AIAC

Associazione Italiana Aritmologia e Cardiostimolazione

CORSI TEORICO-PRATICI

Sleep Apnea 2020

Scompenso cardiaco ed apnea notturna

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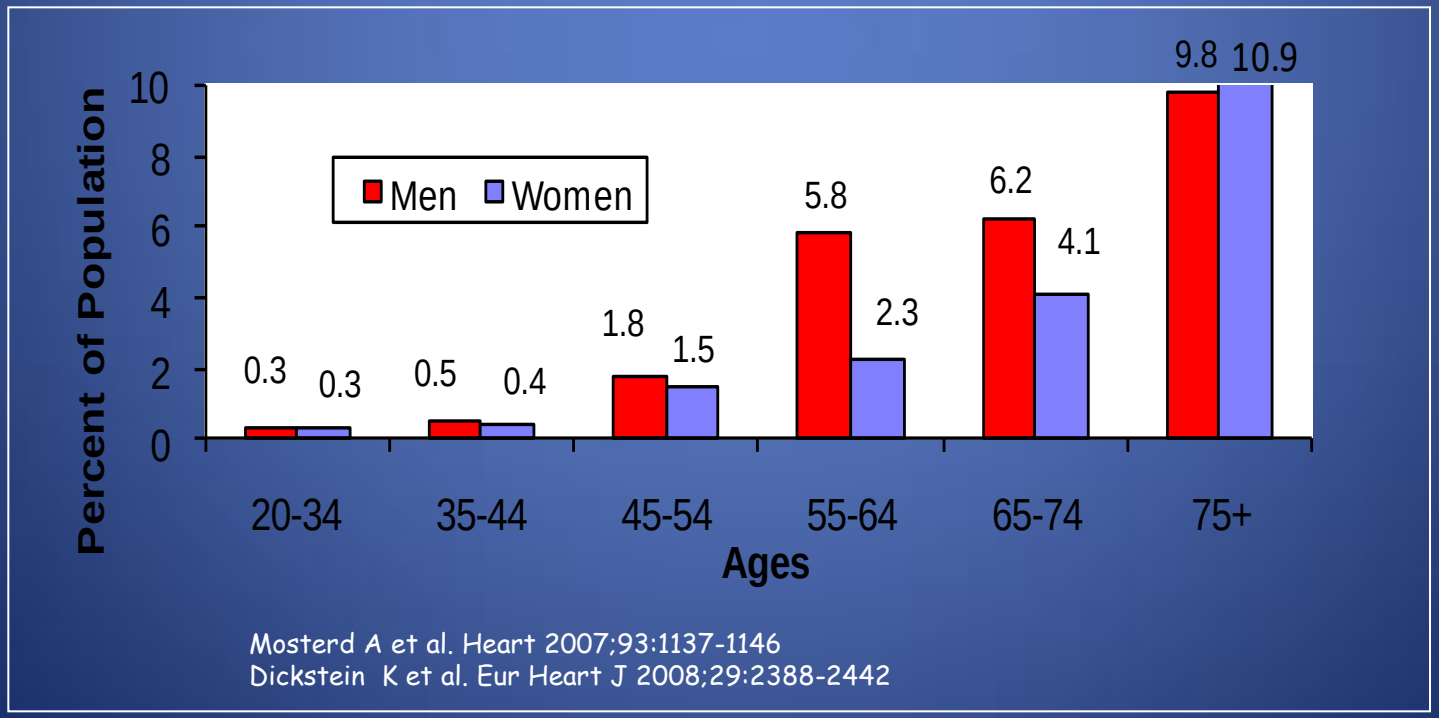
U.O.C. Cardiologia-UTC

Azienda Ospedaliera- Cosenza -

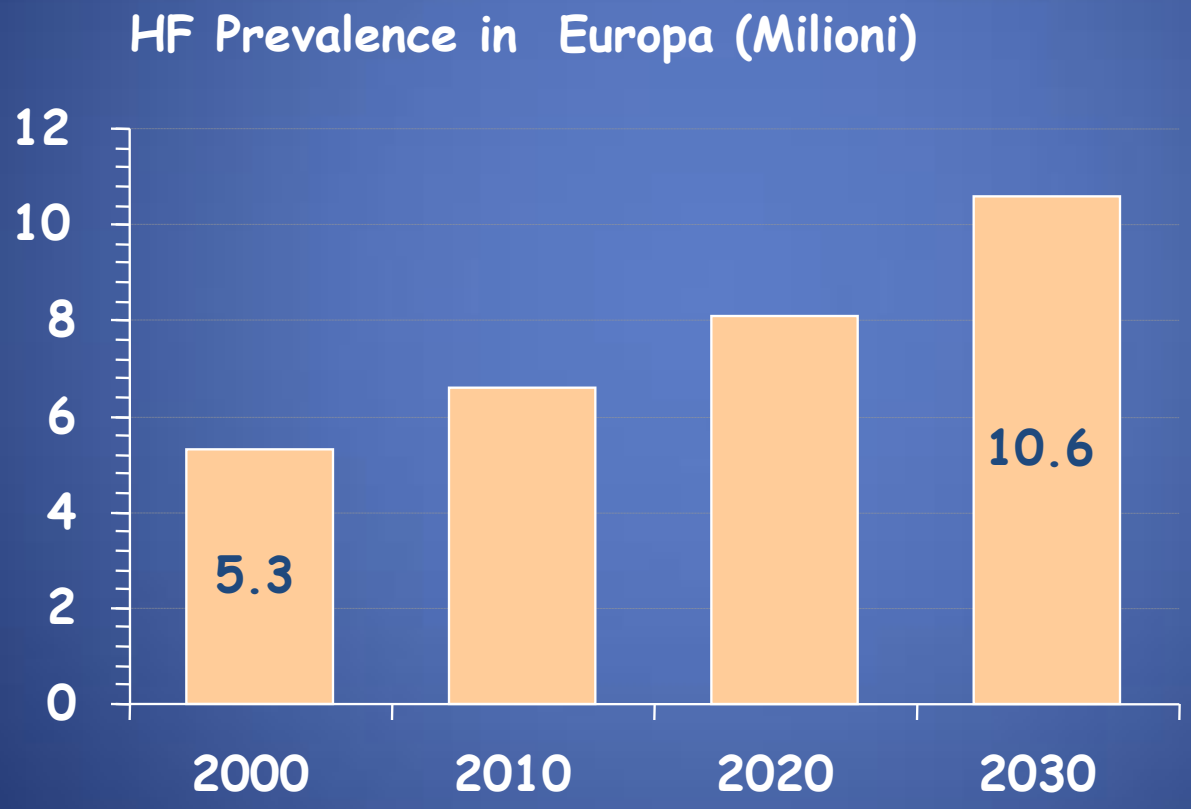
Heart failure – key facts

- Prevalence in total population 2-3%, among 70- to 80-year-old people between 10% and 20%
- Cause of 5% of acute hospital admissions
- Present in 10% of patients in hospital beds
- Economic burden: 2% of national expenditure on health
- Mortality within 5 years after diagnosis of CHF= 50%



Mosterd A et al. Heart 2007;93:1137-1146
Dickstein K et al. Eur Heart J 2008;29:2388-2442

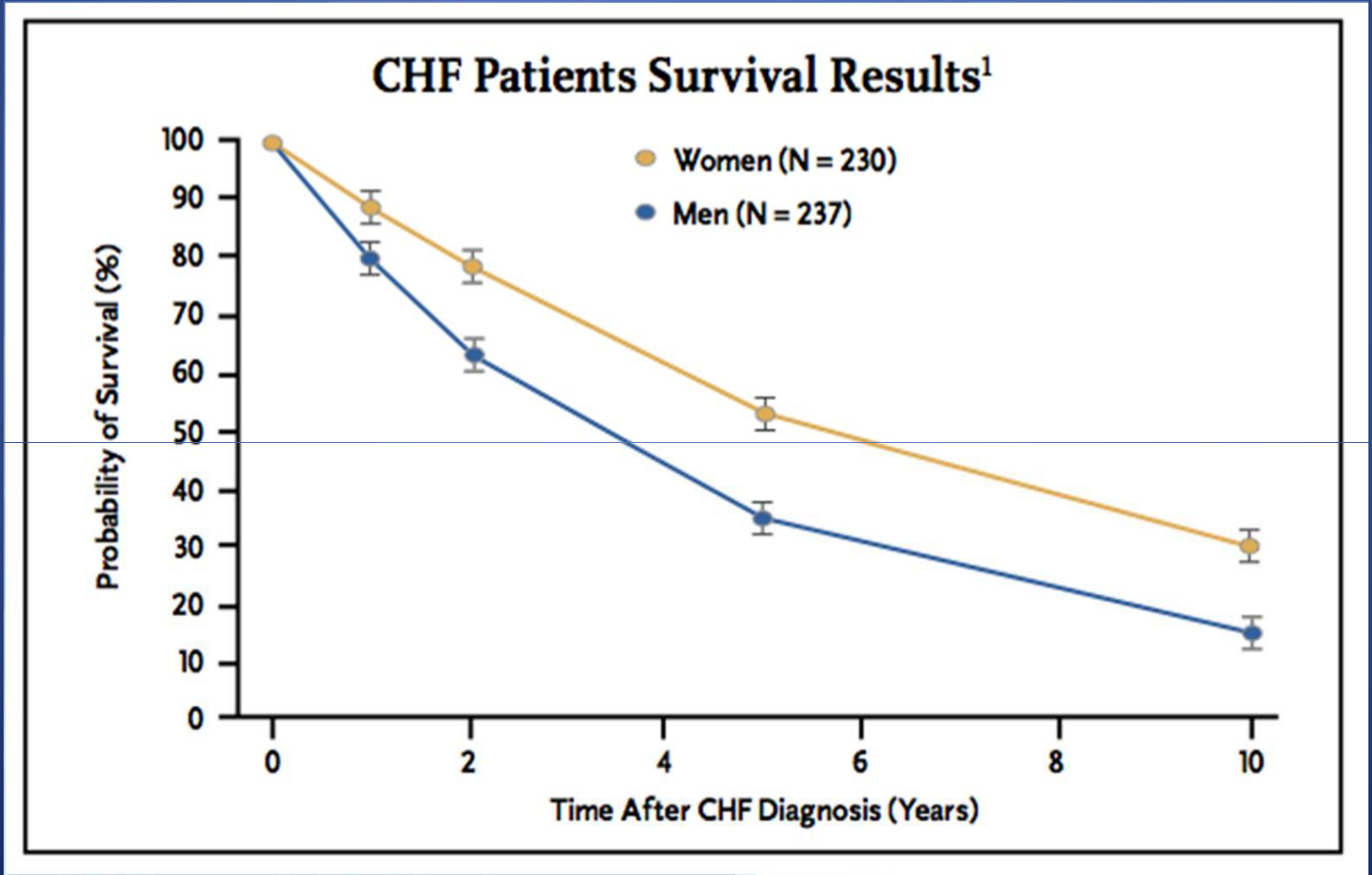
Prevalenza dello scompenso cardiaco è in costante aumento



