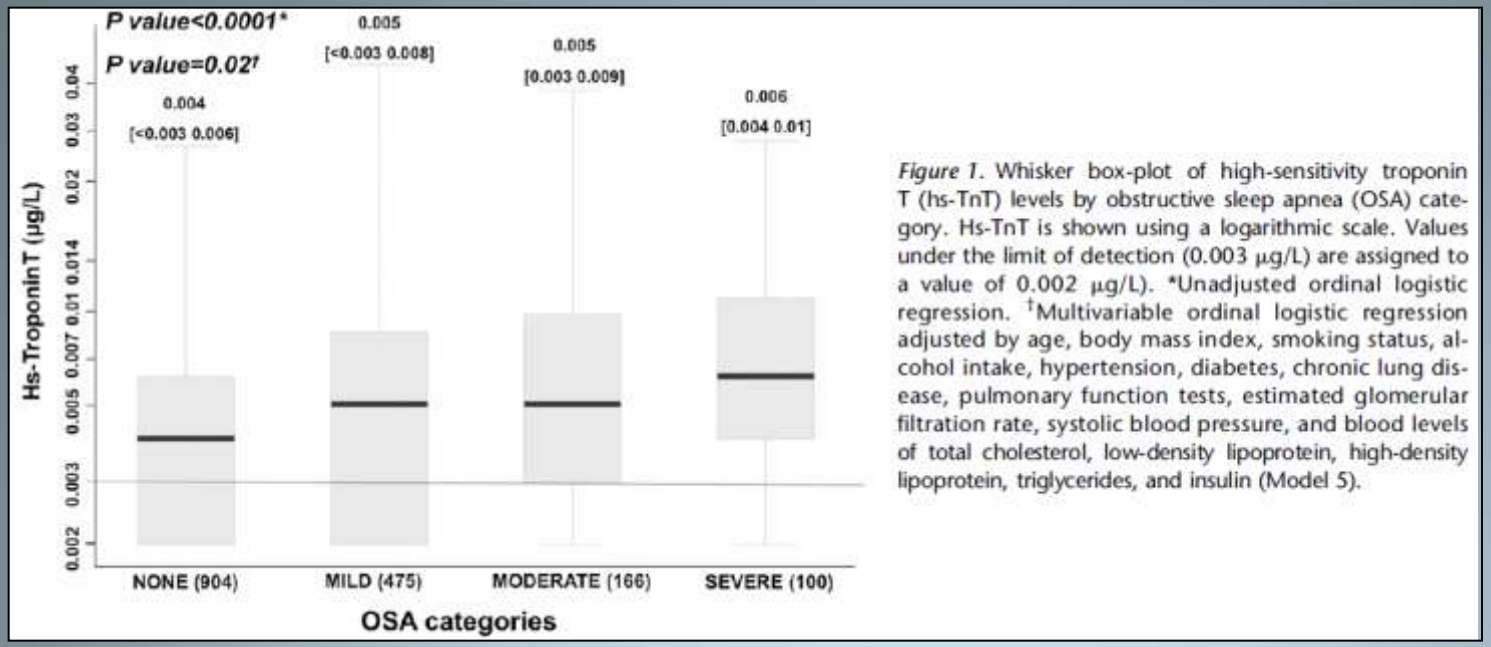


Figure 1. Whisker box-plot of high-sensitivity troponin T (hs-TnT) levels by obstructive sleep apnea (OSA) category. Hs-TnT is shown using a logarithmic scale. Values under the limit of detection (0.003 µg/L) are assigned to a value of 0.002 µg/L). *Unadjusted ordinal logistic regression. †Multivariable ordinal logistic regression adjusted by age, body mass index, smoking status, alcohol intake, hypertension, diabetes, chronic lung disease, pulmonary function tests, estimated glomerular filtration rate, systolic blood pressure, and blood levels of total cholesterol, low-density lipoprotein, high-density lipoprotein, triglycerides, and insulin (Model 5).

Roca CQ et al. Am J Respir Crit Care Med. 2013 Dec 15;188(12):1460-5.

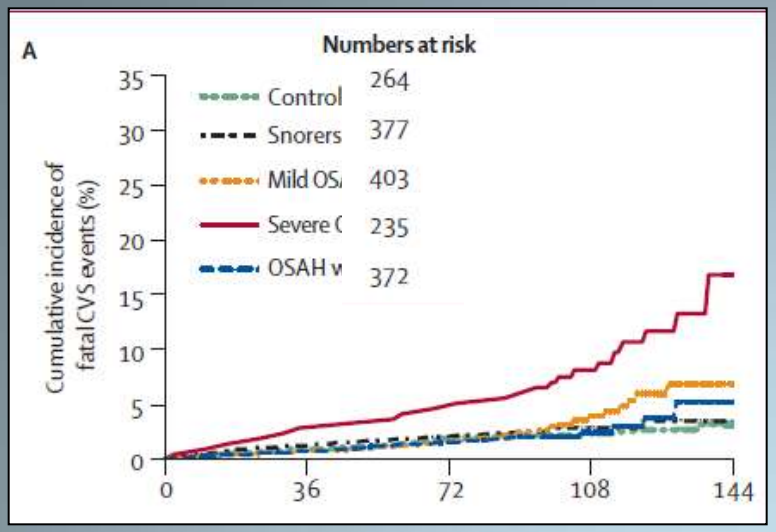
Ljunggren M et al. Sleep. 2012 Nov 1;35(11):1521-7 (n=349 women)

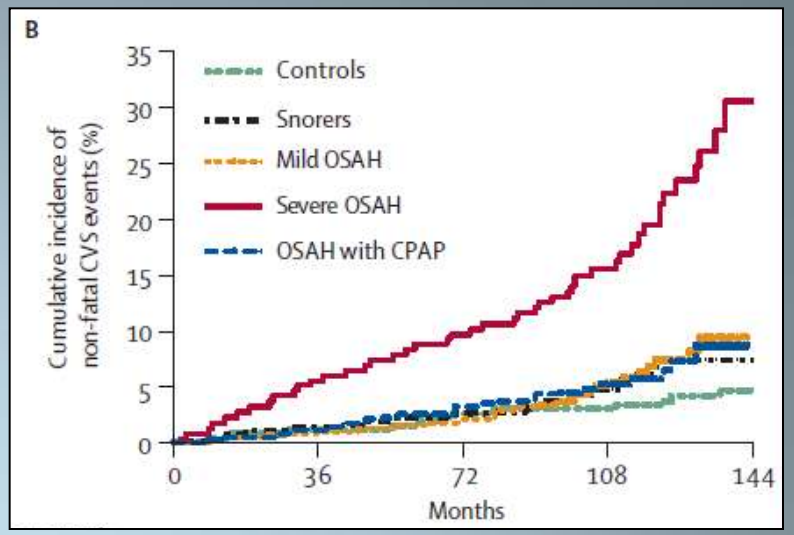
BNP

Table 4—Results of logistic regression analysis with dependent variable p-BNP > 20

	Unadjusted			Adjusted for age and BMI			Adjusted for age, BMI, systolic blood pressure, antihypertensive drugs, and P-creatinine		
Independent variable	OR	(95% CI)	P value	OR	(95% CI)	P value	OR	(95% CI)	P value
AHI < 5	1.0			1.0			1.0		
AHI 5–14.9	2.7	(1.4 – 5.3)	0.002	2.2	1.1– 4.4	0.023	2.2	(1.1 – 4.4)	0.026
AHI 15–29.9	4.4	(2.2 – 8.6)	< 0.001	3.0	1.4 – 6.3	0.004	3.1	(1.4 – 6.5)	0.004
AHI ≥ 30	6.8	(3.0 – 15.4)	< 0.001	4.9	1.9 – 12.6	0.001	4.6	(1.8 – 11.9)	0.002

AHI, apnea-hypopnea index; BMI, body mass index; BNP, type B natriuretic peptide; CI, confidence interval; OR, odds ratio.





	Unadjusted odds ratio (95% CI)	p	Part adjusted odds ratio (95% CI)	p	Fully adjusted odds ratio (95% CI)	p
Age, years	1·09 (1·06–1·11)	<0·0001	1·09 (1·05–1·11)	0·0005	1·09 (1·04–1·12)	0·001
Diagnostic group						
Snoring	1·04 (0·51–1·34)	0·61	1·03 (0·41–1·46)	0·74	1·03 (0·31–1·84)	0·88
Untreated mild-moderate OSAH	1·19 (0·74–1·89)	0·09	1·16 (0·55–2·11)	0·59	1·15 (0·34–2·69)	0·71
Untreated severe OSAH	3·98 (1·74–6·13)	0·003	3·02 (1·44–7·33)	0·015	2·87 (1·17–7·51)	0·025
CPAP	1·06 (0·55–1·91)	0·45	1·05 (0·45–2·09)	0·65	1·05 (0·39–2·21)	0·74
Cardiovascular disease	3·66 (1·98–4·07)	<0·0001			2·54 (1·31–4·99)	0·005

OSAH=obstructive sleep apnoea-hypopnoea; CPAP=continuous positive airway pressure. Variables included in the fully adjusted model were age, diagnostic group, presence of cardiovascular disease, hypertension, diabetes, lipid disorders, smoking status, alcohol use, systolic and diastolic blood pressure, blood glucose, total cholesterol, triglycerides, and current use of antihypertensive, lipid-lowering, and antidiabetic drugs. Variables included in the part adjusted model were those included in the fully adjusted model except hypertension and presence of cardiovascular disease.

Table 3: **Unadjusted, part adjusted, and fully adjusted odds ratio for cardiovascular death associated with clinical variables and diagnosis status, according to the logistic-regression analysis**

	Unadjusted odds ratio (95% CI)	p	Part adjusted odds ratio (95% CI)	p	Fully adjusted odds ratio (95% CI)	p
Age, years	1·11 (1·07–1·14)	<0·0001	1·09 (1·06–1·13)	0·0008	1·09 (1·05–1·13)	0·001
Diagnostic group						
Snoring	1·52 (0·88–2·11)	0·12	1·23 (0·71–2·86)	0·25	1·32 (0·64–3·01)	0·38
Mild-moderate OSAH	1·77 (0·91–2·76)	0·07	1·62 (0·65–3·01)	0·19	1·57 (0·62–3·16)	0·22
Severe OSAH	5·65 (1·92–6·52)	<0·001	3·32 (1·24–7·41)	0·005	3·17 (1·12–7·52)	0·001
CPAP	1·44 (0·61–2·80)	0·24	1·42 (0·53–3·29)	0·28	1·42 (0·52–3·40)	0·29
Cardiovascular disease	2·68 (1·13–2·57)	<0·0001			1·77 (1·03–3·09)	0·02
SBP, mm Hg	1·83 (1·24–5·52)	0·003			1·57 (1·04–4·09)	0·04
Current smoker	1·97 (1·42–6·71)	0·002	1·62 (1·06–6·12)	0·02	1·51 (1·02–5·88)	0·04

OSAH=obstructive sleep apnoea-hypopnoea; CPAP=continuous positive airway pressure; SBP=systolic blood pressure. Variables included in the fully adjusted model were age, diagnostic group, presence of cardiovascular disease, hypertension, diabetes, lipid disorders, smoking status, alcohol use, systolic and diastolic blood pressure, blood glucose, total cholesterol, tryglicerides and current use of antihypertensive, lipid-lowering and antidiabetic drugs. Variables included in the part adjusted model were those included in the fully adjusted model except hypertension and presence of cardiovascular disease.

Table 4: **Unadjusted, part adjusted, and fully adjusted odds ratio for non-fatal cardiovascular events associated with clinical variables and diagnosis status, according to the logistic-regression analysis**

Marin JM. Lancet. 2005;365:1046-1053

Table 3. Relation of OSA to Incident CHD*

	AHI (Events per Hour)				
	<5.0	5.0 to 14.9	15.0 to 29.9	≥30.0	P†
Men					
No. of subjects	829	644	282	172	
No. of CHD events	114	95	47	40	
Covariates in model					
Age, race, BMI, smoking	1.00 (Referent)	0.94 (0.71, 1.24)	1.07 (0.75, 1.52)	1.45 (0.99, 2.13)	0.046
Plus total and HDL cholesterol, lipid-lowering medications, diabetes mellitus	1.00 (Referent)	0.93 (0.70, 1.23)	1.04 (0.73, 1.48)	1.41 (0.96, 2.07)	0.08
Plus SBP, DBP, use of antihypertensive medications	1.00 (Referent)	0.91 (0.69, 1.20)	1.07 (0.75, 1.52)	1.33 (0.91, 1.95)	0.12
Women					
No. of subjects	1605	610	196	84	
No. of CHD events	103	54	17	3	
Covariates in model					
Age, race, BMI, smoking	1.00 (Referent)	1.01 (0.73, 1.45)	0.92 (0.54, 1.55)	0.36 (0.11, 1.16)	0.10
Plus total and HDL cholesterol, lipid-lowering medications, diabetes mellitus	1.00 (Referent)	0.99 (0.71, 1.40)	0.89 (0.52, 1.51)	0.37 (0.12, 1.19)	0.09
Plus SBP, DBP, use of antihypertensive medications	1.00 (Referent)	0.96 (0.69, 1.38)	0.87 (0.51, 1.49)	0.40 (0.12, 1.27)	0.10

*Results are adjusted hazard ratio (95% confidence interval).
†*P* for the overall effect of AHI modeled as a continuous variable.

Obstructive sleep apnea is associated with an increased risk of Incident heart failure in communitydwelling middle-aged and older men; Its association with incident coronary heart disease in this sample is equivocal.

Table 4. Relation of OSA to Incident Heart Failure*

	AHI (Events per Hour)				
	<5.0	5.0 to 14.9	15.0 to 29.9	≥30.0	P†
Men					
No. of subjects	829	644	282	172	
No. of heart failure events	44	46	25	26	
Covariates in model					
Age, race, BMI, smoking	1.00 (Referent)	0.96 (0.63, 1.46)	1.17 (0.71, 1.94)	1.61 (0.95, 2.71)	0.03
Plus total and HDL cholesterol, lipid-lowering medications, diabetes mellitus	1.00 (Referent)	0.90 (0.59, 1.38)	1.08 (0.65, 1.80)	1.59 (0.94, 2.69)	0.02
Plus SBP, DBP, use of antihypertensive medications	1.00 (Referent)	0.88 (0.57, 1.35)	1.13 (0.68, 1.89)	1.58 (0.93, 2.66)	0.02
Women					
No. of subjects	1605	610	196	84	
No. of heart failure events	86	54	19	8	
Covariates in model					
Age, race, BMI, smoking	1.00 (Referent)	1.12 (0.79, 1.59)	1.10 (0.66, 1.83)	1.05 (0.50, 2.23)	0.72
Plus total and HDL cholesterol, lipid-lowering medications, diabetes mellitus	1.00 (Referent)	1.15 (0.81, 1.63)	1.06 (0.64, 1.77)	1.19 (0.56, 2.53)	0.90
Plus SBP, DBP, use of antihypertensive medications	1.00 (Referent)	1.13 (0.80, 1.61)	1.01 (0.60, 1.69)	1.19 (0.56, 2.52)	0.83

*Results are adjusted hazard ratio (95% confidence interval).
†*P* for the overall effect of AHI modeled as a continuous variable.

Gottlieb JD et al. Circulation. 2010;122:352-360

Loke YK et al. Circ Cardiovasc Qual Outcomes. 2012 Sep 1;5(5):720-8.

- AVC i SAOS: meta-anàlisi de 5 estudis: SAOS OR 2.24; 95% CI, 1.57–3.19
- Mortalitat cardiovascular (2 estudis): OR, 2.09; 95% CI, 1.20–3.65
- Mortalitat global: OR: 1.59; 95% CI 1.00-2.55
- Cardiopatia isquèmica: 6 estudis (8785 p), SAOS es va associar de manera no significativa amb la cardiopatia isquèmica (OR, 1.56; 95% CI, 0.83–2.91) (Heterogenicitat important)

Ge X et al. PLoS ONE. 8(7):e69432, n = 11932

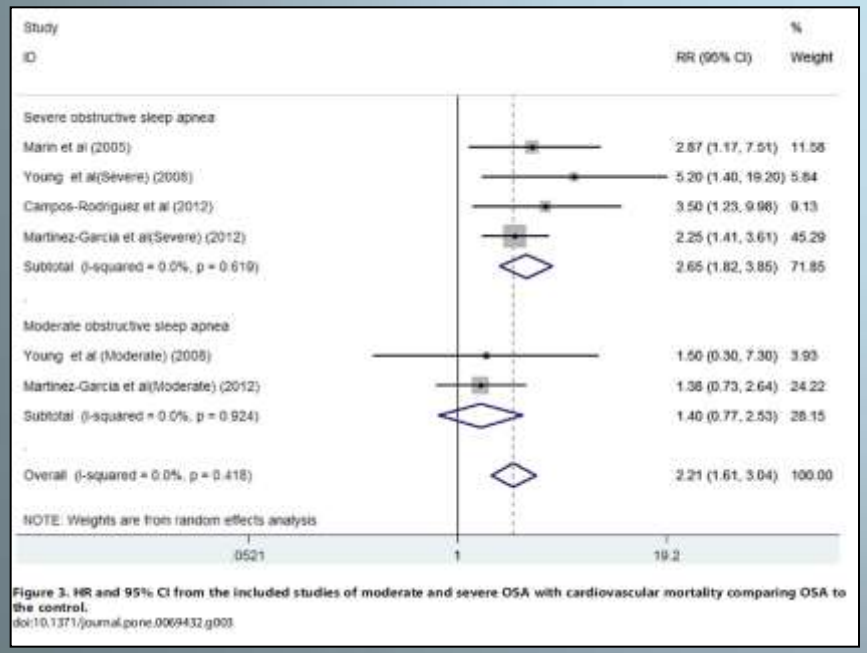


Figure 3. HR and 95% CI from the included studies of moderate and severe OSA with cardiovascular mortality comparing OSA to the control.
doi:10.1371/journal.pone.0069432.g003

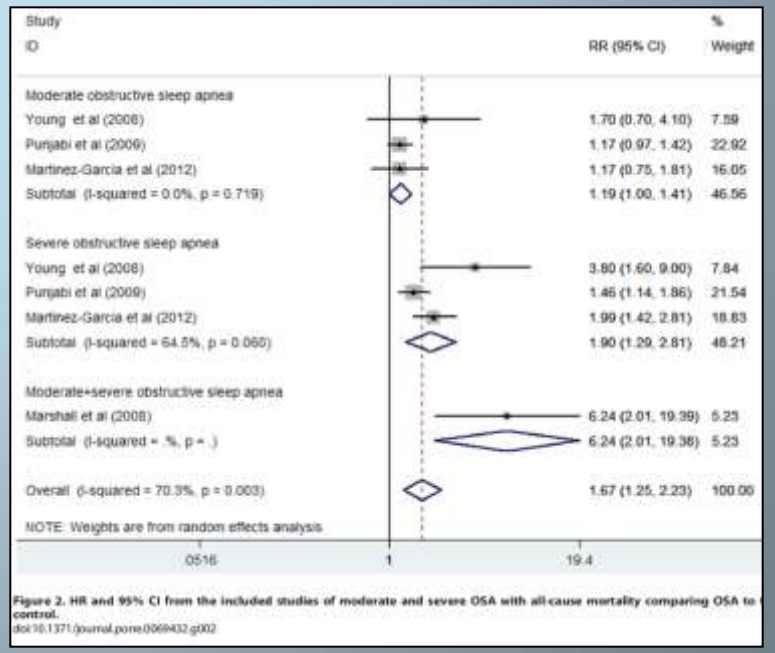


Figure 2. HR and 95% CI from the included studies of moderate and severe OSA with all-cause mortality comparing OSA to control.
doi:10.1371/journal.pone.0069432.g002

CARDIOPATIA ISQUÈMICA

QUINA RELACIÓ HI HA ENTRE SAOS I LA SÍNDROME CORONÀRIA AGUDA?

Conclusions: OSA may impair myocardial tissue perfusion following primary PCI.

Nakashima H et al. Circ J. 2011;75(4):890-6

Conclusions: Considering the independent prognostic and incremental value of suspected OSA, this condition may represent an aggravating factor for patients with non-ST elevation acute coronary syndrome.

Correia LC et al. Sleep. 2012 Sep 1;35(9):1241-5

Conclusions: 42% of the patients admitted with STEMI have undiagnosed severe OSA. Severe OSA carries a negative prognostic impact for this group of patients. It is associated with a lower event-free survival rate at 18-month follow-up.

Lee CH et al. J Clin Sleep Med. 2011 Dec 15;7(6):616-21.

Conclusions: Sleep-disordered breathing was associated with less myocardial salvage and a smaller reduction in infarct size. These findings suggest a contribution of SDB to impaired healing of MI.

Buchner S et al. Eur Heart J. 2014;35(3):192-199

Conclusions: The current study demonstrated that sleep apnea impairs coronary flow rates and is associated with coronary slow-flow phenomenon.

Ozeke O et al. J Cardiovasc Med. 2012 Jun;13(6):376-80

In conclusion, despite the greater incidence of some types of cardiac arrhythmias during an acute MI in OSA, these patients have the same clinical course in hospital and mortality rate as nonOSA patients.

Marin JM et al. Sleep. 1998 Dec 15;21(8):809-15

Conclusions: In the setting of ACS, the prevalence of SDB was very high in this population and was not detected by self-reports of sleepiness or composite risk for SDB. The odds of adverse outcome for ACS up to 6 months were no different in patients with SDB compared to those without SDB, as compared to effects of an older age or presence of diabetes.

Mehra R et al. Sleep Med. 2006 Sep;7(6):521-8

Conclusions: We found a high prevalence of previously undiagnosed OSA in patients admitted with acute myocardial infarction. Diabetes mellitus was independently associated with OSA. No evidence indicated that OSA is associated with impaired microvascular perfusion after primary PCI.

Lee CH et al. Chest 2009 Jun;135(6):1488-95

Conclusions: Using the three angiographic scoring systems, we found no association between AHI and angiographic coronary disease phenotypes, suggesting a limited effect of obstructive sleep apnoea on the amount and distribution of coronary plaques in patients presenting with acute myocardial infarction.

Hein T et al. Acute Card Care. 2013 Jun;15(2):26-33

In summary, there is an association between sleep apnea and collateral vessel growth. We speculate that OSAS may be a significant factor affecting growth of CCVs as a compensatory mechanism.

Steiner S et al. Chest 2010;137:516–20.

Conclusions: Our study demonstrates that patients with OSA have less severe cardiac injury during an acute non-fatal MI when compared to patients without OSA.

Shah N et al. Sleep Breath. 2013 May;17(2):819-26

COM S'EXPLIQUEN AQUESTES DIFERÈNCIES?

- D'una banda, les diferències entre els diferents estudis podrien explicar-se per la diferent població a estudi i diferents end-point als estudis.

- És possible que SAHS no estigui associada només a efectes deleteris?

El potencial efecte cardioprotector de la SAOS podria ser explicat per episodis d'*HIPÒXIA INTERMITENT → PRE I POSTCONDICIONAMENT*

PRECONDICIONAMENT REMOT

23 estudis (954 p intervenció, 924 controls)

Cirurgia cardíaca, intervencionisme coronari percutani i cirurgia vascular

Brevoord D et al. PLoS One. 2012;7(7):e42179.

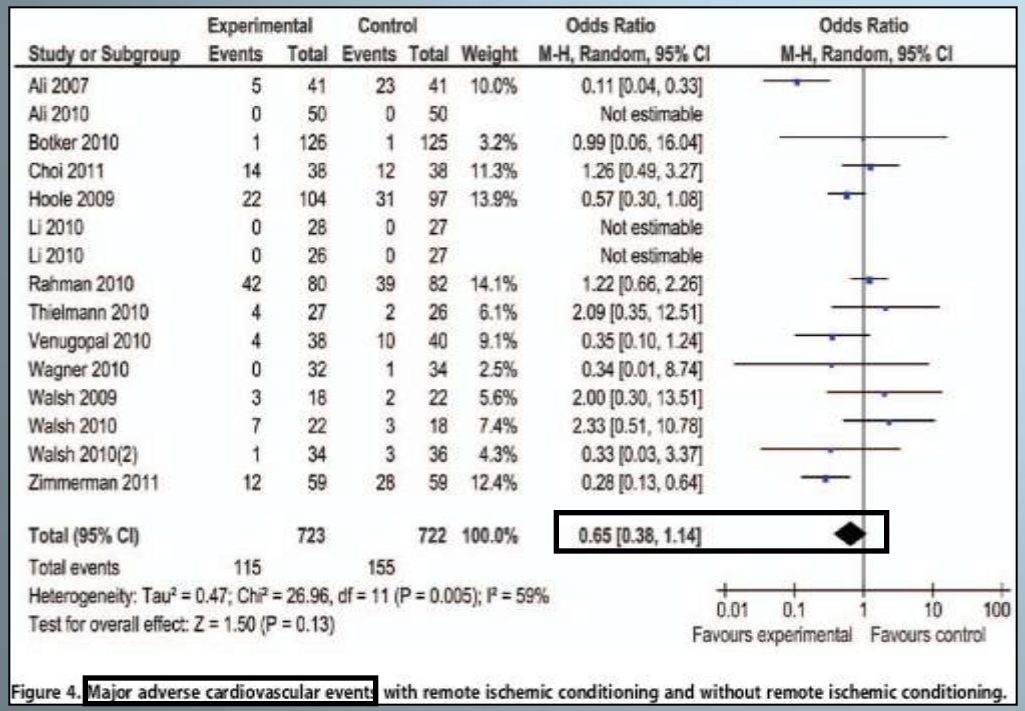


Figure 4. Major adverse cardiovascular events with remote ischemic conditioning and without remote ischemic conditioning.

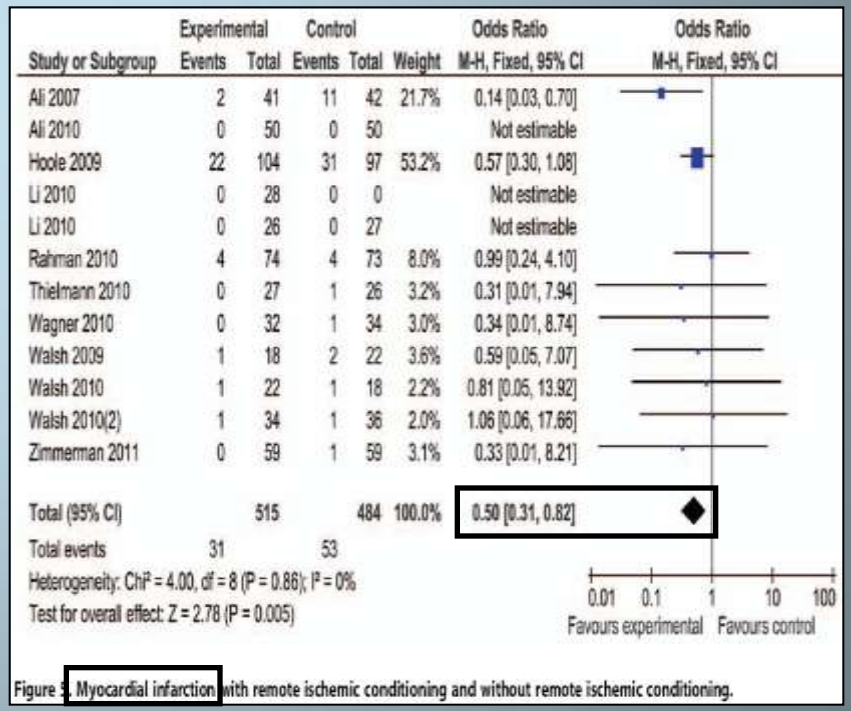


Figure 5. Myocardial infarction with remote ischemic conditioning and without remote ischemic conditioning.

POST/PERICONDICIONAMENT REMOT

	pPCI plus remote conditioning		pPCI		p value
	Patients	Median (IQR)	Patients	Median (IQR)	
Overall population					
Salvage index	73	0·75 (0·50–0·93)	69	0·55 (0·35–0·88)	0·0333
Area at risk (% of left ventricle)	73	26% (20–40)	69	28% (22–42)	0·97
Salvage (% of left ventricle)	73	16% (10–25)	69	12% (5–23)	0·0368
Final infarct size (% of left ventricle)	109	4% (1–14)	110	7% (1–21)	0·10
Vessel patency before procedure*					
Occluded (TIMI flow grade 0–I)					
Salvage index	43	0·74 (0·47–0·87)	42	0·53 (0·35–0·71)	0·0313
Area at risk (% of left ventricle)	43	33% (23–44)	42	34% (24–44)	0·65
Final infarct size (% of left ventricle)	64	9% (3–17)	69	13% (4–24)	0·06
Not occluded (TIMI flow grade II–III)					
Salvage index	30	0·78 (0·50–1·00)	27	0·86 (0·31–1·00)	0·71
Area at risk (% of left ventricle)	30	16% (12–20)	27	16% (10–22)	0·98
Final infarct size (% of left ventricle)	45	1% (0–7)	41	1% (0–5)	0·62
Infarct location†					
Left anterior descending artery					
Salvage index	29	0·78 (0·47–0·93)	29	0·51 (0·38–0·69)	0·06
Area at risk (% of left ventricle)	29	35% (27–41)	29	38% (26–46)	0·72
Final infarct size (% of left ventricle)	43	8% (1–17)	44	16% (4–25)	0·0108
Not left anterior descending artery					
Salvage index	44	0·74 (0·52–0·95)	40	0·67 (0·30–0·96)	0·27
Area at risk (% of left ventricle)	44	22% (13–35)	40	23% (8–33)	0·78
Final infarct size (% of left ventricle)	66	4% (1–13)	66	4% (1–12)	0·94

TIMI=thrombolysis in myocardial infarction. *For interaction of vessel patency before procedure with remote conditioning, p=0·96 for area at risk, p=0·15 for salvage index, and p=0·35 for final infarct size. †For interaction of infarct location with remote conditioning, p=0·99 for area at risk, p=0·86 for salvage index, and p=0·13 for final infarct size.

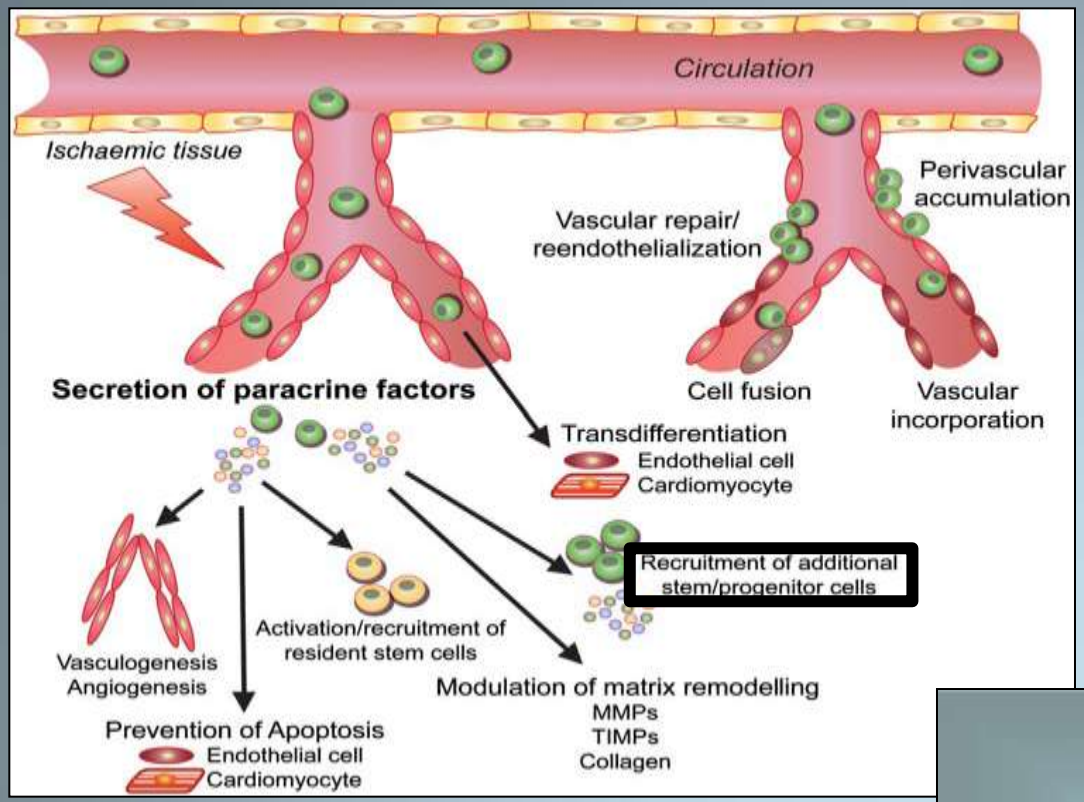
Bøtker HE et al. Lancet 2010; 375: 727–34

QUINA POT SER L'EXPLICCIÓ FISIOPATOLÒGICA D'AQUESTS RESULTATS?