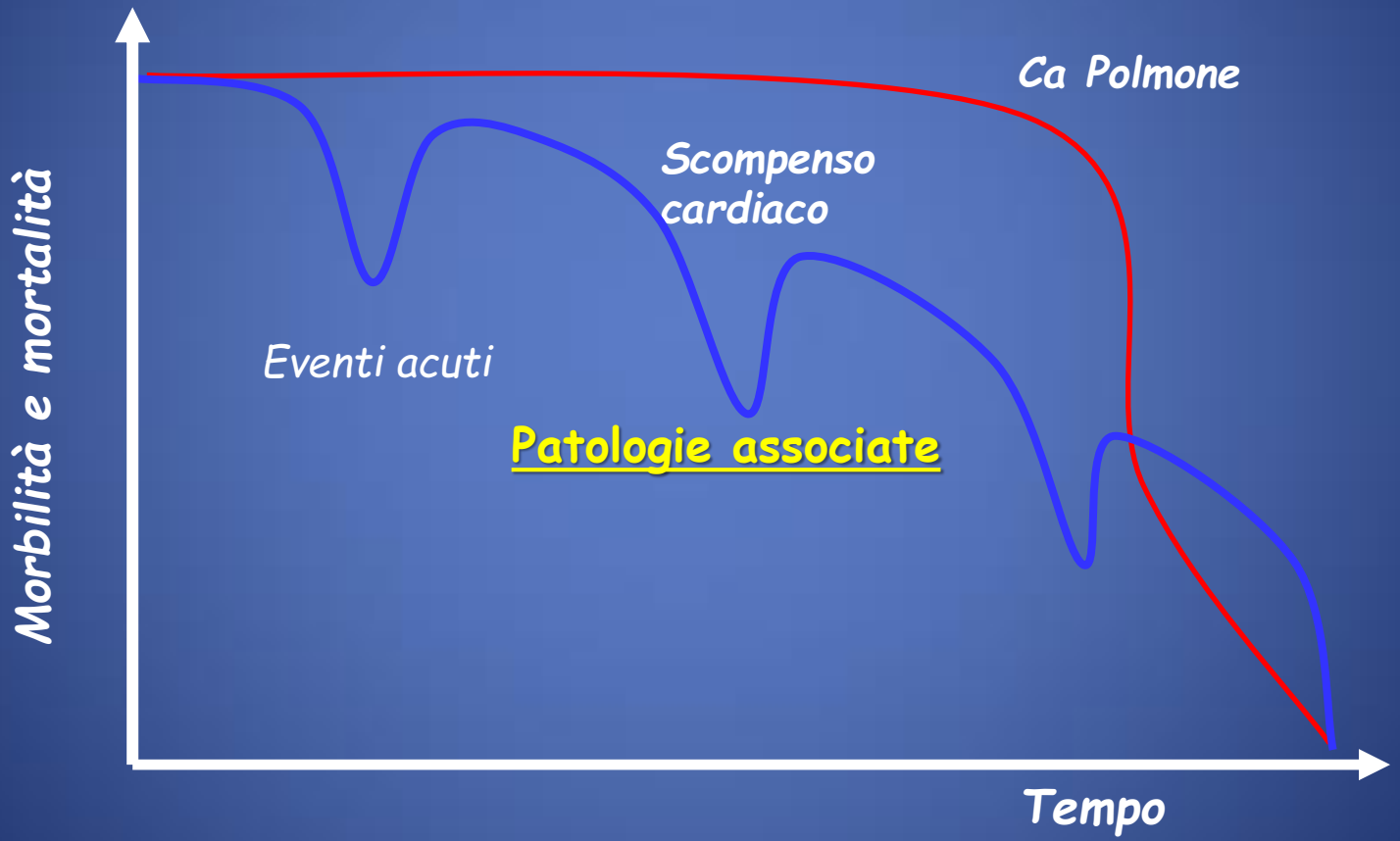
- Aumento eta' media
- Gestione della fase acuta

Source: New Medicine Reports 1997 ; 1999 Heart and Stroke Statistical Update, AHA

Prognosi


CHF Patients Survival Results[1]
Women (N = 230)
Men (N = 237)
Probability of Survival (%)
100
90
80
70
60
50
40
30
20
10
0
0
2
4
6
8
10
Time After CHF Diagnosis (Years)

Progressione



- Patients with almost all forms of cancer have a much better survivals

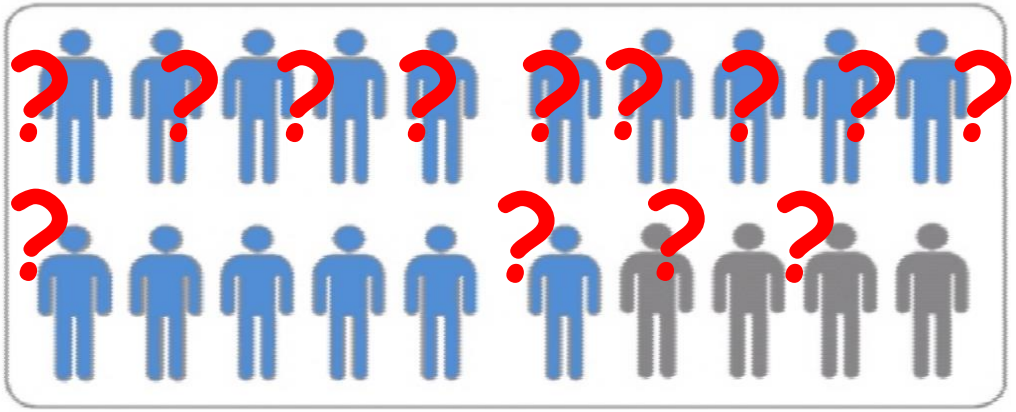
Source: More 'malignant" than cancer? Five-year survival following a first admission for heart failure. Eur J Heart Failure 2001; 3:315-22

Quesito

- Qual è quella "patologia associata"che ha una prevalenza fino all' 70% **nella popolazione con Scompenso Cardiaco (HF)** (di cui circa l' **80% non diagnosticata**) con pesanti ricadute clinico-prognostiche ?

Maggiore rischio di FA e di SCD nella popolazione ICD e CRT

Maggiore mortalità e complicanze con HF



Risposta: la Sleep Apnea

- **Sleep Apnea: Interruzione della respirazione durante il sonno**

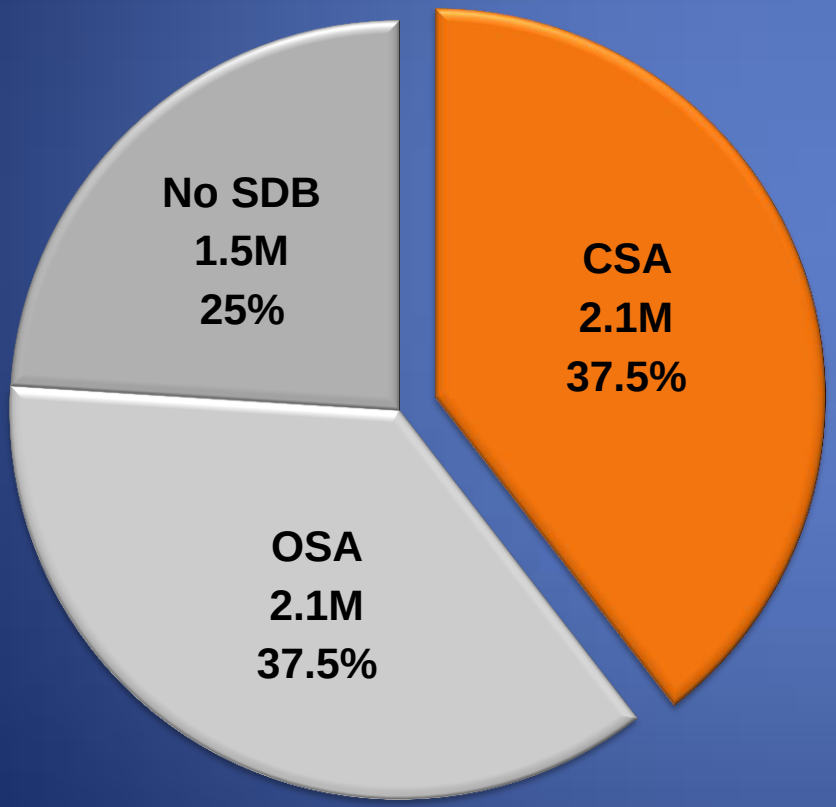
Sleep Apnea Centrale (CSA): Il cervello smette di dare il segnale di respirare