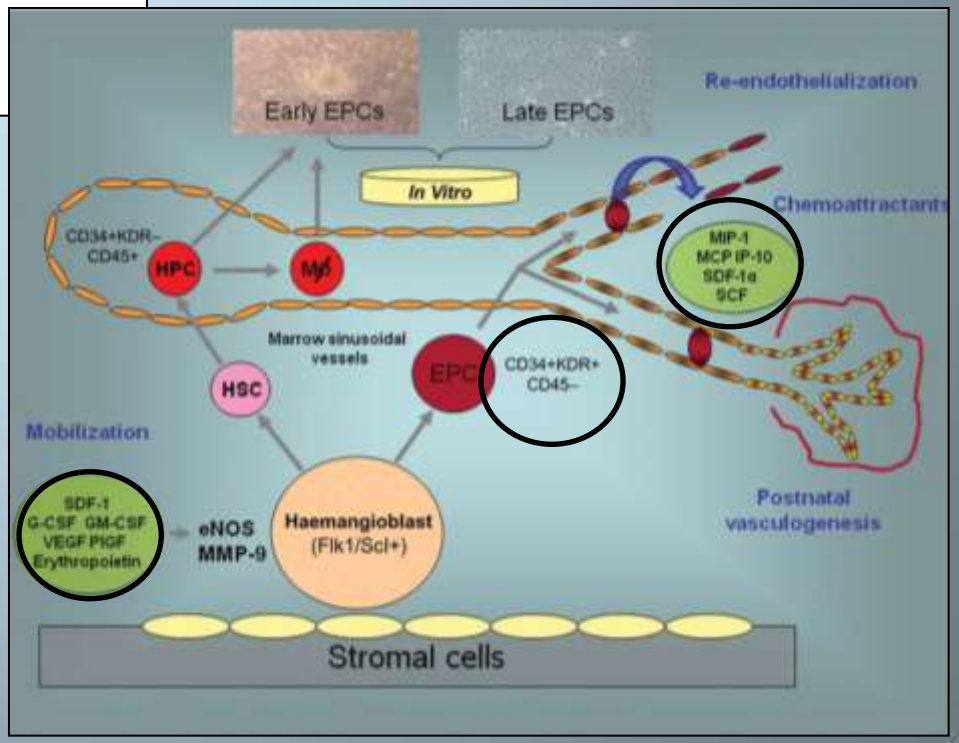
- L'endoteli és una superfície complexa i dinàmica, que respon a una gran varietat d'estímuls, tant locals con sistèmics, amb la intenció de mantenir l'homeostasi vascular.

- L'exposició crònica a diferents factores de risc cardiovascular altera les funcions reguladores de l'endoteli, es produeixen canvis proinflamatoris, que finalment condueixen a la mort cel·lular i apoptosi.

- Com a conseqüència, l'endoteli presentarà una funcionalitat alterada i perdrà la seva integritat.



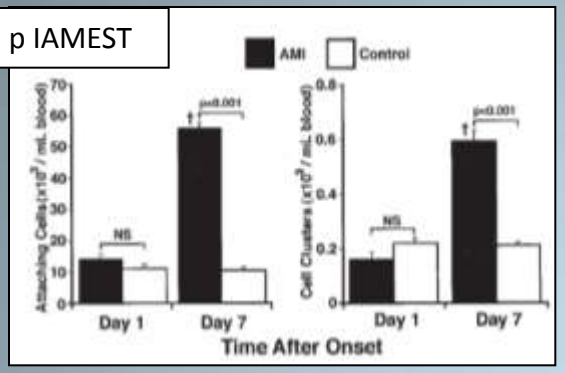
Tongers et al. Eur Heart J. 2011;32,1197–1206



Leone AM et al. Eur Heart J. 2009;30,890–899

ENDOTHELIAL PROGENITOR CELLS i IAM

15 p IAMEST



Shintani et al. Circulation. 2001 Jun 12;103(23):2776-9.

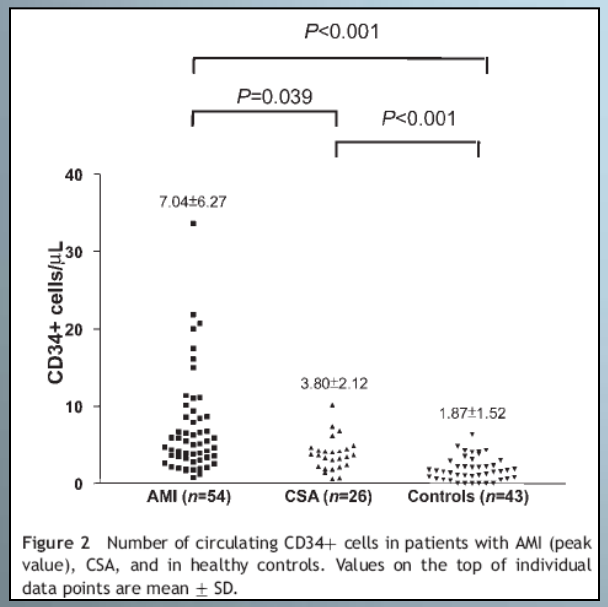
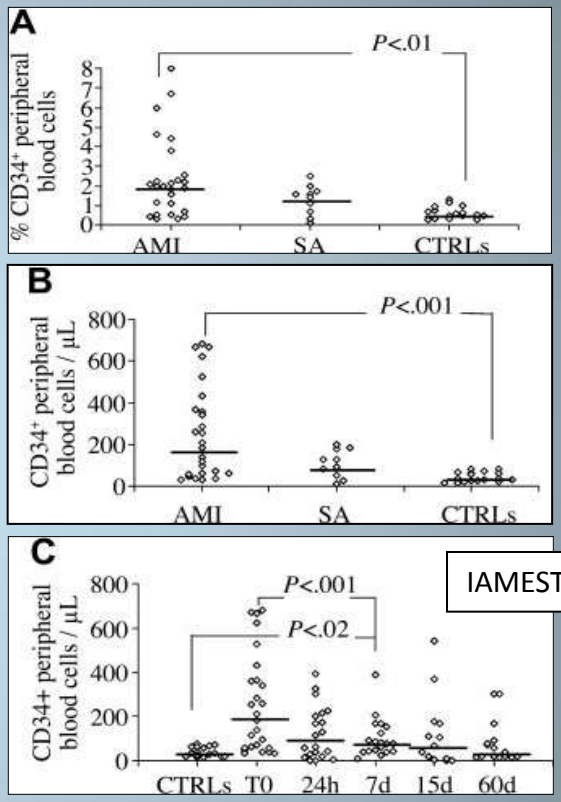


Figure 2 Number of circulating CD34+ cells in patients with AMI (peak value), CSA, and in healthy controls. Values on the top of individual data points are mean ± SD.

Leone et al. Eur Heart J. 2005:26;1196–1204

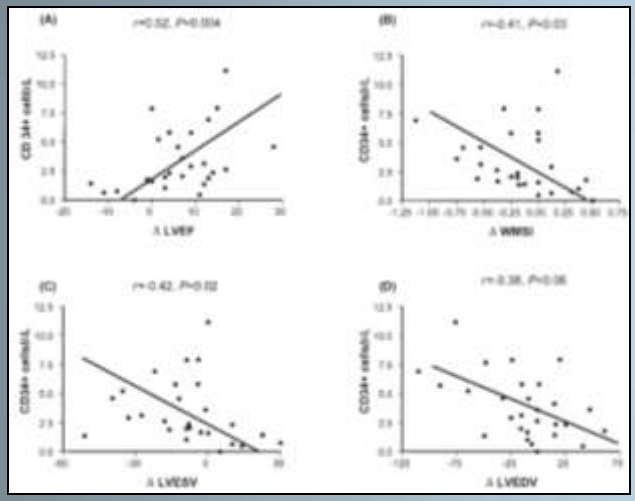


IAMEST, 26 p

Massa et al. Blood. 2005;105:199-206

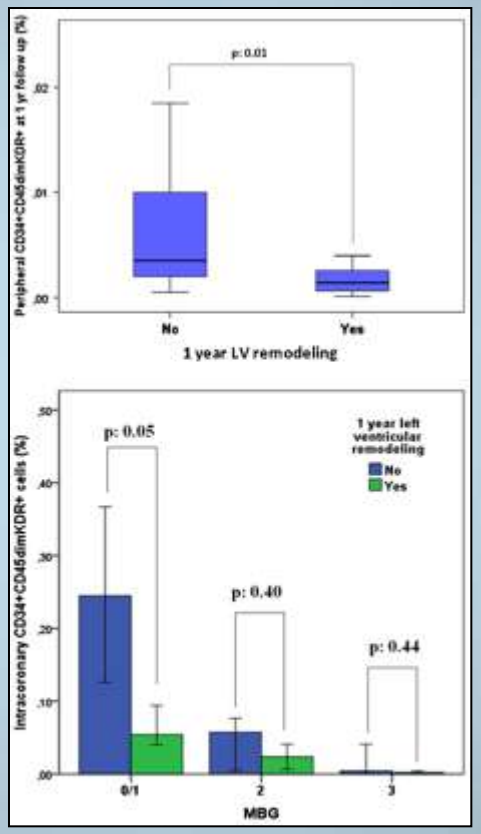
VALOR PRONÒSTIC?

54 p IAMEST, 26 angina estable, 43 control



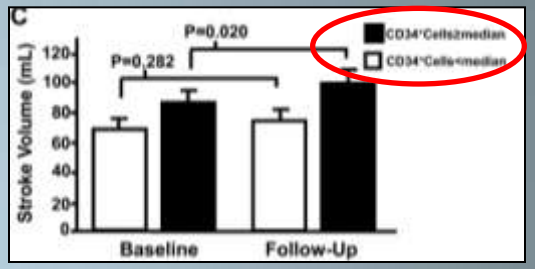
Leone AM, Eur Heart J. 2005:26;1196–1204

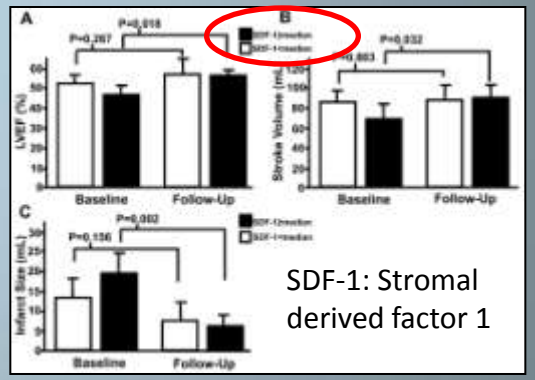
78 p IAMEST- ICPP



Porto I et al.
Am J Cardiol 2013;112:782-791

40 p IAMEST- ICPP

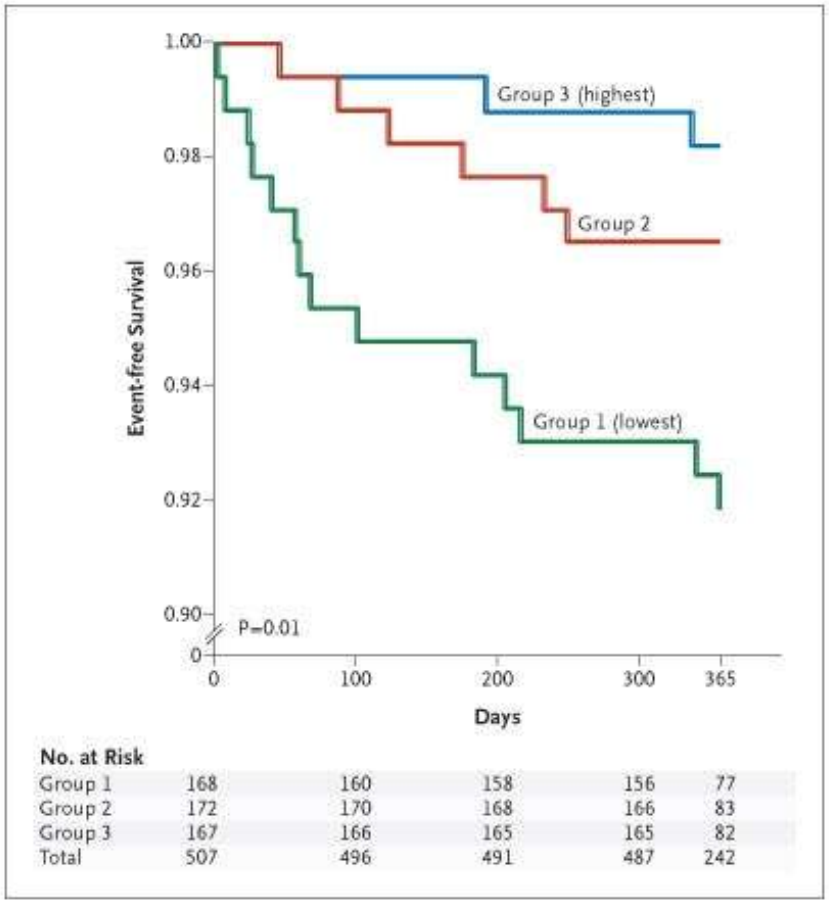




SDF-1: Stromal derived factor 1

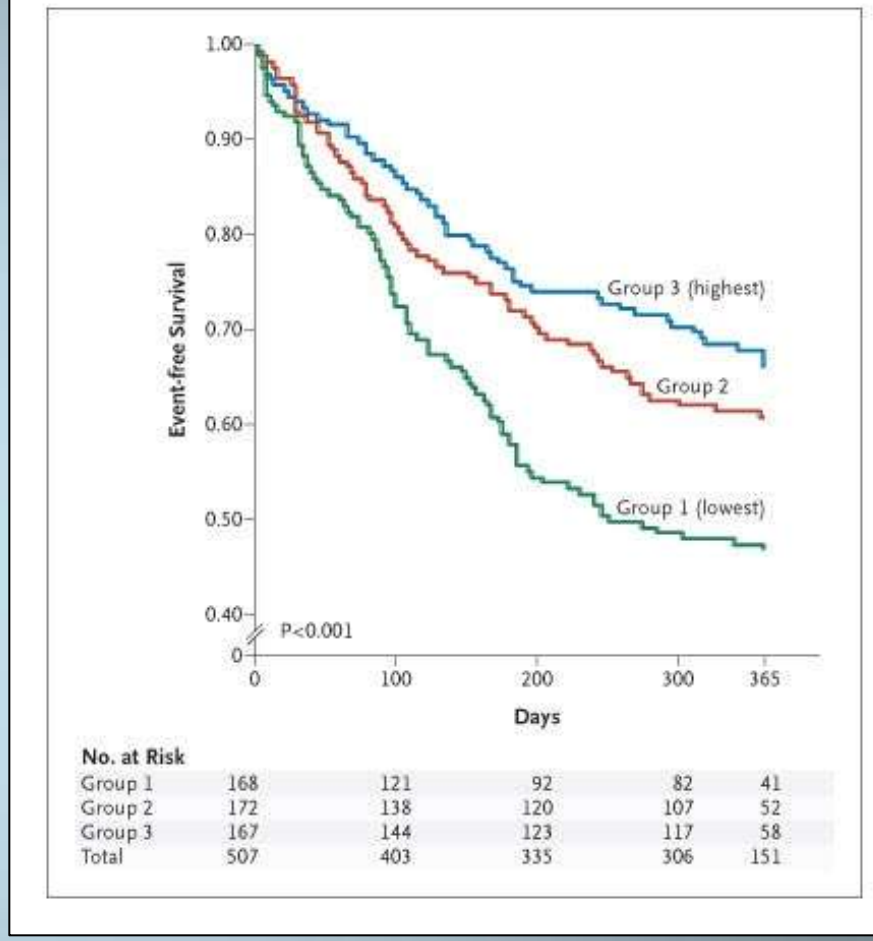
Geisler T el al. Eur J Radiol. 2012 Apr;81(4):e486-90

Werner N et al. N Engl J Med 2005;353:999-1007



No. at Risk					
Group 1	168	160	158	156	77
Group 2	172	170	168	166	83
Group 3	167	166	165	165	82
Total	507	496	491	487	242

Cumulative Event-free Survival in an Analysis of Death from Cardiovascular Causes at 12 Months, According to Levels of Circulating CD34+KDR+ Endothelial Progenitor Cells at the Time of Enrollment.