Sleep Apnea Ostruttiva (OSA): Ostruzione delle vie aeree superiori

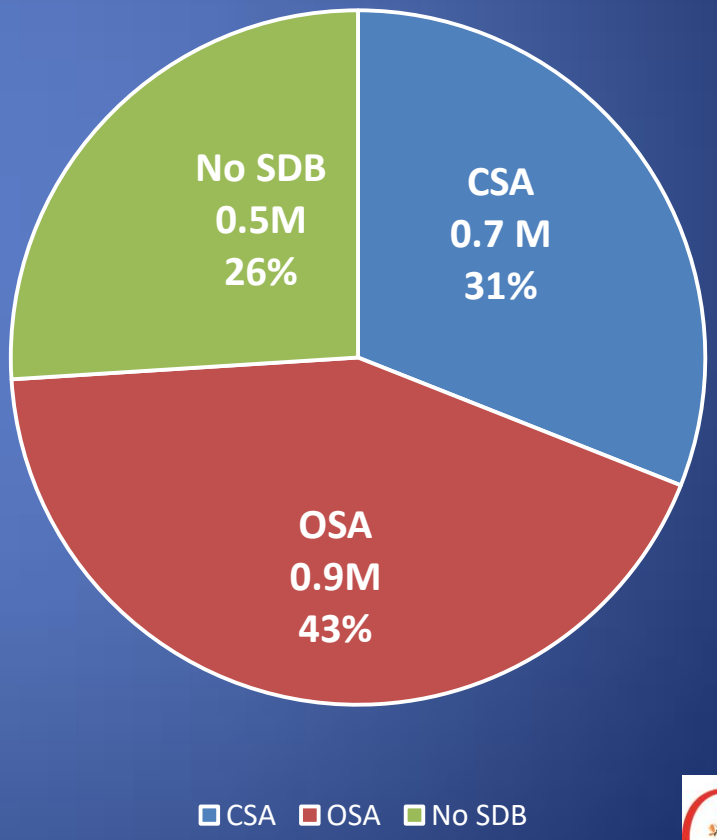
- **Hypopnea: Riduzione della respirazione piuttosto che interruzione completa**
- **Sleep Disorder Breathing (SDB)**
- **Sleep Apnea Syndrome (SAS)**

Central Sleep Apnea is Common in Heart Failure and Atrial Fibrillation Patients

United States
Heart Failure Population
5.7 Million

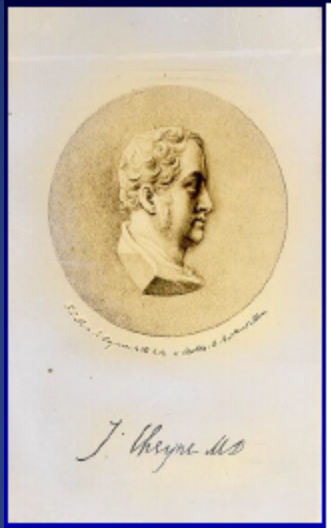


United States
Atrial Fibrillation Population
2.1 Million



Roger et al. Circulation 2011;123:e18-209
Oldenburg et al. Eur J Heart Fail;20079:251-7

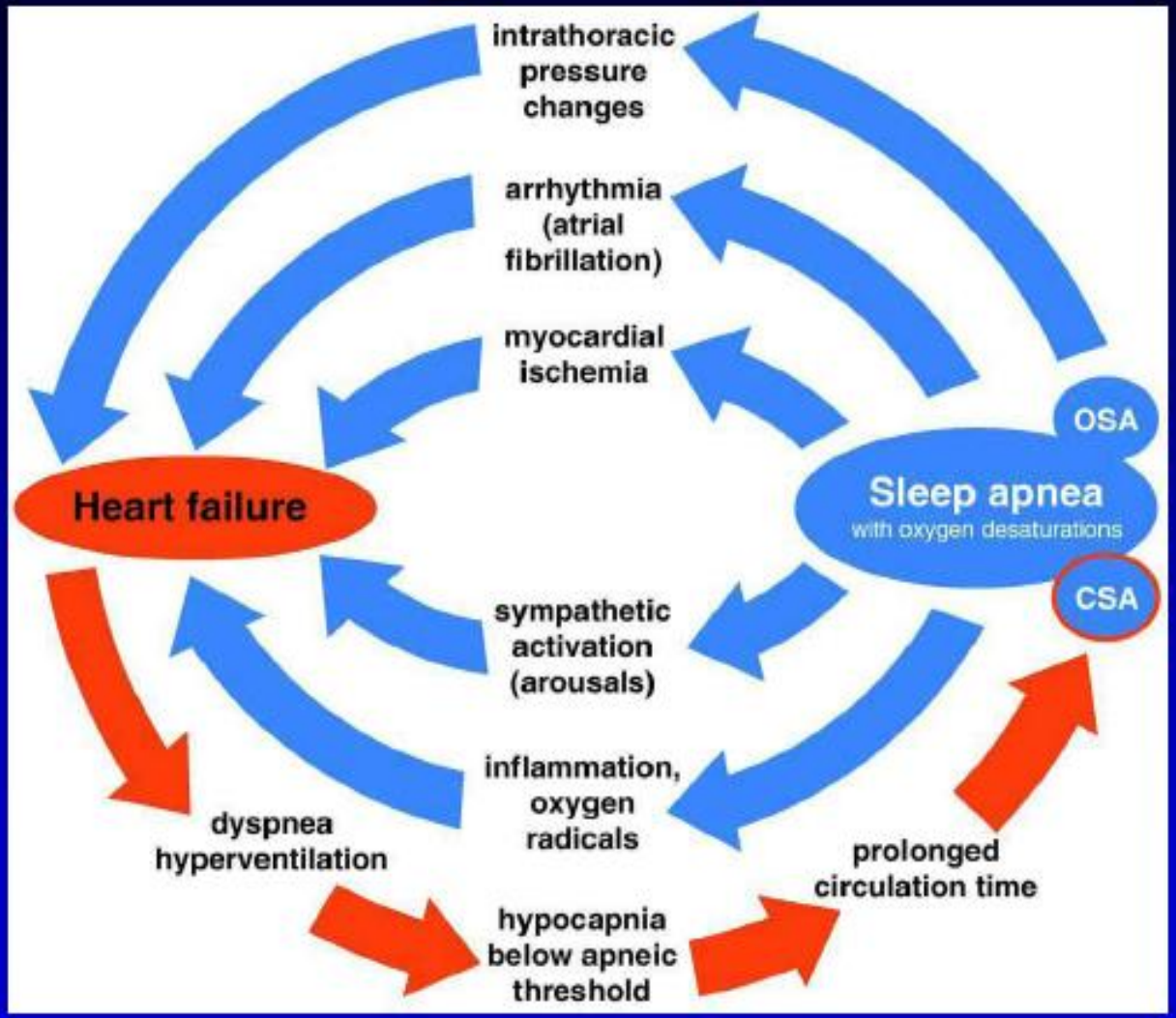
Bitter et al. Dtsch Arztebl Int 2009;106:164–70



. . . The only peculiarity in the last period of his illness, which lasted eight or nine days, was in the state of the respiration. For several days, his breathing was irregular; it would cease for a quarter of a minute, then it would become perceptible, though very low, then by degrees it became heaving and quick, and then it would gradually cease again. This revolution in the state of his breathing occupied about a minute, during which there were about thirty acts of respiration"

John Cheyne. *A case of apoplexy, in which the fleshy part of the heart was converted into fat.*
Dublin Hosp Rep. 1818:2:216-223

Cycle of SDB Intertwined with Cycle of Heart Failure



Brenner et al. *Trends Cardiovasc Med* 2008;18:240-7

Sleep apnoea in heart failure

Problems with nomenclature (and perception)

Sleep apnoea in heart failure
Problems with nomenclature (and perception)

Cardiologist

Prevalent in obese & HTN pts

Snoring problem

Affecting QoL

Sleep Physician

Sleep disordered breathing

- **obstructive sleep apnoea**
- **central sleep apnoea**

Nomenclature accepted

Prevalent and relevant for M&M and QoL

Target for intervention

Breathing abnormality

- Cheyne-Stokes respiration
- During sleep (also at rest)

Nomenclature accepted ?

Prevalent and relevant for M&M and QoL

Target for intervention ?

Heart Failure Specialist

Sleep apnoea in heart failure
Problems with nomenclature (and perception)

- **Obstructive sleep apnoea**

  episodes of complete upper airway obstruction; prevalent in non-HF pts;

  apnoea and hypoxia & arousals from sleep

  CV consequences: hypertension, arrhythmias, myocardial ischaemia

- **Central sleep apnoea**

  temporary withdrawal of central respiratory drive

  more specific and prevalent in HF

  complex (unclear) pathophysiology; ominous consequences;

  emerging target for intervention

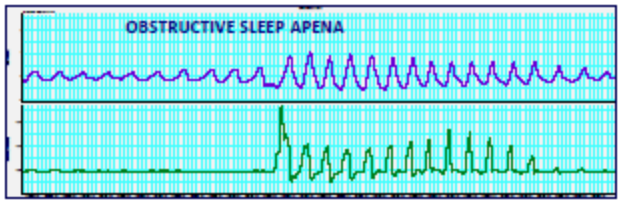
Sleep apnoea in heart failure
Problems with nomenclature (and perception)

- **Obstructive sleep apnoea**

  episodes of complete upper airway

  apnoea and hypoxia & arousals fro

  CV consequences: hypertension, a

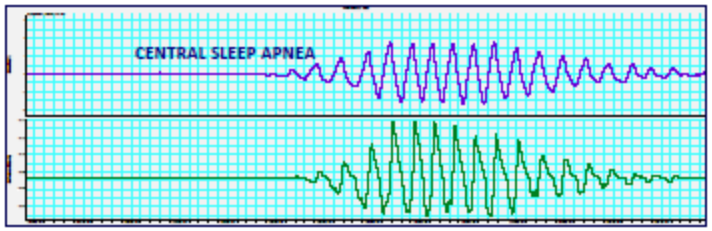


Abdominal and chest movement without airflow indicates obstructive apnea

- **Central sleep apnoea**

ory drive

nous consequences;



Lack of abdominal and chest movement indicates central apnea

Clinical Definitions

- **Central apnea**
  - ≥10 second cessation of airflow, without effort
- **Obstructive apnea**
  - ≥10 second cessation of airflow, while effort continues
- **Hypopnea**
  - 30% reduction in airflow for 10 sec with a 4% fall in oxygen saturation
- **Apnea-Hypopnea Index (AHI)**
  - Number of apneas and hypopneas per hour of sleep
  - Mild (5-14/hour), Moderate (15-29/hour), and Severe (≥ 30/hour)
- **Arousals**
  - Number of arousals per hour of sleep
- **Oxygen Desaturation Index (ODI) 4%**
  - Number of times oxygen saturation drops by 4% or more per hour

2007 AASM Guidelines

Sleep apnoea in heart failure

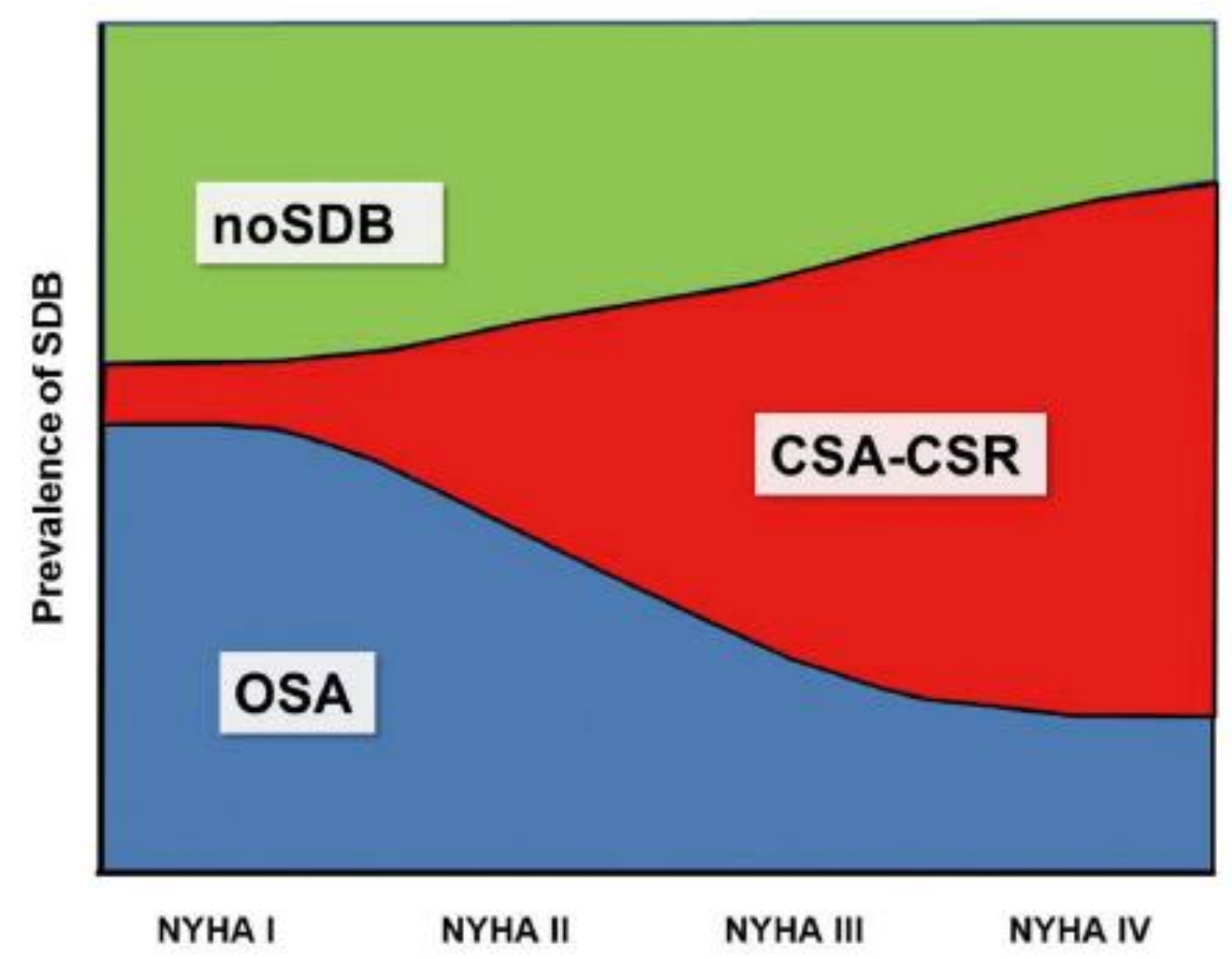
1. Problems with nomenclature (and perception)
2. Prevalence

Prevalence of sleep apnea in patients with HFrEF

Country [year] Author	N	AHI ≥ 15/h	CSA	OSA	β-blockers
*USA [2006] Javaheri	100	49%	37%	12%	10%
USA [2008] MacDonald	108	61%	31%	30%	82%
*Canada [2007] Wang	287	47%	21%	26%	80%
*UK [2007] Vazir	55	53%	38%	15%	78%
Germany [2007] Oldenburg	700	52%	33%	19%	85%
*Germany [2009] Hagenah	50	64%	44%	20%	100%
*Germany [2010] Jilek	273	64%	50%	14%	88%
*Portugal [2010] Ferreira	103	46%	NA	NA	90%
Total	1676	54%	34%	20%	81%

Krawczyk M et al. Cardiol J 2013

SDB in Heart Failure



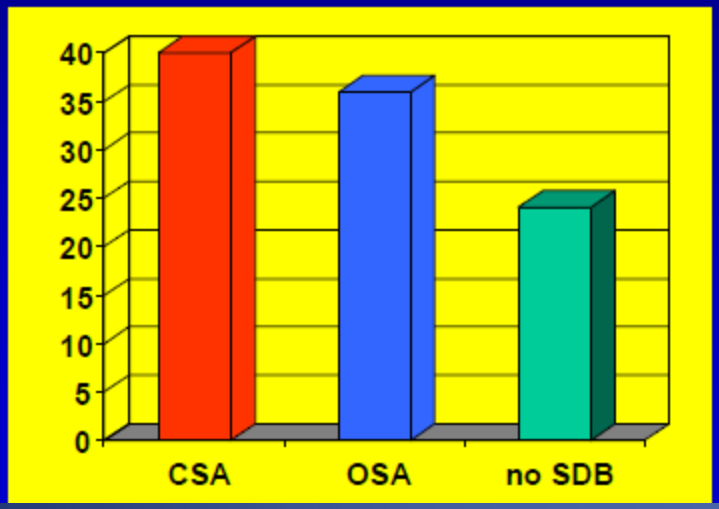
Sleep-disordered breathing in patients with symptomatic heart failure
A contemporary study of prevalence in and characteristics of 700 patients

Olaf Oldenburg [a,*], Barbara Lamp [a], Lothar Faber [a], Helmut Teschler [b], Dieter Horstkotte [a], Volker Töpfer [a]

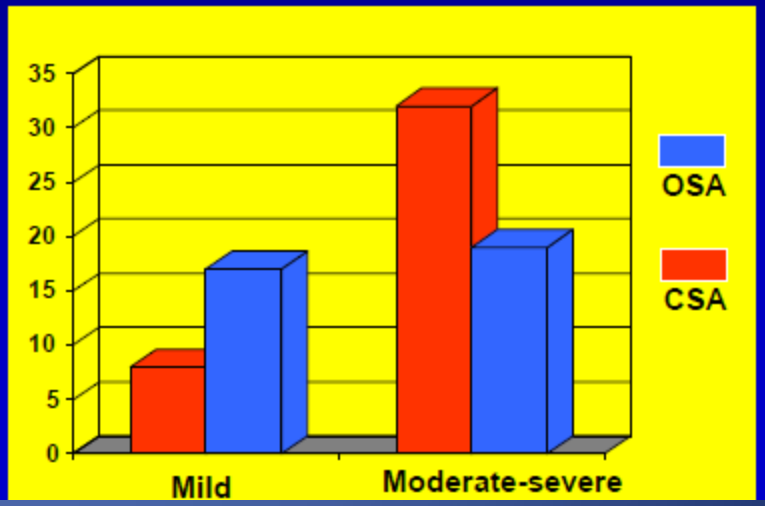
European Journal of Heart Failure 2007

- **700 CHF pts, 561 men, age: 65 yrs**
- **NYHA class – 2.7, LVEF – 28%, peakVO2 – 14.4 ml/kg/min**
- **Therapy: 95% - ACEi/ARB, 85% - beta-blocker, 90% - diuretics**
- **Sleep studies with cardiorespiratory polygraphy: nasal air flow, chest and abdominal effort, pulse oximetry, snoring and body position**

Prevalence of SDB (% CHF pts)



Severity of SDB (% CHF pts)