No. at Risk					
Group 1	168	121	92	82	41
Group 2	172	138	120	107	52
Group 3	167	144	123	117	58
Total	507	403	335	306	151

Cumulative Event-free Survival in Analysis of a First Major Cardiovascular Event (Myocardial Infarction, Hospitalization, Revascularization, or Cardiovascular Death) at 12 Months, According to Levels of Circulating CD34+KDR+ Endothelial Progenitor Cells at the Time of Enrollment.

- Si la noxa (isquèmia) provoca mobilització de EPC, i a major EPC, (sembla) millor pronòstic,

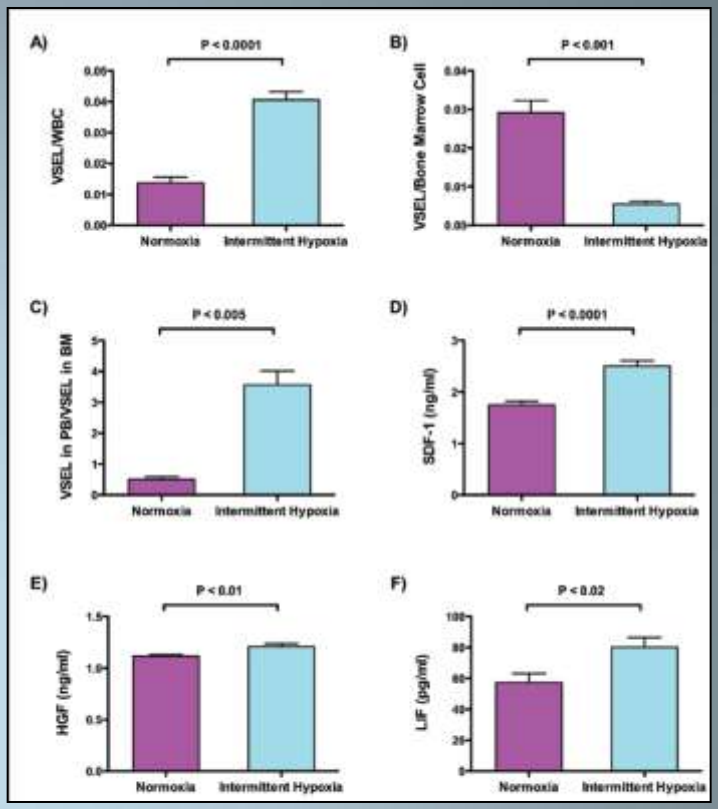
- Com afecta la SAOS (hipòxia intermitent) a la mobilització de EPC i altres cèl·lules?

Table 1 | Bone marrow-derived stem cell studies in patients with obstructive sleep apnea (OSA) and animal models.

Reference	Species	Groups (*n*)	Main results
EPCs			
Kizawa et al. (2009)	Human	Control (38) OSA (37)	EPCs were increased threefold in OSA patients with respect to controls and decreased after 12 weeks of CPAP treatment.
Martin et al. (2008)	Human	Control (10) OSA (17)	EPCs: no changes between OSA and control groups.
Yun et al. (2010)	Human	Control (22) OSA (82)	EPCs: similar values in both groups. Endothelial impairment in OSA group.
de la Peña et al. (2009)	Human	Control (13) OSA (13)	EPCs from OSA were reduced fivefold with respect to control group. OSA also presented increased levels of VEGF but endothelial function was unaltered.
Jelic et al. (2008)	Human	Control (15) OSA (30)	OSA group presented a fourfold reduction in circulating EPCs with respect to controls. Levels were normalized after 4 weeks of CPAP. In addition, OSA patients presented increased levels of oxidative stress and inflammation.
Jelic et al. (2009)	Human	Control (16) OSA (16)	EPCs were reduced threefold with respect to controls and were inversely related to the presence of endothelial microparticles. EPCs increased after 4 weeks of CPAP treatment.
Mum et al. (2011)	Human	OSA (16)	Negative correlation of circulating EPCs with severity of OSA and oxidative stress. EPCs values returned to control values after 1 month of CPAP treatment.
Kheirandish-Gozal et al. (2010)	Human	Control (20) OSA (40)	Circulating EPCs were reduced in those OSA children with impaired endothelial function (20 patients) and increased in those without it (20 patients).
VSELs			
Gharib et al. (2010)	Mice	Control (30) (21% O_2 for 48 h) Int. hyp. (30) (21.0 and 5.7% O_2 every 180 s 12 h/day for 48 h.	Intermittent hypoxia (IH) induced migration of VSELs from bone marrow to peripheral blood. More than 1,100 genes were differentially expressed in VSELs in response to IH.
Gharib et al. (2011)	Mice	Control (6) (21% FiO_2 for 24 h) Chr. Hyp. (6) (8% FiO_2 for 24 h)	Hypoxia mobilized VSELs from the bone marrow to peripheral blood and induced a distinct genome-wide transcriptional signature.
MSCs			
Carreras et al. (2009)	Rat	Control (10) OSA (10) (60 h 15 s each) for 5 hours	Circulating MSCs were three times higher in rats subjected to OSA than in controls.
Carreras et al. (2010a)	Rat	Cont. (30) OSA (30) (60 h 15 s each) for 5 h	Serum from apneic rats increased MSCs migration, adhesion and endothelial wound healing compared to serum from control rats.
Carreras et al. (2010b)	Rat	Cont. (10) OSA (10) (60 h 15 s each) for 5 h	IL-1α was higher in rats subjected to recurrent obstructive apneas than in controls. MSCs injection reduced the IL-1α levels induced by recurrent obstructive apneas.

EPCs, endothelial progenitor cells; MSCs, mesenchymal stem cells; VSELs, very small embryonic-like cells

Almendros I et al. Front. Neurol. 2012 Jul 11;3:112



Gharib SA et al. Sleep. 2010;33(11):1439-46

Table 2 Association between sleep parameters, endothelial progenitor cells, and advanced glycation end-products

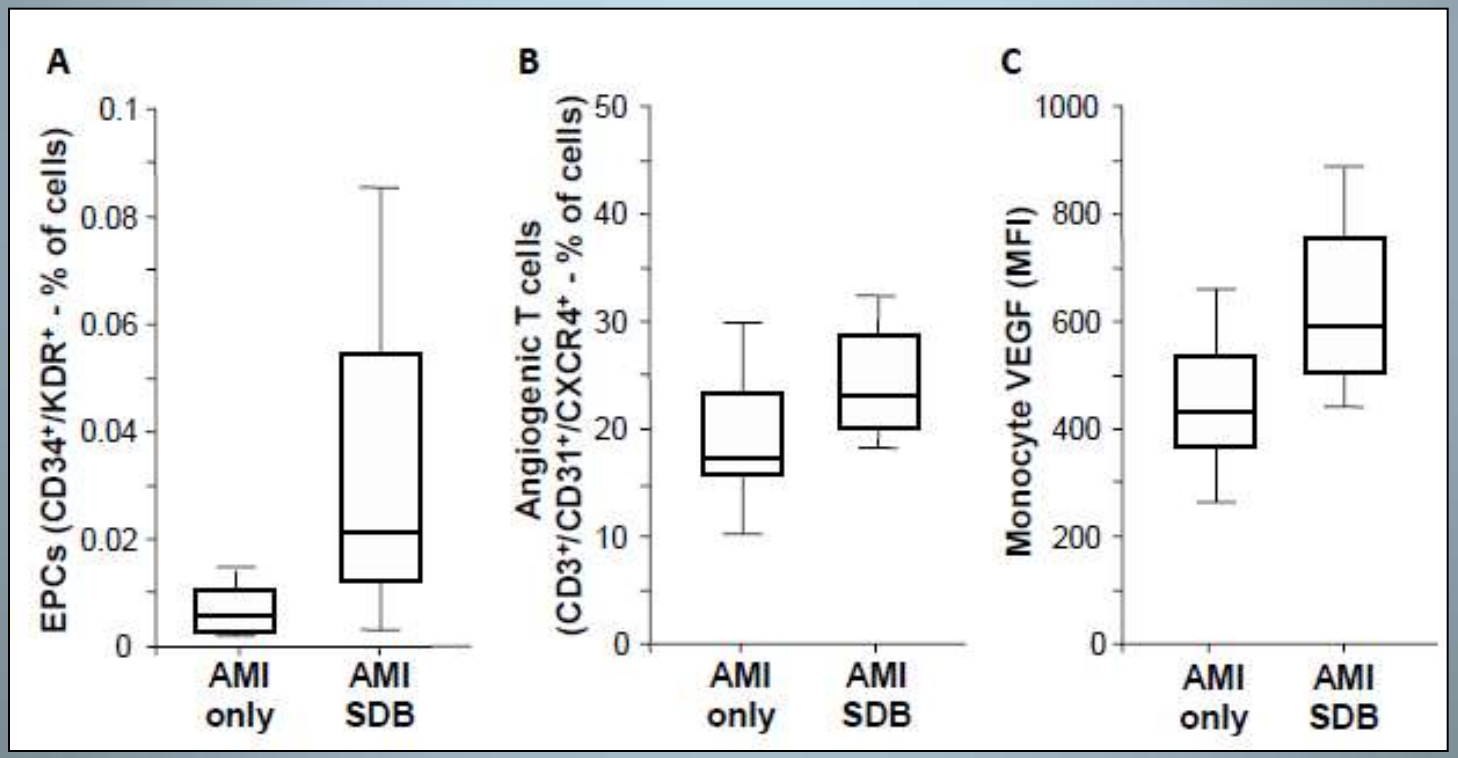
p values (correlation coefficient)	ODI	T90	Min SaO_2	Arousal index	AHI	AGE
CD34+ count	0.041 (0.250)	0.033 (0.261)	0.044 (−0.247)	NS	NS	NS
CD133+ count	NS	NS	NS	0.048 (0.242)	NS	0.021 (−0.281)
CD133 + KDR + count	NS	NS	NS	0.017 (0.291)	NS	NS

Number in bracket = correlation coefficient, *AHI* apnea–hypopnea index, *ODI* oxygen desaturation index, *T90* time with oxygen saturation <90 %, *AGE* advanced glycation end-products, *Min SaO_2* minimal oxygen saturation

Lui MM et al. Sleep Breath. 2013;17:937-942

IAM, SAOS I EPC?

- 40 pacients: 21 pacients sense SAOS i 19 amb SAOS
- Inclusió ~ 5 dies de l'IAM



Berger S et al. Am. J. Respir. Crit. Care Med. 2013 Jan 1;187(1):90-8.

CONCLUSIONS

- Els episodis d'hipòxia/reoxigenació associats a la SAOS poden produir disfunció endotelial per estrès oxidatiu i inflamació vascular.

- Tot i que la SAOS té múltiples efectes negatius a nivell cardiovascular, no tots els pacients amb SAOS desenvoluparan complicacions cardiovasculars.

- Las EPC poden tenir un paper crucial en la protecció del sistema cardiovascular ja que contribueixen al manteniment de la funció endotelial.

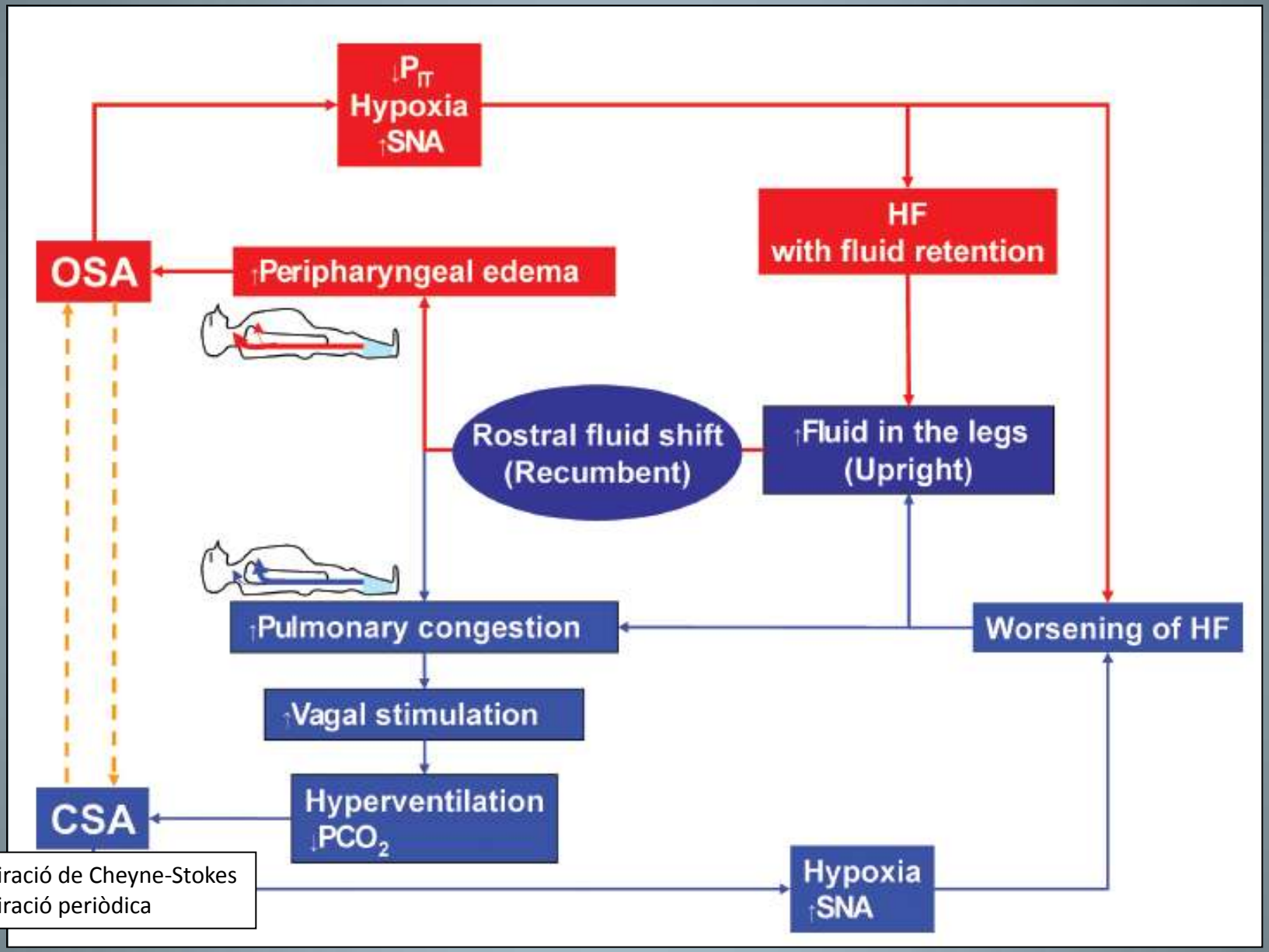
INSUFICIÈNCIA CARDÍACA

PREVALENÇA

- OSA en IC entre 12-53% (població general 5-10%)
- CSA en IC entre 21-37% (població general <1%).

- La prevalença es similar entre FE preservada i deprimida

Kasai T et al. Circulation. 2012;126:1495-1510



Respiració de Cheyne-Stokes
Respiració periòdica

↑ producció metabòlica de pCO2 -> hiperventilació -> ↓ pCO2 per sota el nivell de l'apnea
Relacionada amb l'augment de la pressió d'ompliment de VE

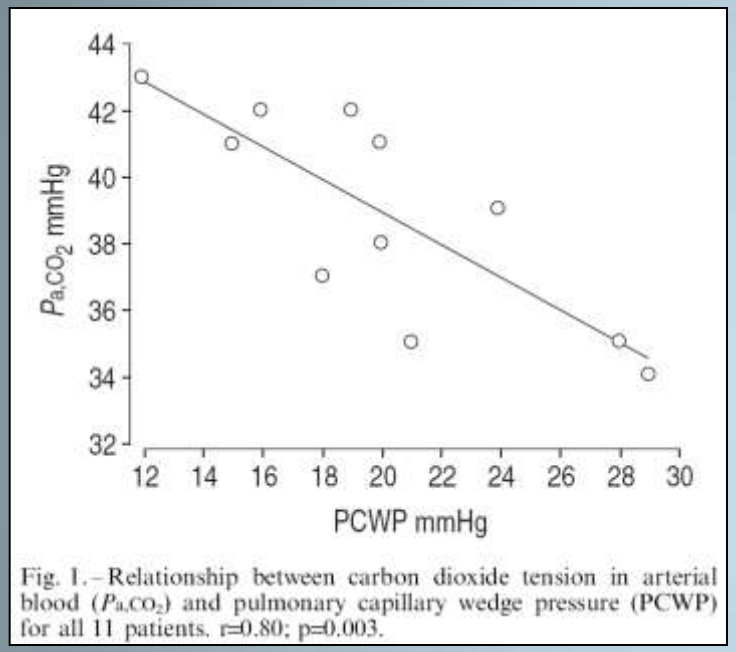


Fig. 1.–Relationship between carbon dioxide tension in arterial blood (P_{a,CO_2}) and pulmonary capillary wedge pressure (PCWP) for all 11 patients. r=0.80; p=0.003.