Sleep apnoea in heart failure

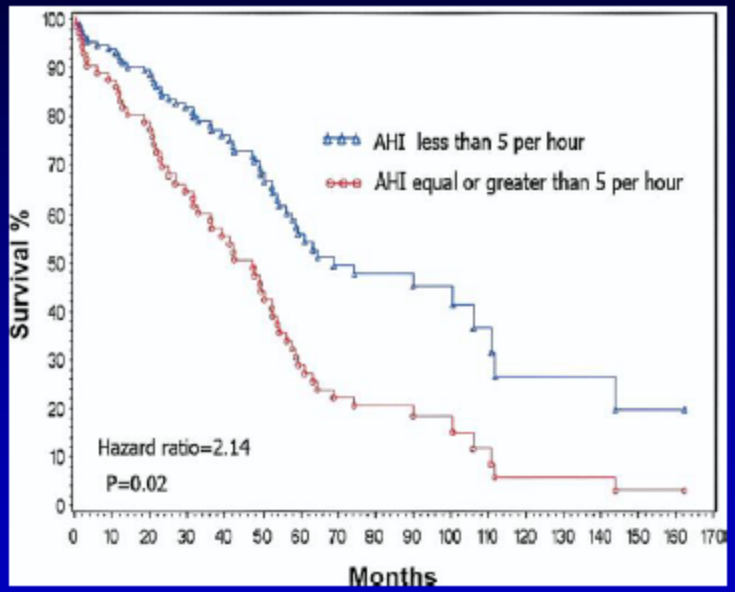
1. Problems with nomenclature (and perception)
2. Prevalence
3. Diagnosis (in cardiology practice)

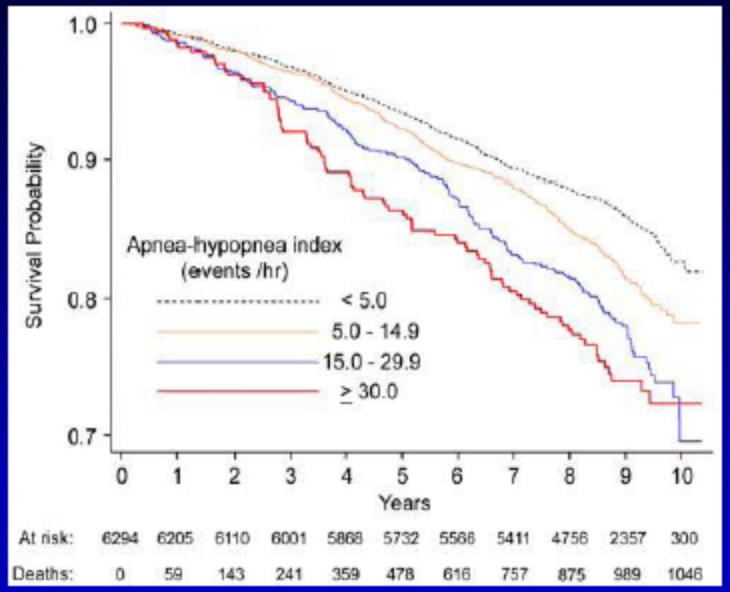
Sleep disordered breathing in HF

Diagnosis in cardiology practice

- **Polysomnography („gold standard")**
  - sleep study / sleep laboratory
  - portable polysomnograph monitors
  - polygraphy / pulse oximetry
- **Questionnaires**
- **Other techniques**
  - heart rate (blood pressure) variability
  - thoracic bioimpedance (pacemakers)

CSA Increases Mortality in Heart Failure Patients



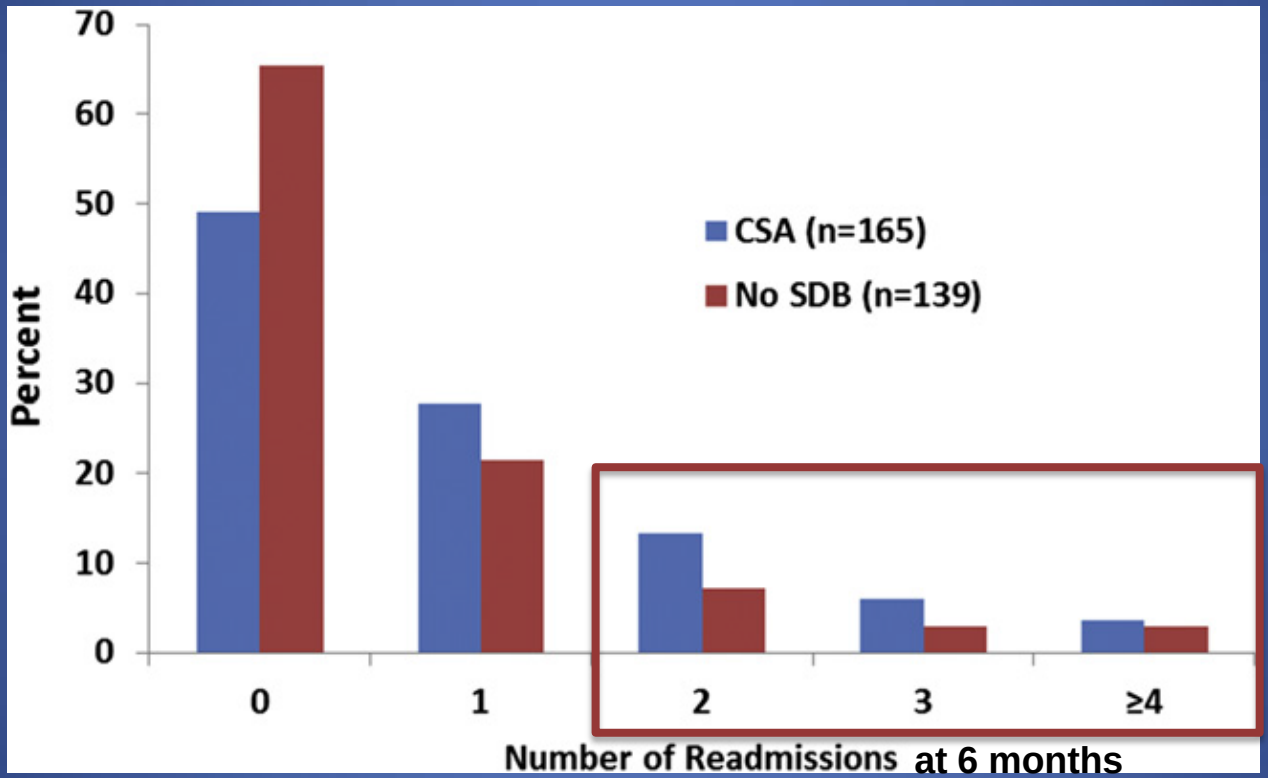


- Relationship of increased mortality and CSA constant across all levels of severity of CSA
- Mortality increases with increased AHI in patients with SDB
- Mortality remains high even with optimal current therapies

Javaheri et al. *JACC.* 2007;49:2028-34
Punjabi et al. *PLoS Medicine.* 2009;6:1-9

Central Sleep Apnea Increases the Risk for HF Readmissions

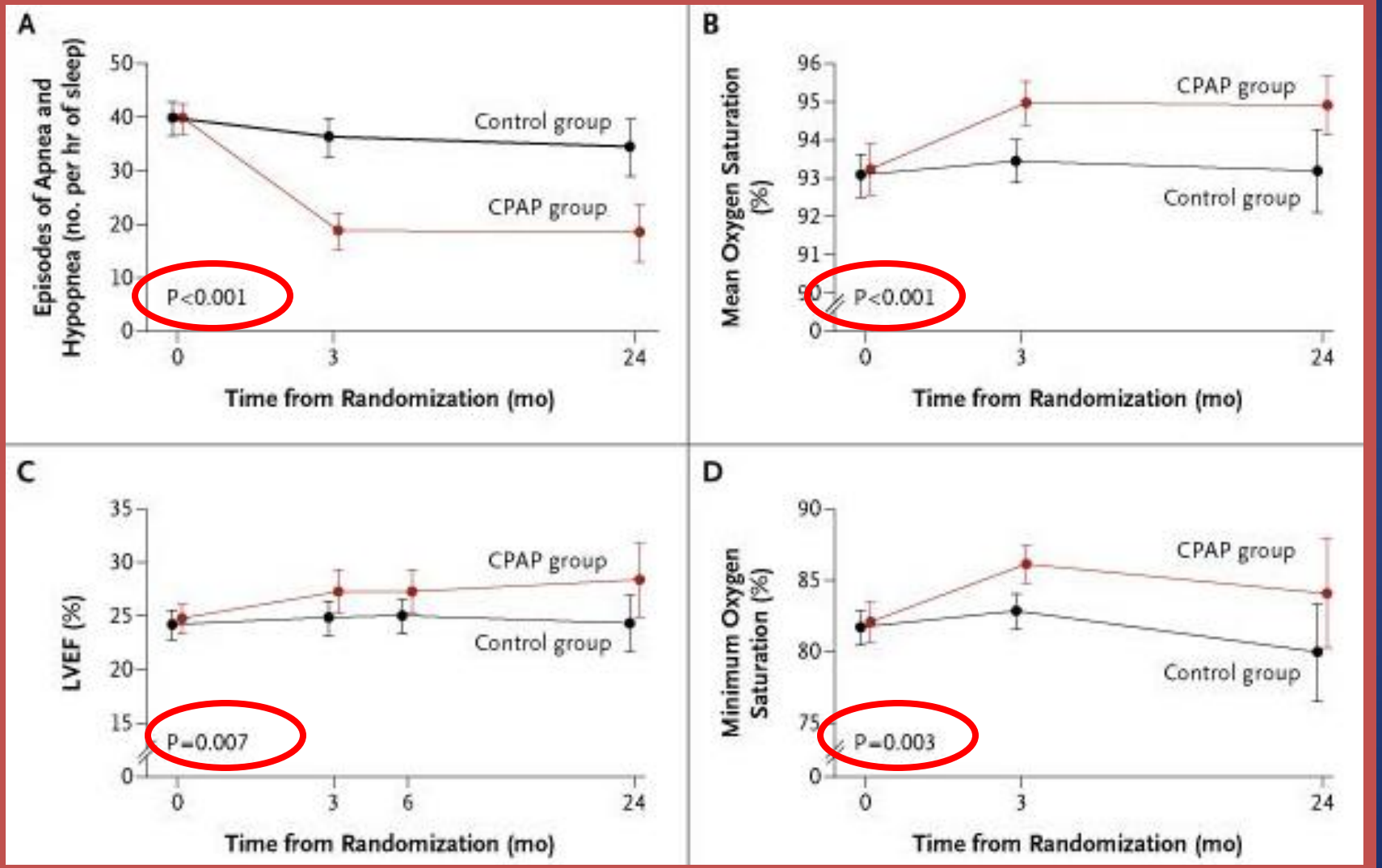
*50% of heart failure patients with central sleep apnea were **readmitted** at 6 months*