Lorenzi-Filho G et al. Eur Respir J 2002;19:37-40

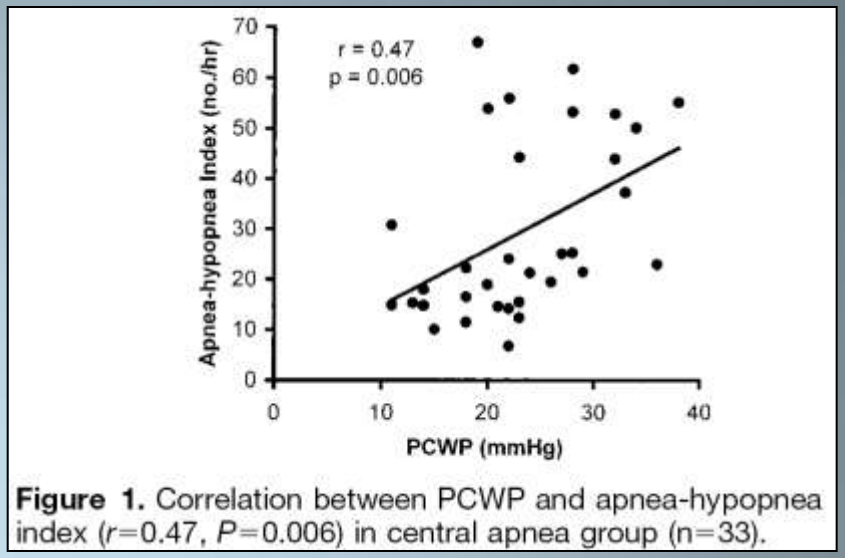
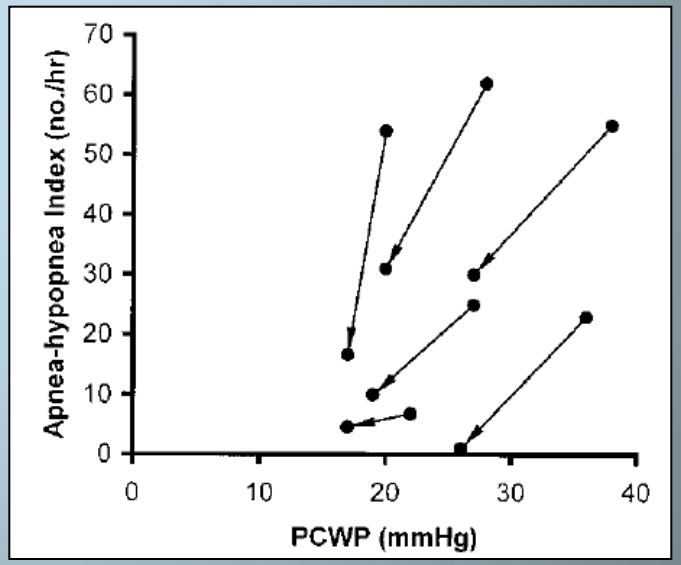
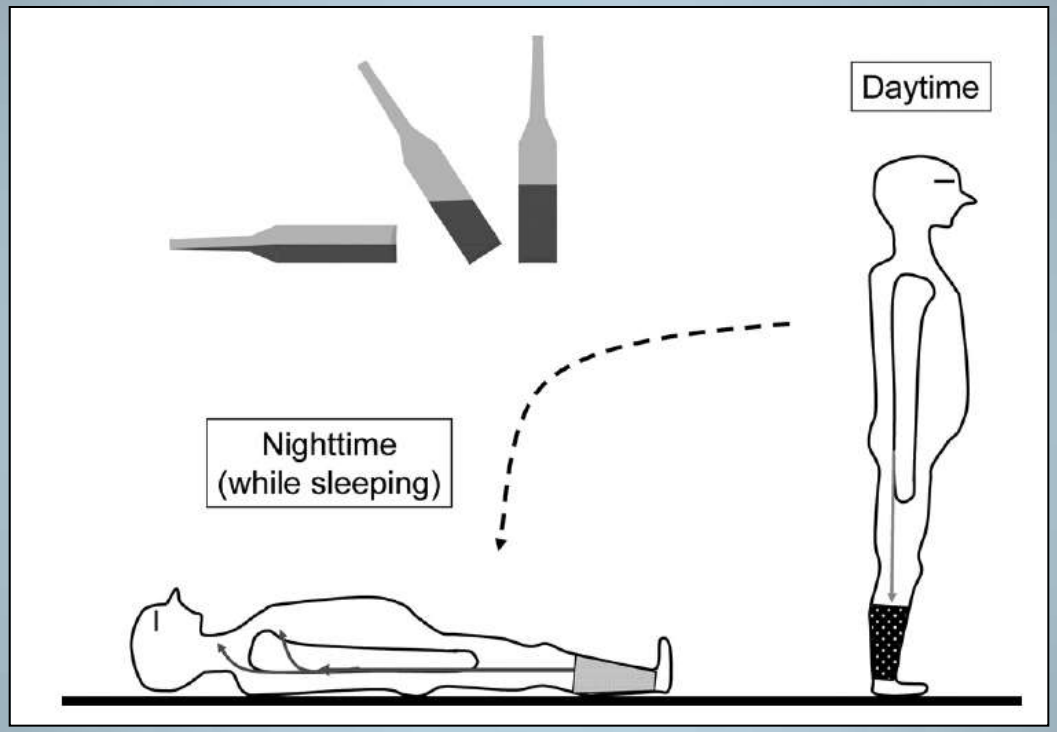


Figure 1. Correlation between PCWP and apnea-hypopnea index (r=0.47, P=0.006) in central apnea group (n=33).



Solin P et al. Circulation 1999;99:1574-1579


Daytime
Nighttime
(while sleeping)

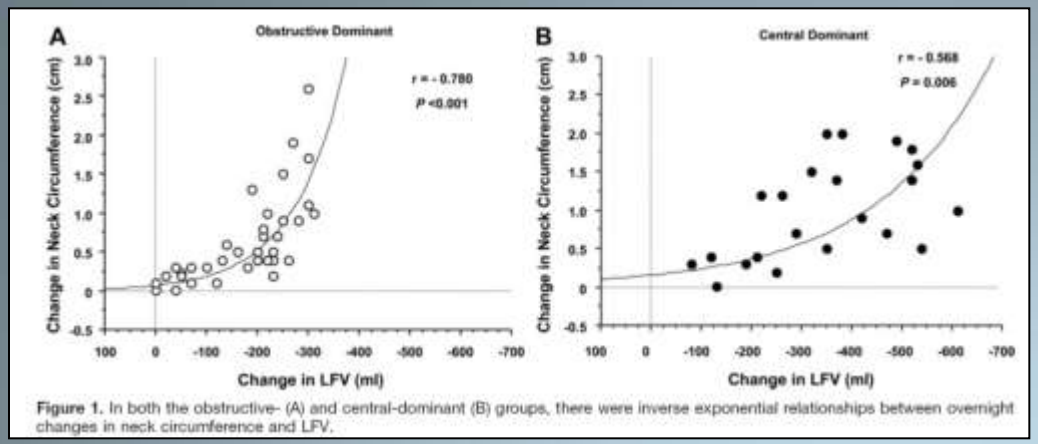
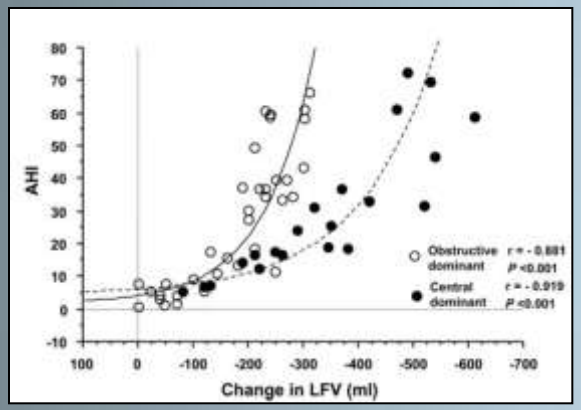
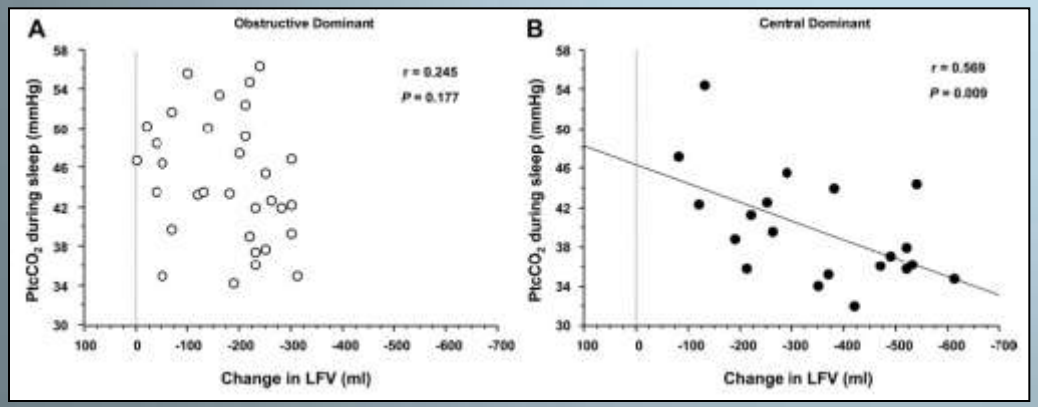
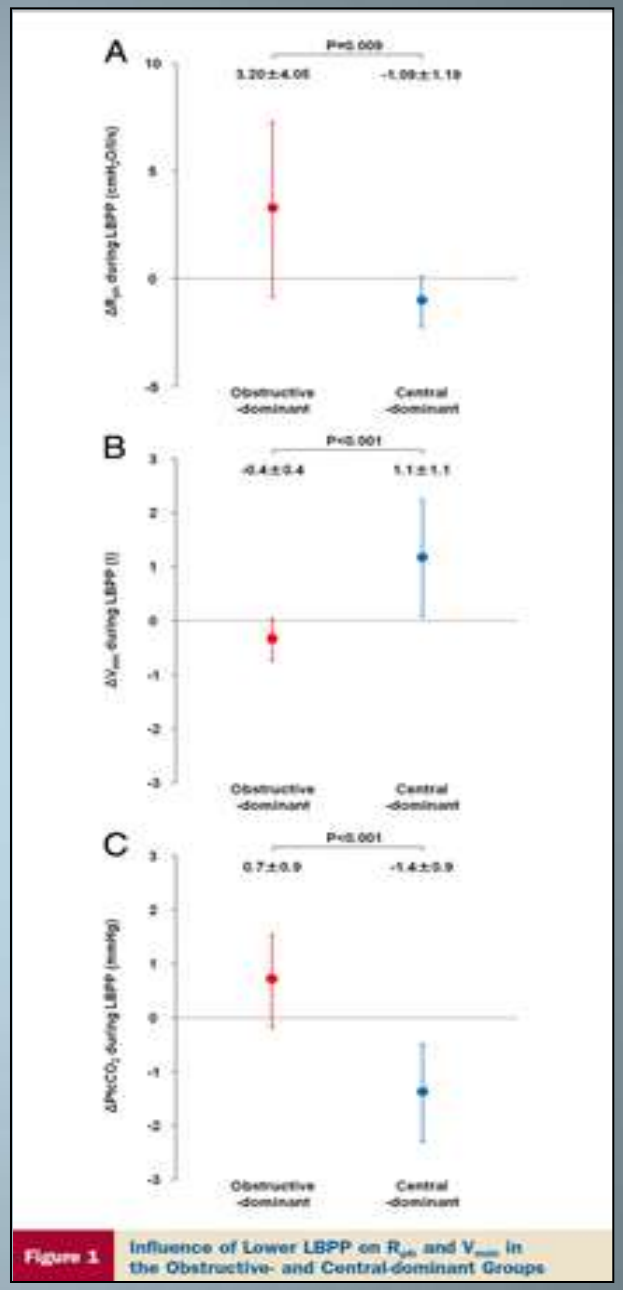


Figure 1. In both the obstructive- (A) and central-dominant (B) groups, there were inverse exponential relationships between overnight changes in neck circumference and LFV.



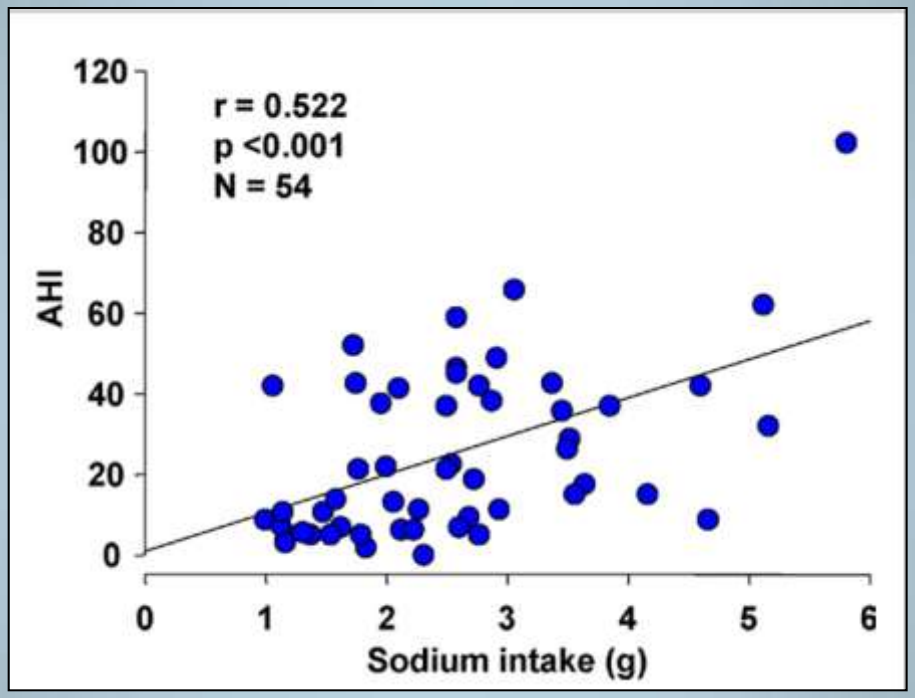
Leg fluid volume





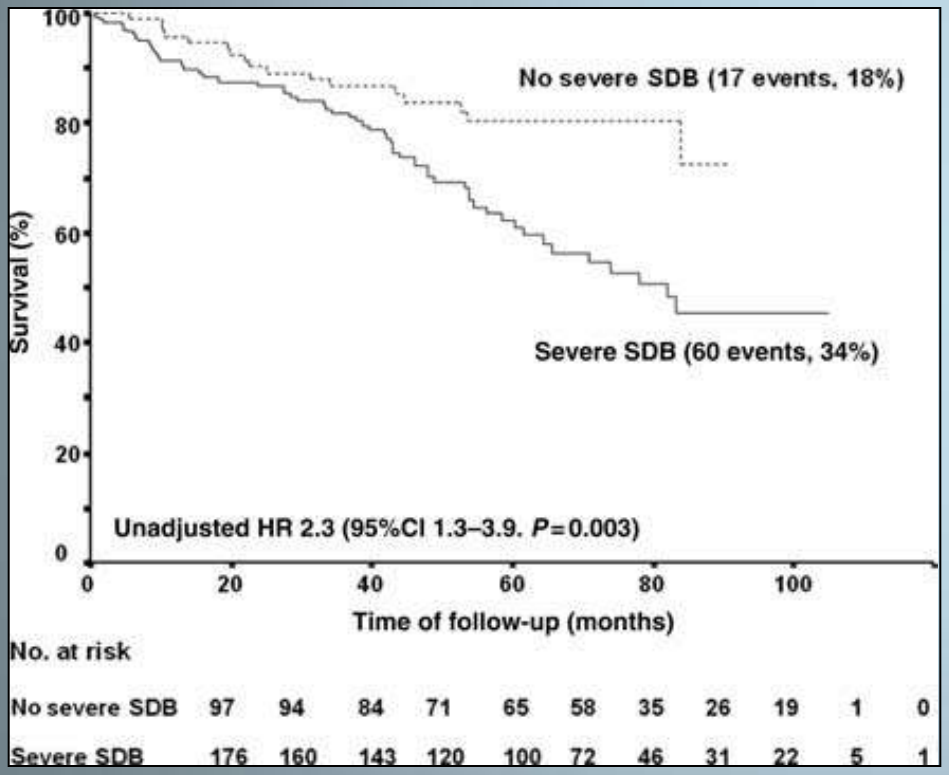
Yumino D et al. Circulation 2010;121:1598-1605

Kasai T et al. J Am Coll Cardiol 2013;61:1157-66

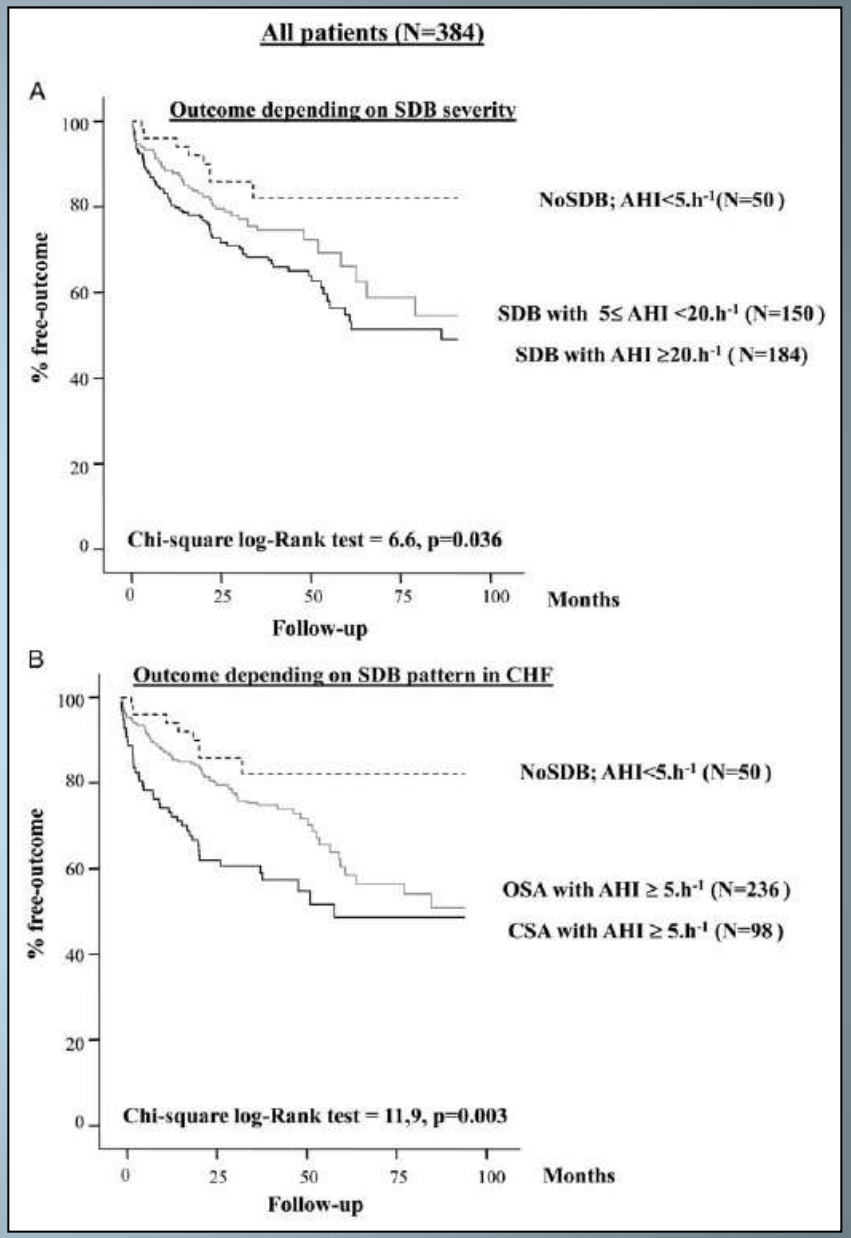


Kasai T et al. J Am Coll Cardiol 2011;58:1970-4

VALOR PRONÒSTIC?



Jilek C et al. European Journal of Heart Failure. 2011;13:68–75



Damy T et al. European Journal of Heart Failure. 2012; 14:1009–1019

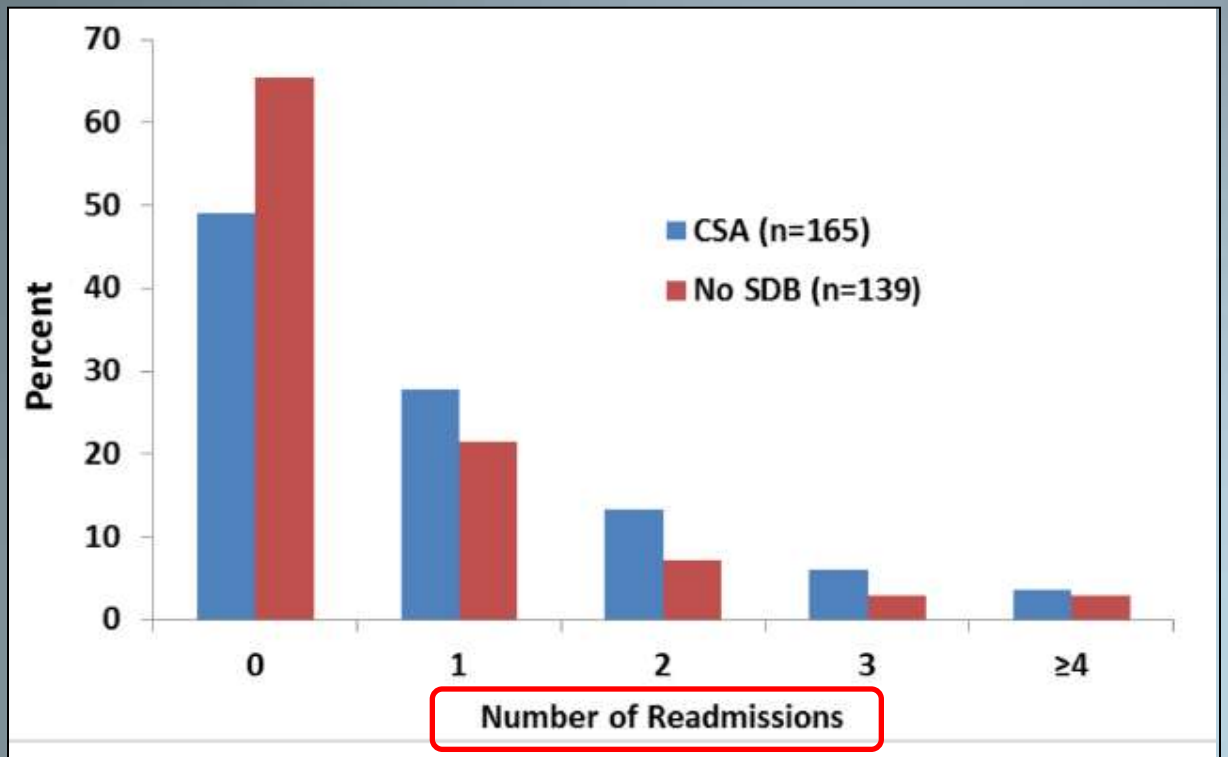


Figure-2. Comparison of Distribution of Cardiac readmissions in 6 months between patients with CSA and patients with no SDB

Distribution of cardiac readmission counts within 6 months; SDB: Sleep Disordered breathing; CSA: central sleep apnea; Note the higher percent of patients readmitted for each count in the CSA group.

Effect of CSA on 6 month Cardiac readmissions

Model	Rate Ratio (confidence interval), p value
Univariable model	1.63 (1.1, 2.4), p=. 01
Multivariable model (adjusted for listed covariates*)	1.53 (1.1, 2.2), p=. 03

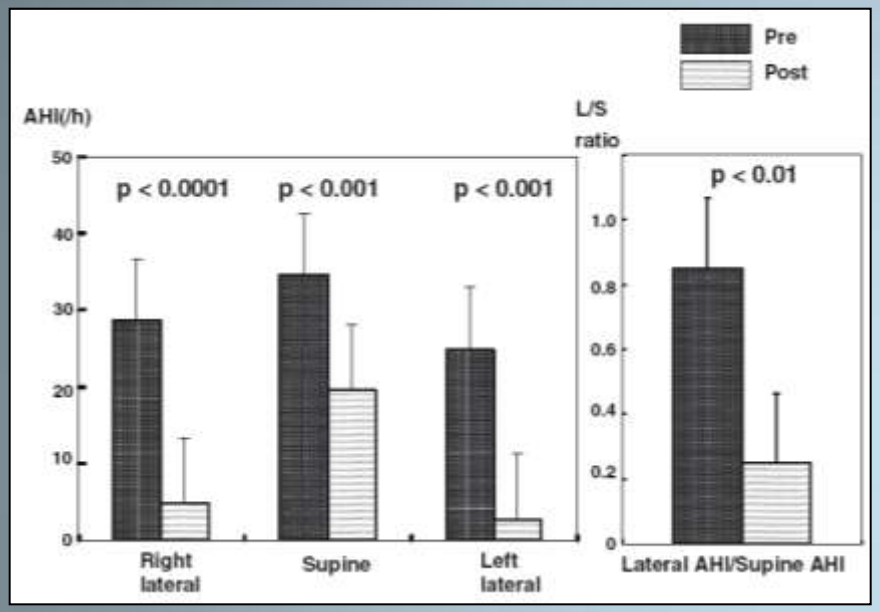
Left ventricular ejection fraction, age, body mass index, sex, creatinine, diabetes, type of cardiomyopathy, coronary artery disease, discharge SBP (<110 vs. 110), discharge angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, discharge beta blocker, initial length of stay, admission sodium, and admission hemoglobin.

Khayat R et al. J Card Fail. 2012;18(7):534-540

TRACTAMENT

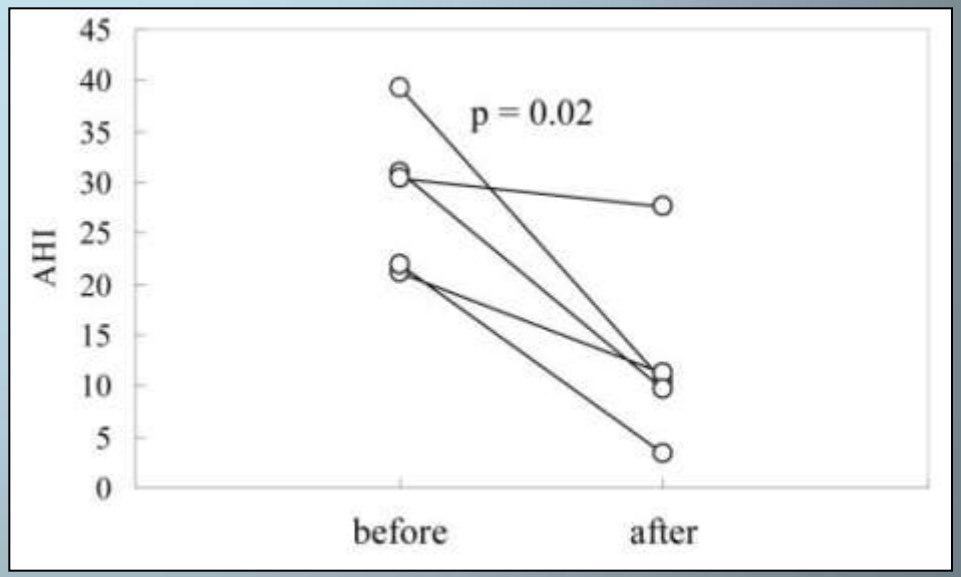
- Optimització del tractament
- CPAP
- Servoventilació
- Altres: estimulació frènica, O2…

OPTIMITZACIÓ DEL TRACTAMENT

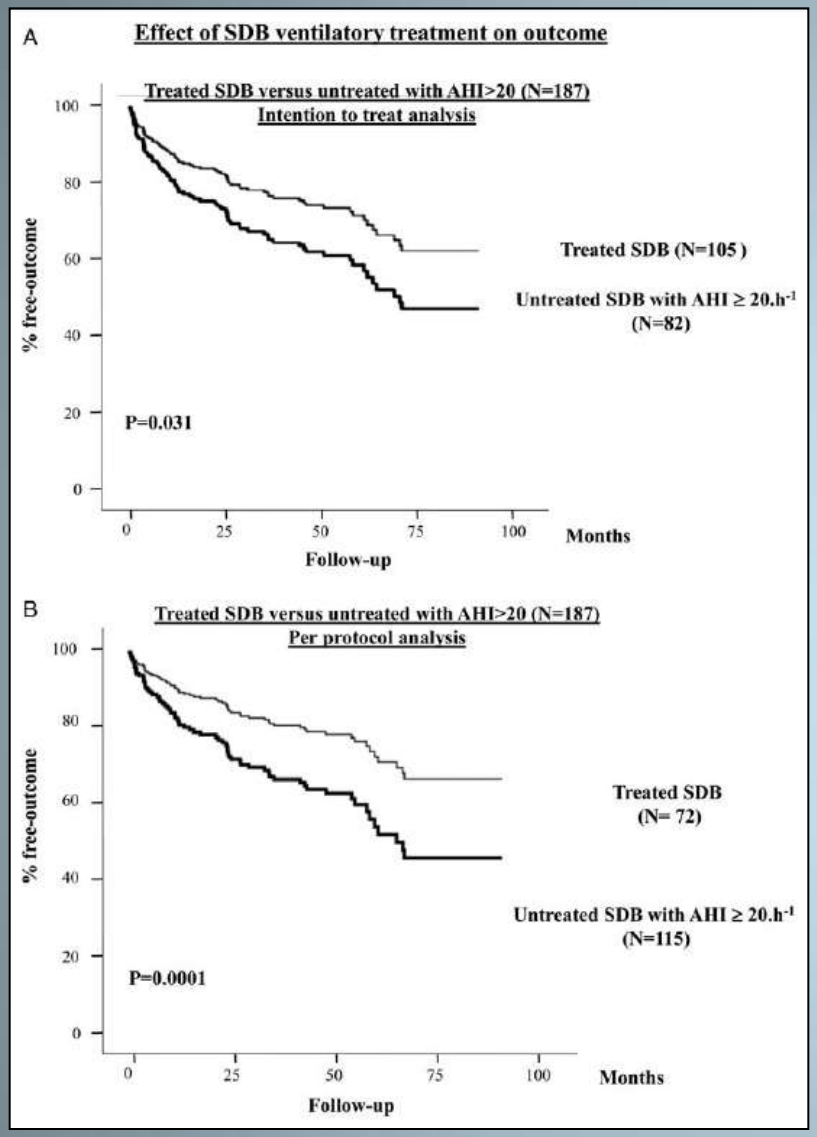


Joho S et al. Sleep Medicine 2010;11:143-148

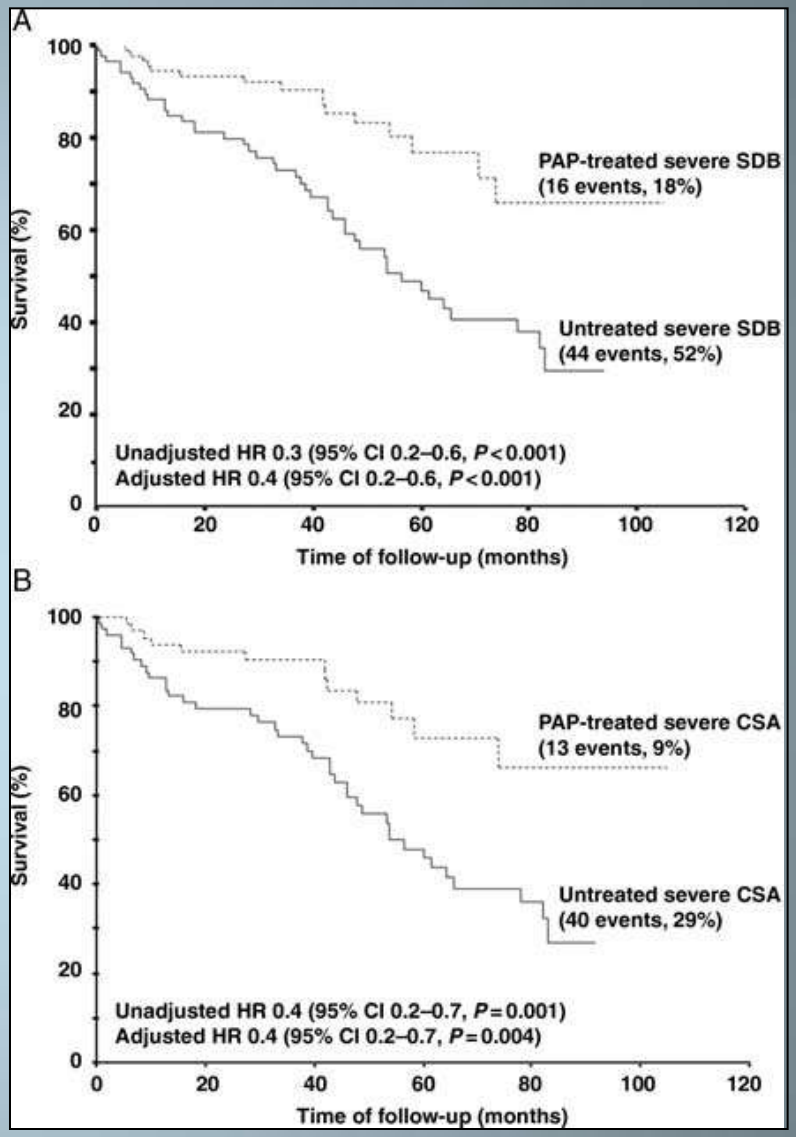
6 mesos de tractament amb carvedilol, n=5