*Over 25% of heart failure patients with central sleep apnea had **2 or more readmissions** within 6 months*

Khayat et al. J Card Fail 2012;18:534-540

Effect of CPAP on the Frequency of Episodes of Apnea and Hypopnea, Mean and Minimal Nocturnal Oxygen Saturation, and Left Ventricular Ejection Fraction



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

The NEW ENGLAND JOURNAL of MEDICINE

Conclusions

- Both OSA and CSA are ***highly prevalent*** in patients with HF and significantly increase their morbidity and mortality.
- In HF patients with OSA ***mask-based therapies*** have consistently improved both clinical signs/symptoms and outcomes.
- ***Screening for SDB should be included in evaluation of all patients with HF.***

HF patients should be diagnosed & treated for CSA

Sleep disturbance and sleep-disordered breathing

Sleep-disordered breathing (SDB) occurs in more than one-third of patients with HF,[484] being even more prevalent in patients with AHF.[485] The **most common types** are: central sleep apnoea (**CSA**, similar to Cheyne Stokes respiration, CSR), obstructive sleep apnoea (OSA), and a mixed pattern of the two. Other causes of sleep disturbance include anxiety, depression, decubitus or paroxysmal pulmonary congestion (orthopnoea and paroxysmal nocturnal dyspnoea) and diuretic therapy causing nocturnal diuresis. **Reviewing sleep history (including asking a partner) is part of the holistic care of patients with HF** (see Section 14). CSA/OSA have been shown to be assoc. with a worse prognosis in HF.[485,486]

OSA is associated with an increased risk of incident HF in men.[487]

CSA is the most common form of SDB in HFrEF, and HFrEF is the most common cause of CSA, so they are closely linked. Screening for, and the diagnosis and treatment of sleep apnoea is discussed in detail elsewhere.[484,488]

Diagnosis used to require overnight polysomnography, although advanced home testing equipment which can distinguish the type of sleep apnoea has been developed.

*Ponikowski P et al. Eur Heart J **2016**. ESC GLs diagnosis/treatment of acute and chronic HF*

Conclusioni → Brainstorming

- **"Storicamente" la sleep apnea → puro "disturbo del sonno"**
- Oggi sappiamo che sleep apnea è un marker di severità delle malattie CV:
  - Elevata prevalenza nello **SCC** ed anche nella **FA**

    Elevata **ricorrenza di FA quando NON si trattano le OSA**

- Ancor oggi, **è ampiamente SOTTO-DIAGNOSTICATA nei pz CV**

- "Cambio di mentalita" **per il cardiologo -→SCREENING/DIAGNOSI di sleep apnea**, in collabor. con pneum. / spec. sonno

- ***Nelle indicaz. canoniche (pacing/CRT), il DEVICE può aiutare:***
  - ***screening per Sleep Apnea(Apnea Scan)***
  - ***monitoraggio della terapia***

STUDIO DASAP

Diagnosis And treatment of Sleep Apnea
in Patient with Heart Failure

Prof. Luigi Padeletti Ospedale Careggi - Firenze -Italy
Dr.ssa Maria Teresa La Rovere Fondazione S. Maugeri – Montescano (PV) - Italy Dr. Michele Emdin CNR – Pisa - Italy
Dr. Gianfranco Sinagra Ospedali Riuniti – Trieste - Italy

STUDIO DASAP

Obiettivo primario

Lo scopo è stato quello di valutare le performance dell 'algoritmo APNEA SCAN presente nei dispositive Boston Scientific impiantati in pazienti bisognosi sia di CRTD che di ICD convenziolane.

Obiettivo secondario

È stato poi quello di valutare l'incidenza di eventi clinici dopo 24 mesi dall'arruolamento in correlazione con l'indice RDI dell' algoritmo dell APNEA SCAN.

Studio DASAP

REVIEV:

- Ultimo arruolamento è stato eseguito il 29-giugno-2016
- Sono stati arruolati 261 pazienti, di questi 170 per la valutazione dell'obiettivo primario
- Chiusi anche tutti gli arruolamenti a 12 mesi

Studio DASAP andamento europeo

Centre	EC submission	EC meeting (and opinion)	EC written approval availability	Contract signature -CA approval (only for Italy)	SIV	First Pt. enrolled	No. of Pt enrolled
1- Prof. Padeletti (Firenze)	Not applicable	27/05/2013	Available	Not applicable 25/06/13	21/02/14	10/03/14	29 (+1 screening failure)
2 – Prof. Capucci (Ancona)	30/12/13	06/03/14	Available	04/06/14 26/05/14	17/06/14	17/06/14	23
3 – Prof. Emdin (Pisa)	17/03/14	27/03/14 10/07/14 (II meeting) 09/10/14 (III meeting)	Available/ Suspensive opinion Available/ Suspensive opinion Available	11/11/14 31/10/14	18/12/14	13/01/15	12
4 - Prof. Sinagra (Trieste)	20/01/14	17/03/14	Available	Not applicable 26/03/14	14/05/14	17/06/14	18
5 – Prof. D'Onofrio (Napoli)	29/01/14	16/04/14	Available	04/06/14 04/06/14	03/06/14	27/06/14	52 (+1 screening failure)
6 – Prof. Boriani – Dr Diemberger (Bologna)	11/02/14	11/03/14 13/05/14 (II meeting)	Available/ Suspensive opinion Available/ Positive	16/07/14- 06/07/14	31/07/14	15/09/14	4
7 – Prof. Pisanò (Lecce)	23/12/13	18/02/14	Available	24/02/14 06/03/14	10/04/14	14/05/14	40
8 – Prof. Indolfi (Catanzaro)	07/01/14	05/03/14	Available	10/04/14 10/04/14	18/04/14	05/05/14	12
9 – Prof. Tespili (Seriate)	14/01/14	26/02/14	Available	27/03/14 31/03/14	05/05/14	09/05/14	27
10 –Dr Checchinato (Moncalieri)	02/07/14	12/11/14	Available	23/12/14 07/01/15	15/01/15		2
12 – Dr. Russo (Taranto)	14/01/14	30/01/14	Available	Not applicable 10/04/14	22/04/14	06/05/14	1
13– Az. Osp. Di Cosenza(Talarico)	08/04/14	27/06/14	Available	15/10/14 15/10/14	19/09/14	28/10/14	22 (+1 screening failure)
14 – Dr. Rapacciuolo (Napoli)	15/04/14	21/05/14 10/09/14 (II meeting)	Available/ Suspensive opinion Available/ Positive	18/11/14 15/10/14	27/10/14	04/11/14	16
22 – Dr. Miguel Angel Arias (Toledo)	03/07/14	04/09/14 07/10/14 (II meeting)	Available/ Suspensive opinion Available/ Positive	23/03/2015	27/04/15	20/10/15	4
25 - Dr. João de Sousa (Lisbon)	31/07/14	17/12/14	Available/ Positive	02/03/15	02/04/15	Site closed with no patients enrolled	

Implantable cardioverter-defibrillator–computed respiratory disturbance index accurately identifies severe sleep apnea: The DASAP-HF study

Antonio D'Onofrio, MD,* Maria Teresa La Rovere, MD,† Michele Emdin, MD, PhD,‡§ Alessandro Capucci, MD, PhD,‖ Gianfranco Sinagra, MD, PhD,¶ Valter Bianchi, MD,* Ennio C.L. Pisanò, MD,# Paolo Pieragnoli, MD,** Maurizio Tespili, MD,†† Mario Luzi, MD,‖ Antonello Talarico, MD,‡‡ Massimo Zecchin, MD,¶ Antonio Rapacciuolo, MD, PhD,§§ Marcello Piacenti, MD,§ Ciro Indolfi, MD, PhD,‖‖ Miguel Angel Arias, MD,¶¶ Igor Diemberger, MD,## Catia Checchinato, MD,*** Giuseppe Boriani, MD, PhD,††† Luigi Padeletti, MD, PhD‡‡‡

*From the *Ospedale Monaldi, Naples, Italy, †Fondazione 'Salvatore Maugeri', IRCCS, Istituto Scientifico di Montescano, Montescano (PV), Italy, ‡Institute of Life Sciences, Scuola Superiore Sant'Anna, Pisa, Italy, §Fondazione Toscana Gabriele Monasterio, Pisa, Italy, ‖Università Politecnica delle Marche, Ancona, Italy, ¶University of Trieste, Trieste, Italy, #Vito Fazzi Hospital, Lecce, Italy, **University of Florence, Florence, Italy, ††"Bolognini" Hospital, Seriate (BG), Italy, ‡‡Ospedale SS. Annunziata, Cosenza, Italy, §§Federico II University, Naples, Italy, ‖‖"Magna Graecia" University, Catanzaro, Italy, ¶¶Hospital Virgen de la Salud, Toledo, Spain, ##University of Bologna, Policlinico S.Orsola-Malpighi, Bologna, Italy, ***Ospedale Santa Croce, Moncalieri (TO), Italy, †††University of Modena and Reggio Emilia, Modena, Italy, and ‡‡‡IRCCS MultiMedica, Sesto San Giovanni, Milan, Italy.*

BACKGROUND Sleep apnea (SA) is a relevant issue in the management of patients with heart failure for risk stratification and for implementing treatment strategies.