Tamura A et al. Chest 2007;131:130-135



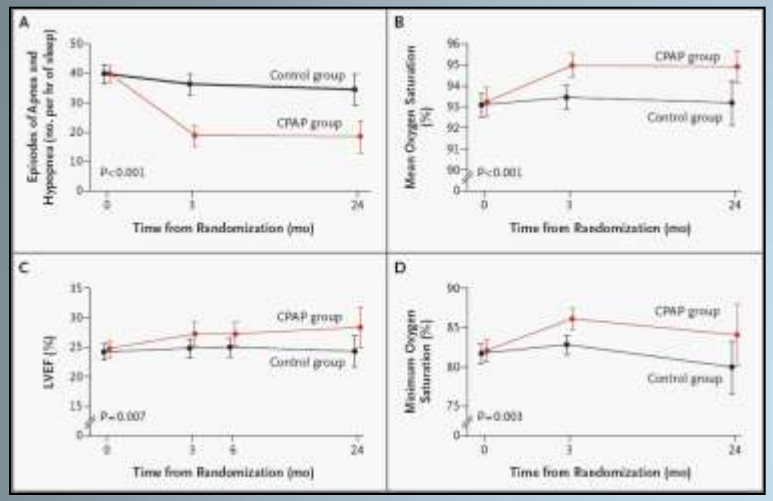
Damy T et al. European Journal of Heart Failure (2012) 14, 1009–1019

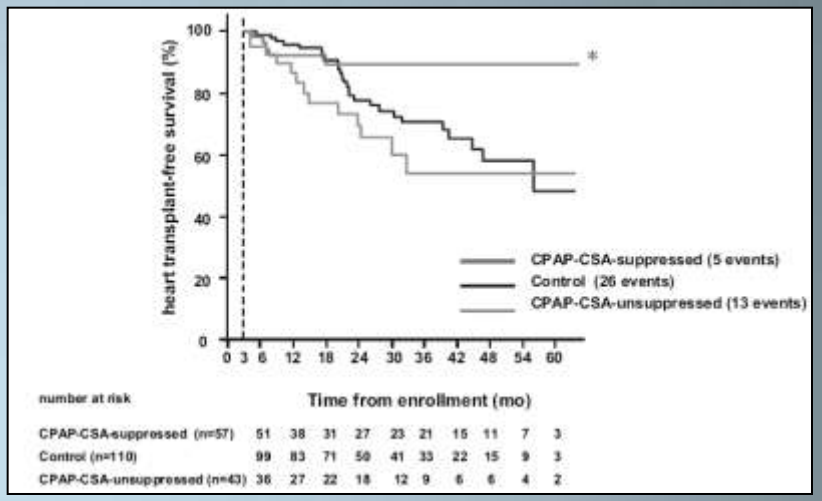


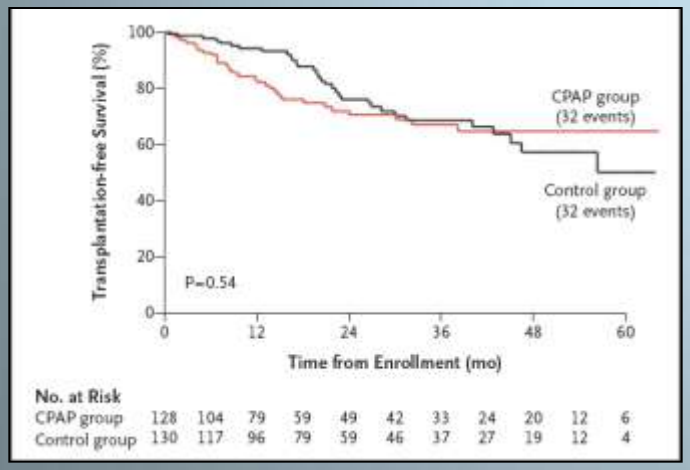
Jilek C et al. European Journal of Heart Failure (2011) 13, 68–75

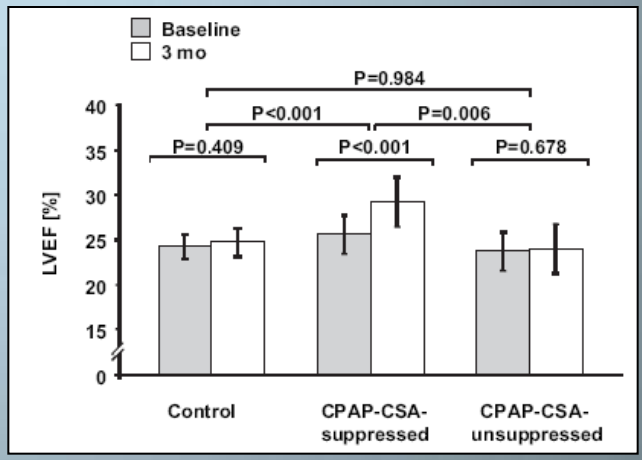
CPAP – APNEA CENTRAL

CANAP estudi randomitzat, 258 p IC i CSA





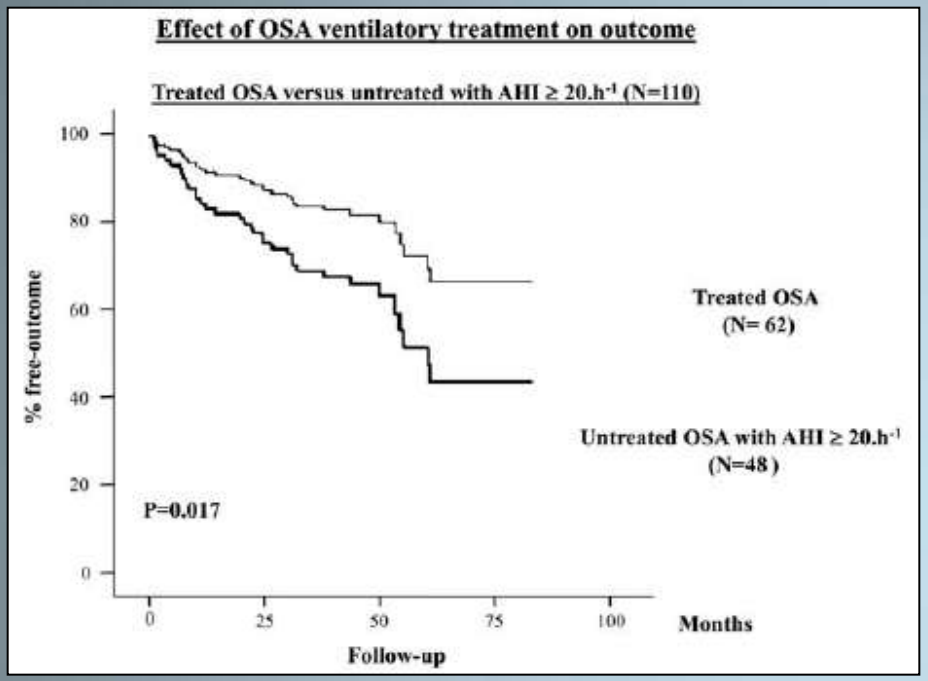




Bradley TD et al. N Engl J Med 2005; 353:2025-2033

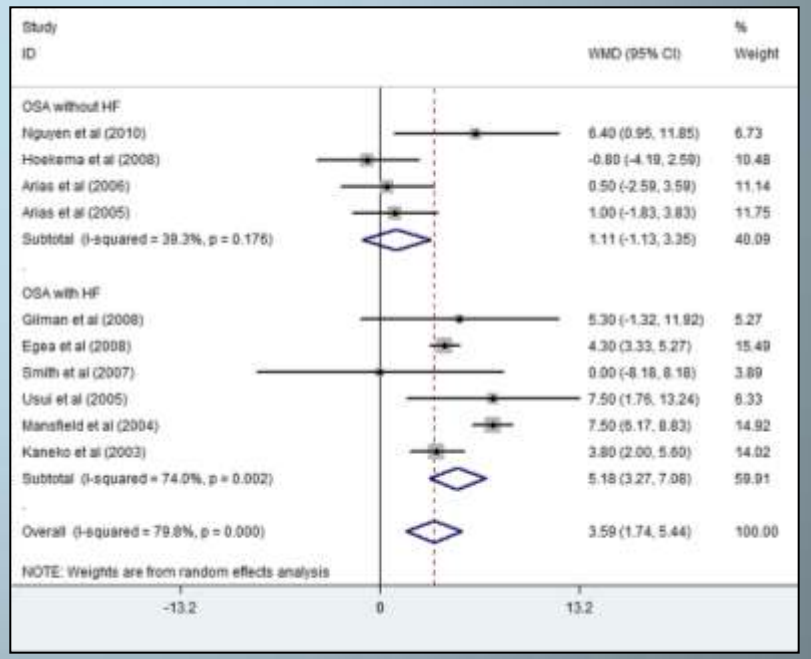
Artz M et al. Circulation. 2007;115:3173-3180

CPAP – APNEA OBSTRUCTIVA



Damy T et al. European Journal of Heart Failure (2012) 14, 1009–1019

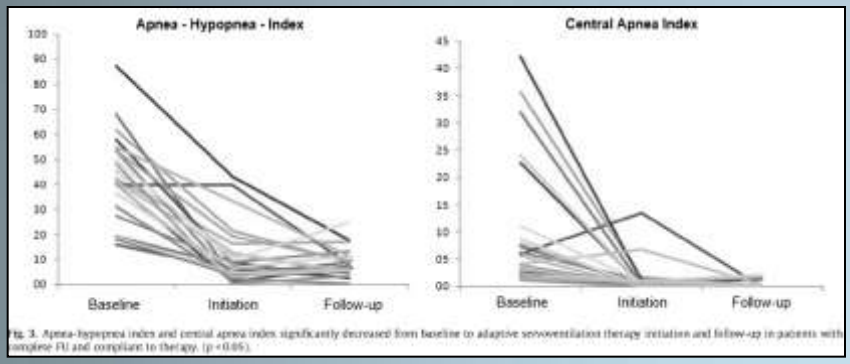
Conclusions: Our meta-analysis supports the notion that CPAP may improve the LVEF among patients with OSA.



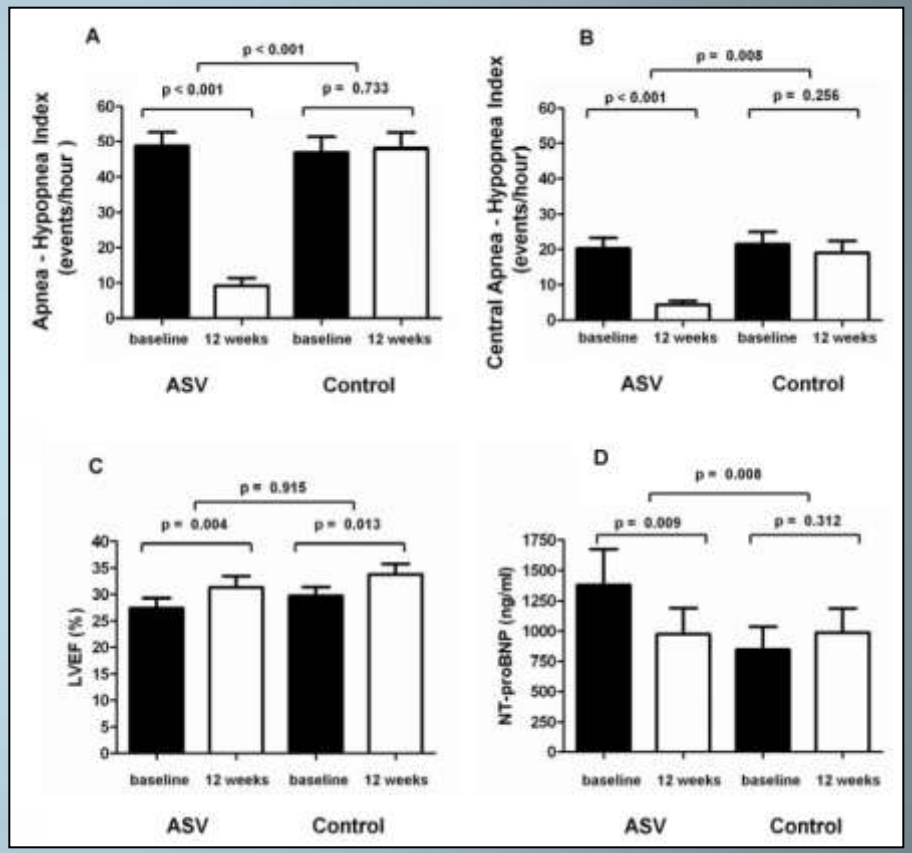
Sun H et al. PLoS One. 2013;1;8(5):e62298

SERVO-VENTILACIÓ

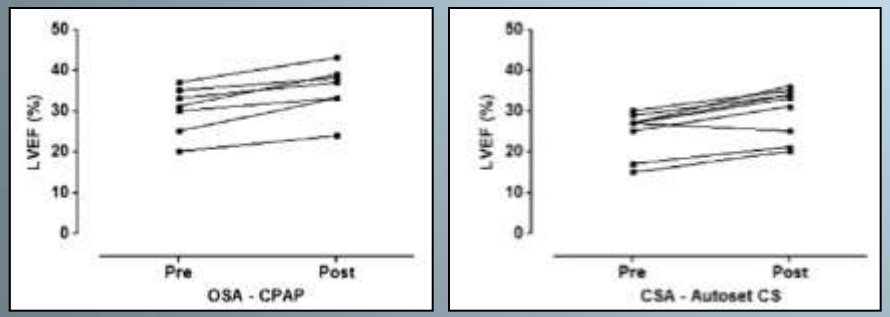
45 pacients. FE Preservada i deprimida



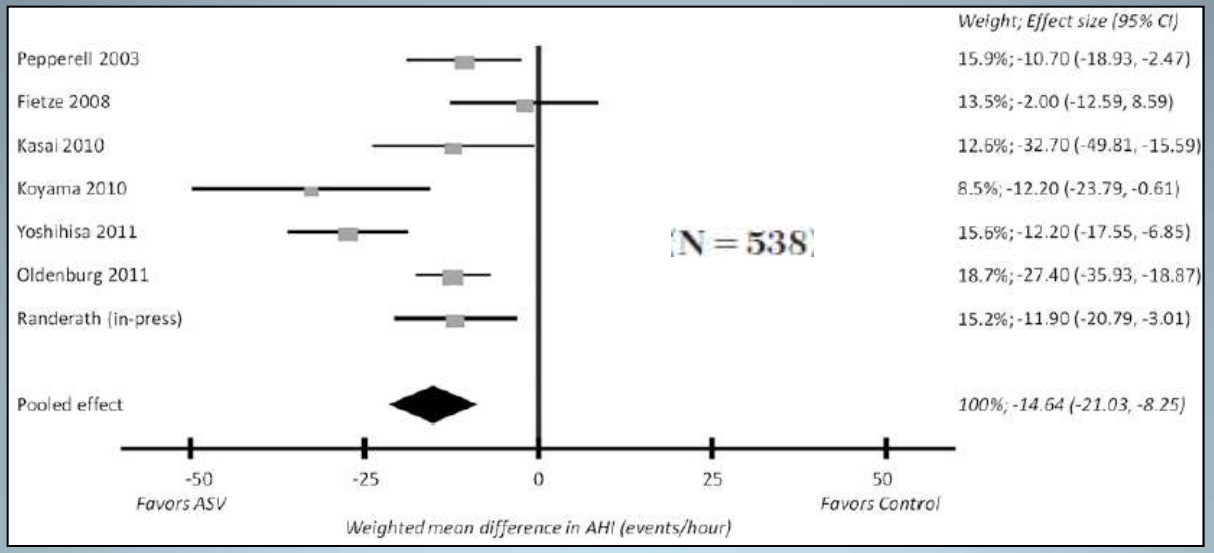
Oldenburg O et al. Sleep Med. 2013 May;14(5):422-7