OBJECTIVE The purpose of this study was to evaluate in patients with implantable cardioverter-defibrillators (ICDs) the performance of the respiratory disturbance index (RDI) computed by the ApneaScan algorithm (Boston Scientific Inc., Natick, MA) as a discriminator of severe SA.

METHODS ICD-indicated patients with left ventricular ejection fraction ≤35% were enrolled. One month after implantation, patients underwent a polysomnographic study. We evaluated the accuracy of the RDI for the prediction of severe SA (apnea-hypopnea index [AHI] ≥30 episodes/h) and the agreement between RDI and AHI during the sleep study night.

RESULTS Two hundred sixty-five patients were enrolled to obtain the required sample of 173 patients with AHI and RDI data for analysis. The mean AHI was 21 ± 15 episodes/h and severe SA was diagnosed in 38 patients (22%), while the mean RDI was 33 ± 13 episodes/h. On the basis of the receiver operating characteristic curve analysis of RDI values, the area under the curve was 0.77 (95% confidence interval [CI] 0.70–0.83; $P < .001$). At an RDI value of 31 episodes/h, severe SA was detected with 87% (95% CI 72%–96%) sensitivity and 56% (95% CI 48%–66%) specificity. RDI closely correlated with AHI recorded during the same night ($r = 0.74$; 95% CI 0.57–0.84; $P < .001$), and the Bland-Altman agreement analysis revealed a bias of 11 episodes/h, with limits of agreement being −10 to 32 episodes/h.

CONCLUSION The RDI accurately identified severe SA and demonstrated good agreement with AHI. Therefore, it may serve as an efficient tool for screening patients at risk of SA.

KEYWORDS Heart failure; ICD; Respiratory disturbances; Sleep apnea; Thoracic impedance

(Heart Rhythm 2018;15:211–217)


"Molte cose ,non è perche sono difficili che non osiamo farle
ma perché non osiamo farle che sono difficili"
Lucio Anneo SENECA

Aula Magna - ASST GOM Niguarda
16 marzo 2017 - MILANO

Sistema Socio Sanitario
Ospedale Niguarda
Regione Lombardia

Nuove tecnologie e nuovi modelli di gestione del paziente cardiovascolare

Sleep Apnea, HF e cardio-stimolazione

Dr. Maurizio LUNATI

Direttore Cardiologia 3 - Elettrofisiologia

ASST GOM Niguarda - MILANO

Prevalenza di Sleep Apnea nei pz con patologie cardiovascolari

AF 30%

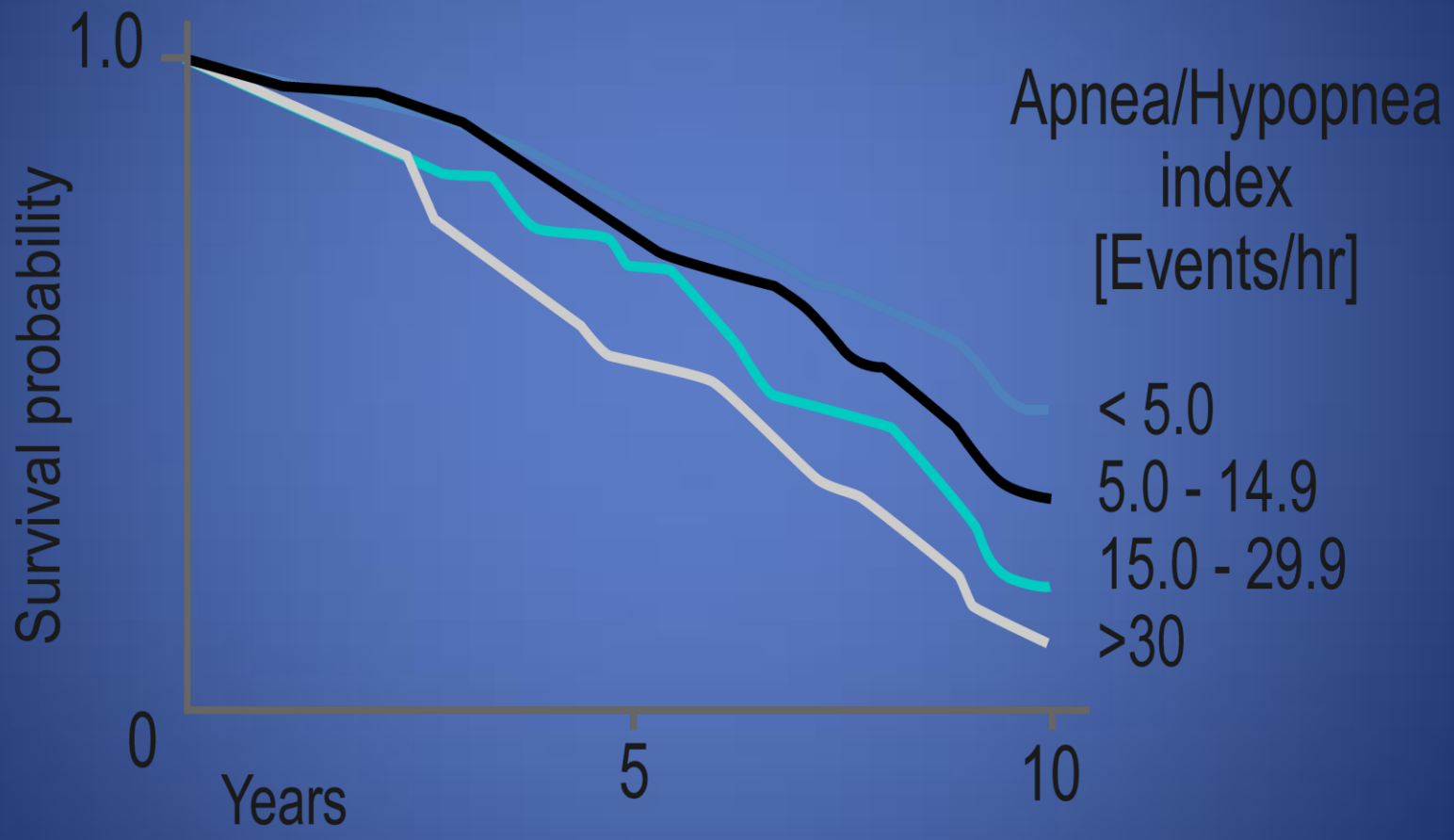
HYPERTENSION >30%

CORONARY ARTERY DISEASE 30%- 50%

HEART FAILURE 50%

HF WITH LVEF <40% >60%

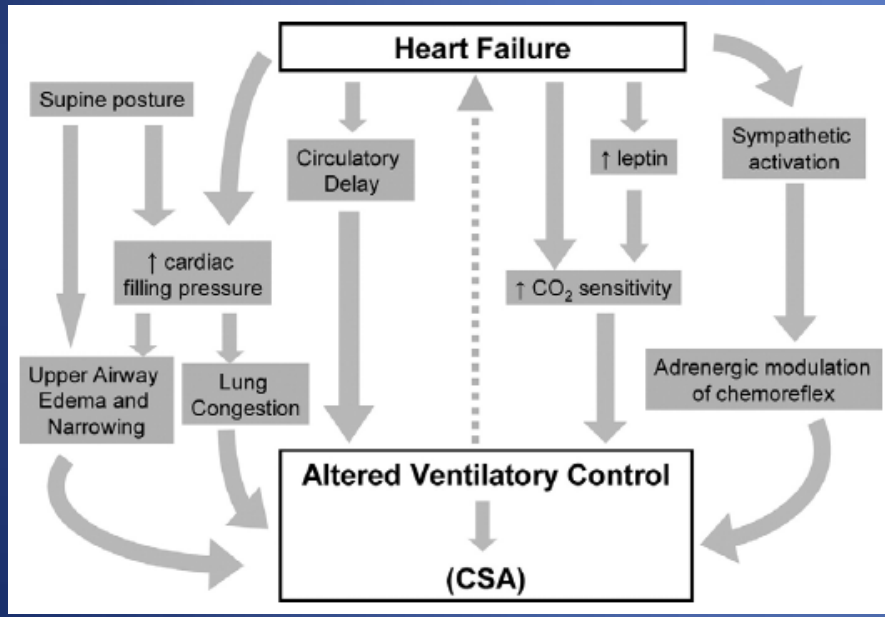
Severità di Sleep Apnea ⇔ Mortalità



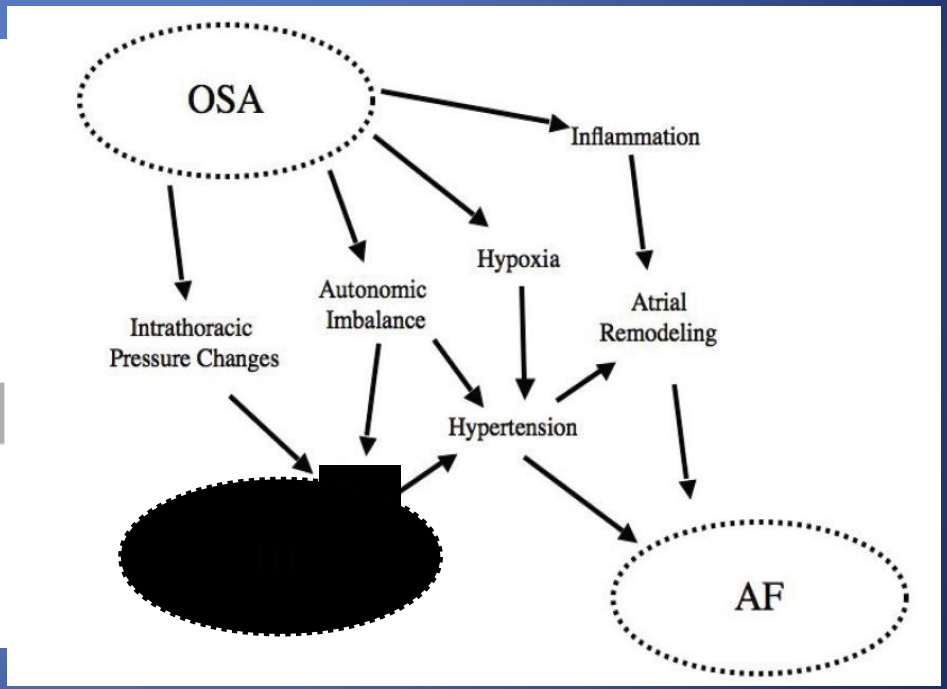
* J Punjabi NM et al. Sleep-Disordered Breathing and Mortality: A Prospective Cohort Study. PLoS Med **2009**;6(8)
* Chung F et al. STOP Questionnaire A Tool to Screen Pts for OSAs. Anesthesiology **2008**;108:812–21