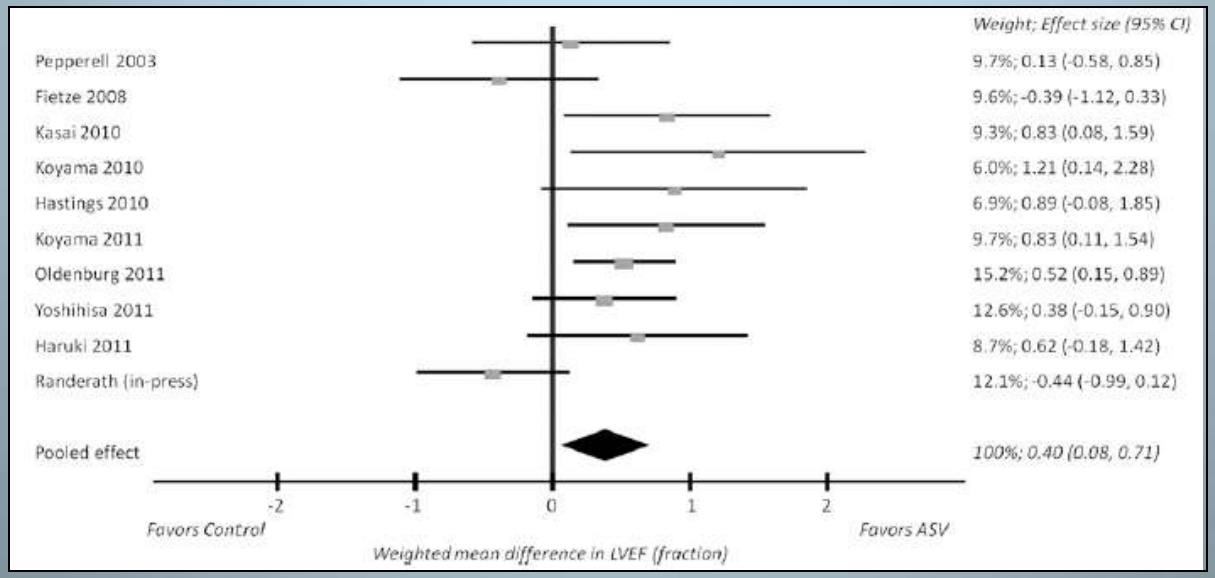


Artz M et al. Eur Respir J Express. Published on December 6, 2012



Kourouklis SP et al. Int J Cardiol. 2013;168(1):157-62





Sharma BK et al. Chest 2012;142(5):1211-1221

FUNCIÓ PRESERVADA

Table 4 Time course of cardiac function by echocardiography

		ASV	Non-ASV	*P*-value
LVEF (%)	Baseline	56.1 ± 7.4	54.0 ± 8.2	0.423
	6 months	61.1 ± 9.9	51.9 ± 9.7	
	Δ	5.1 ± 7.7	−2.0 ± 7.7	0.066
LVMI (g/m^2)	Baseline	144.9 ± 52.6	118.0 ± 30.2	0.071
	6 months	136.6 ± 42.5	155.0 ± 71.9	
	Δ	−8.2 ± 28.6	36.5 ± 74.2	0.023
LAVI (mL/m^2)	Baseline	48.6 ± 25.1	39.9 ± 31.0	0.384
	6 months	42.6 ± 20.4*	49.3 ± 31.2	
	Δ	−6.2 ± 15.1	9.6 ± 16.4	0.023
E/E'	Baseline	12.8 ± 7.1	12.0 ± 5.5	0.692
	6 months	7.1 ± 2.8*	13.1 ± 7.5	
	Δ	−5.8 ± 7.6	1.2 ± 4.8	0.004
MR score	Baseline	1.6 ± 0.9	1.2 ± 1.3	0.298
	6 months	1.0 ± 0.7	1.4 ± 1.3	
	Δ	−0.6 ± 0.6	0.2 ± 0.9	0.087

There were no significant differences in baseline parameters between non-ASV and ASV groups.
*P <0.0125 vs. baseline.
ASV, adaptive servo-ventilation; E/E', ratio of the peak transmitral velocity during early diastole to the peak mitral valve annular velocity during early diastole; LAVI, left atrial volume index; LVMI, left ventricular mass index; MR, mitral regurgitation.

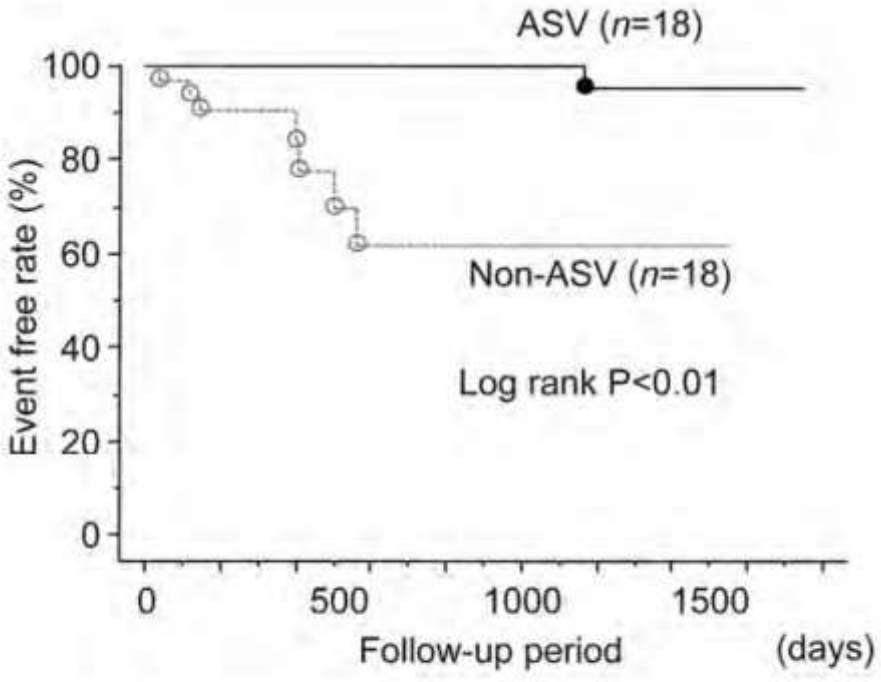
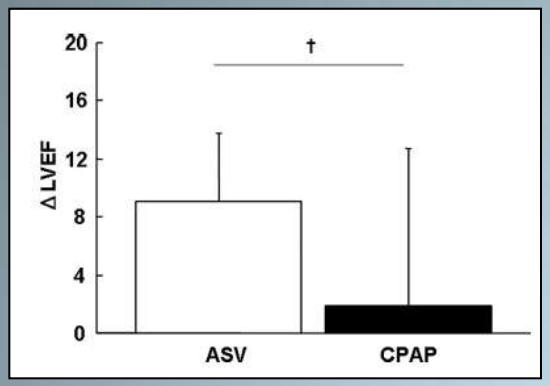
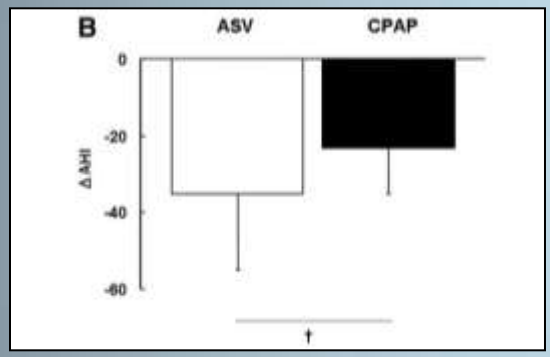


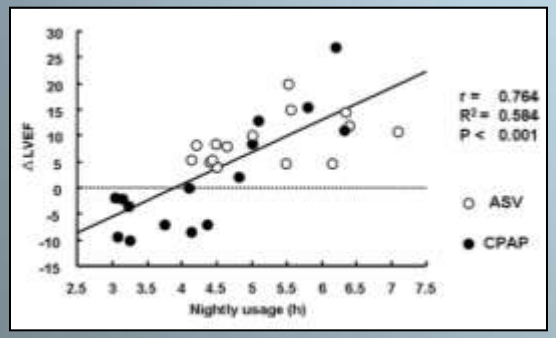
Figure 1 Kaplan–Meier analysis for cardiac events (cardiac death and worsening heart failure) between patients in the adaptive servo-ventilation (ASV) and non-ASV groups.

Yoshihisa A et al. Eur J Heart Fail. 2013;15:543-550

CPAP vs SERVO

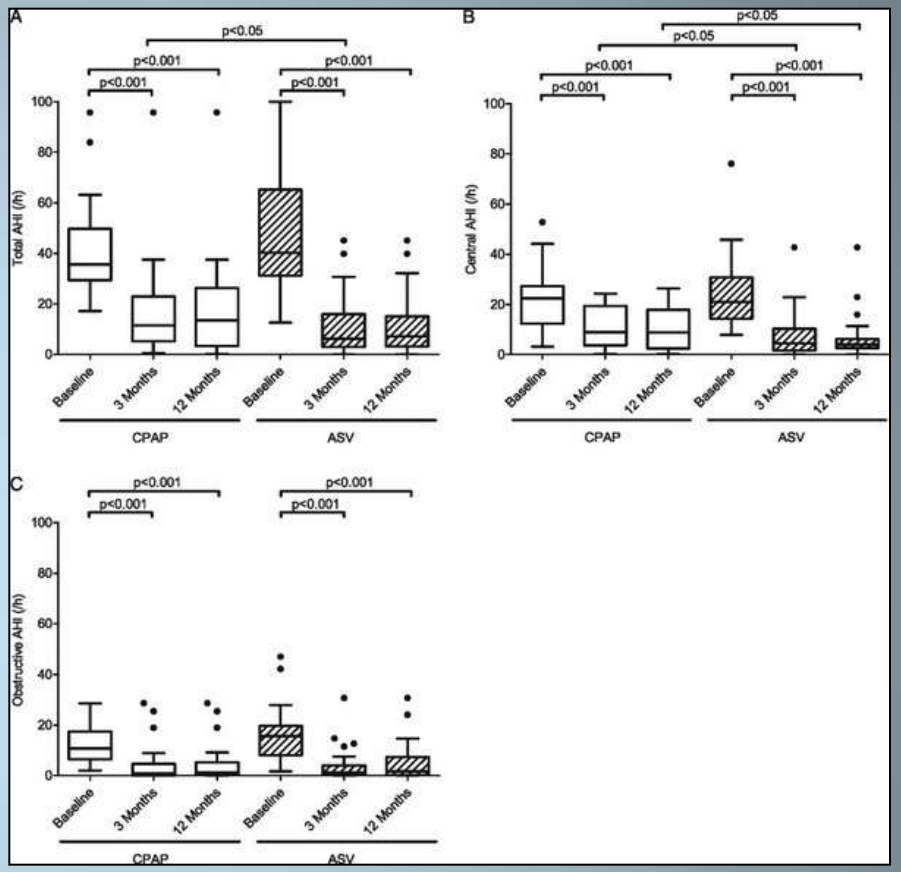






31 pacients amb OSA i CSA randomitzats

Kasai T et al. Circ Heart Failure 2010;3(1): 140-8



71 pacients, randomitzat

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ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012

European Heart Journal (2012) **33**, 1787–1847

11.19 Sleep disturbance and sleep-disordered breathing

Patients with HF frequently have sleep disturbance; the causes are many, including pulmonary congestion (leading to orthopnea and paroxysmal nocturnal dyspnoea) and diuretic therapy causing nocturnal diuresis. Anxiety and other psychological problems can also lead to insomnia, and reviewing sleep history is part of the holistic care of patients with HF (see Section 14). Up to one-third of patients with HF have sleep-disordered breathing.[211,212] Sleep apnoea is of concern in patients with HF because it leads to intermittent hypoxaemia, hypercapnia, and sympathetic excitation. Obstructive sleep apnoea also causes recurrent episodes of negative intrathoracic pressure and increases in LV afterload. It is more common in patients who are obese and whose sleeping partners report that the patient snores or exhibits daytime somnolence (the patient may not be aware of these). However, not all patients with obstructive sleep apnoea are obese. The prevalence of central sleep apnoea (including Cheyne–Stokes respiration) in HF is uncertain and may have declined since the widespread use of beta-blockers and CRT. Screening for and the diagnosis and treatment of sleep apnoea is discussed in detail elsewhere.[211,212] Diagnosis currently requires overnight polysomnography. Nocturnal oxygen supplementation, continuous positive airway pressure, bi-level positive airway pressure, and adaptive servo-ventilation may be used to treat nocturnal hypoxaemia.

15.2 Co-morbidity

The long-term safety and efficacy of many treatments for co-morbidities are unknown, but are of great interest and importance.

Anaemia—erythropoiesis-stimulating agents, iron?

Depression—selective serotonin reuptake inhibitors, cognitive therapy?

Diabetes—metformin, GLP-1 agonists/analogues, DPP IV inhibitors, SGLT-2 inhibitors?

Sleep-disordered breathing—positive airways pressure therapies?

2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

Clyde W. Yancy, Mariell Jessup, Biykem Bozkurt, Javed Butler, Donald E. Casey, Jr, Mark H. Drazner, Gregg C. Fonarow, Stephen A. Geraci, Tamara Horwich, James L. Januzzi, Maryl R. Johnson, Edward K. Kasper, Wayne C. Levy, Frederick A. Masoudi, Patrick E. McBride, John J.V. McMurray, Judith E. Mitchell, Pamela N. Peterson, Barbara Riegel, Flora Sam, Lynne W. Stevenson, W.H. Wilson Tang, Emily J. Tsai and Bruce L. Wilkoff

Circulation. 2013;128:e240-e327; originally published online June 5, 2013; doi: 10.1161/CIR.0b013e31829e8776

7.3.1.4. Treatment of Sleep Disorders: Recommendation

Class IIa

1. **Continuous positive airway pressure can be beneficial to increase LVEF and improve functional status in patients with HF and sleep apnea.[393–396] *(Level of Evidence: B)***

Sleep disorders are common in patients with HF. A study of adults with chronic HF treated with evidence-based therapies found that 61% had either central or obstructive sleep apnea.[397] Despite having less sleep time and sleep efficiency compared with those without HF, patients with HF, including those with documented sleep disorders, rarely report excessive daytime sleepiness.[398] Thus, a high degree of suspicion for sleep disorders should be maintained for these patients. The decision to refer a patient to a sleep study should be based on clinical judgment.

The primary treatment for obstructive sleep apnea is nocturnal continuous positive airway pressure. In a major trial, continuous positive airway pressure for obstructive sleep apnea was effective in decreasing the apnea–hypopnea index, improving nocturnal oxygenation, increasing LVEF, lowering norepinephrine levels, and increasing the distance walked in 6 minutes; these benefits were sustained for up to 2 years.[394] Smaller studies suggest that continuous positive airway pressure can improve cardiac function, sympathetic activity, and HRQOL in patients with HF and obstructive sleep apnea.[395,396]

See Online Data Supplement 15 for additional data on the treatment of sleep disorders.

CONCLUSIONS

- L'apnea del son en pacients amb insuficiència cardíaca és freqüent i s'associa a pitjor pronòstic.
- Els pacients presenten tant apnea central com obstructiva, i ambdós s'associen amb efectes deleteris sistèmics.
- El diagnòstic d'aquesta patologia és complex ja que precisa de polisomnografia a l'hospital.
- L'optimització del tractament és la base del tractament en l'apnea central
- La CPAP és d'elecció en pacients amb apnea obstructiva, mentre que en pacients amb apnea central es beneficien de la servo-ventilació (tot i que la CPAP també és útil)
- Per ara, les guies de pràctica clínica no recomanen el seu estudi ni tractament.

GRÀCIES PER L'ATENCIÓ