Relazione HF ⇔ Sleep Apnea (OSA/CSA)

- **SAS, HF** (e **AF**) sono patologie con forti inter-correlazioni
- Molto ancora è da indagare soprattutto sul versante HF ⇔ CSA …



Somers et al.
*JACC Vol. 52, No. 8, **2008***



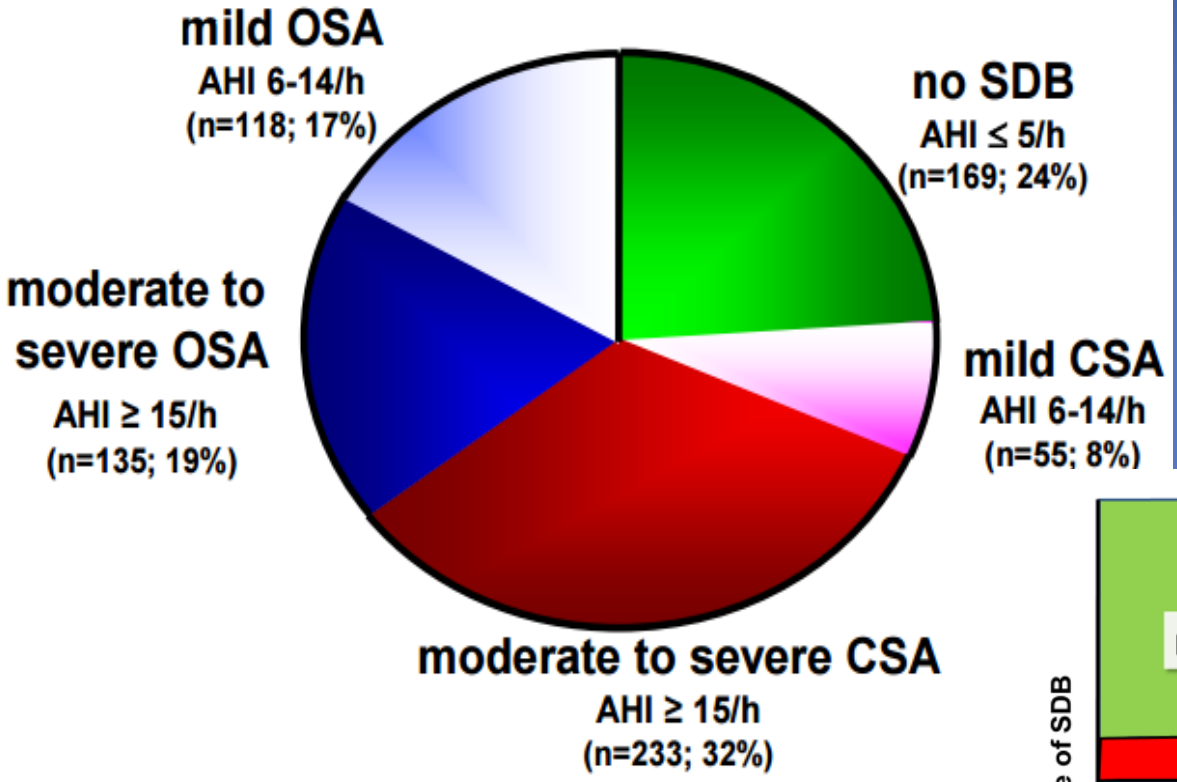
Digby, Baranchuk et al.
*Current Cardiology Reviews **2012**;8(4)*

HF e CSA: alcuni numeri

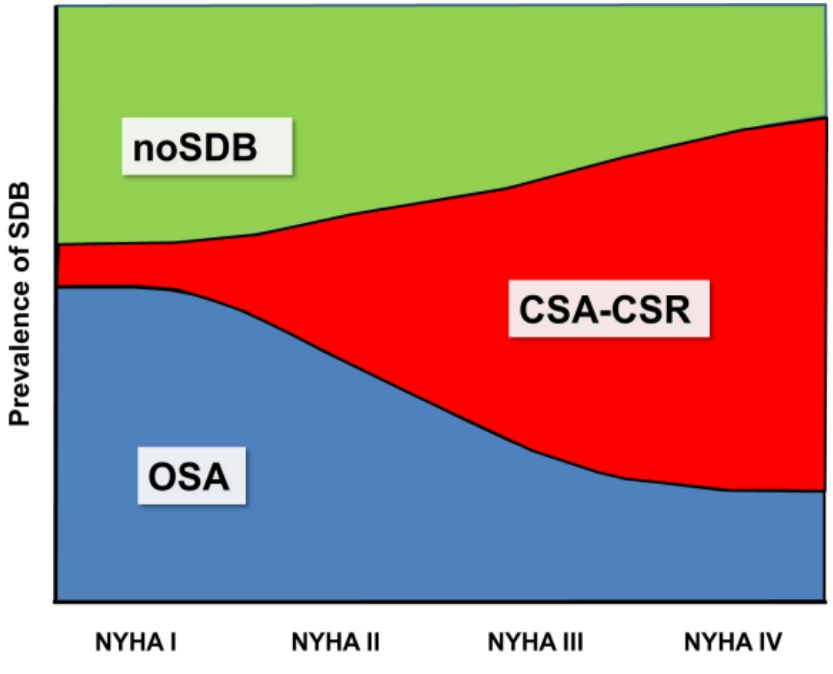
- Prevalenza HF negli over-25Y: circa 3-4% [1–3]
- Prevalenza HF negli over-75Y: circa 8% [4]
- **Prevalenza CSA nei pz HF: 40-60%** [5-8]
- **Prevalenza CSA nei pz HFpEF: circa 30%** [9]

1. *Mc Donagh TA et al. Symptomatic and asymptomatic LV systolic dysfunction in an urban population. Lancet 1997;350:829–33.*
2. *Ceia F et al. Prevalence of chronic HF in Southwestern Europe: the EPICA study. Eur J Heart Fail 2002;4:531–9.*
3. *Guha K et al. Heart Failure Epidemiology: European Perspective. Curr Cardiol Rev 2013;9:123–7.*
4. *Kupari M et al. CHF in old age: prevalence, mechanisms and 4Y prognosis in the Helsinki Ageing Study. J Intern Med 1997.*
5. *Javaheri S et al. Sleep Apnea in 81 Ambulatory Male Patients With Stable Heart Failure : Types and Their Prevalences, Consequences, and Presentations. Circulation 1998;97:2154–9.*
6. *Lanfranchi PA et al. Prognostic value of nocturnal CSR in CHF. Circulation 1999;99:1435–40.*
7. *Oldenburg O et al. Sleep-disordered breathing in patients with symptomatic heart failure A contemporary study of prevalence in and characteristics of 700 patients. Eur J Heart Fail 2007;9:251–7.*
8. *Lévy P et al. Prevalence and Impact of Central Sleep Apnea in Heart Failure. Sleep Medicine Clinics 2007;2:615–21.*
9. *Bitter T et al. Sleep-disordered breathing in HF with normal LVEF. Eur J Heart Fail 2009;11:602–8.*

SBDs in pz HF con FE ridotta (HFrEF) → indicazioni CRT



n=710 pz
NYHA ≥ 2
LVEF < 40%



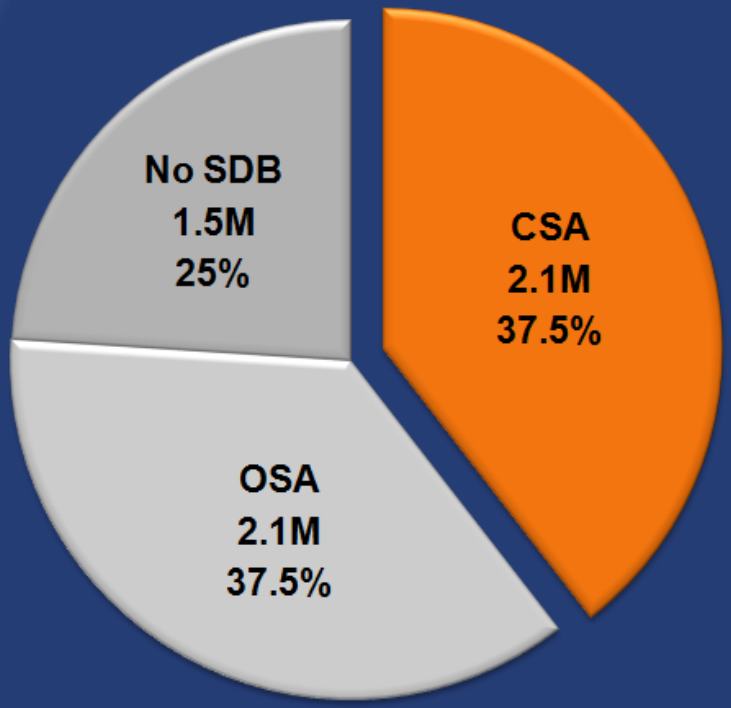
• *Oldenburg O et al. Eur J of HF **200***

• *Oldenburg O et al. Circulation **201***

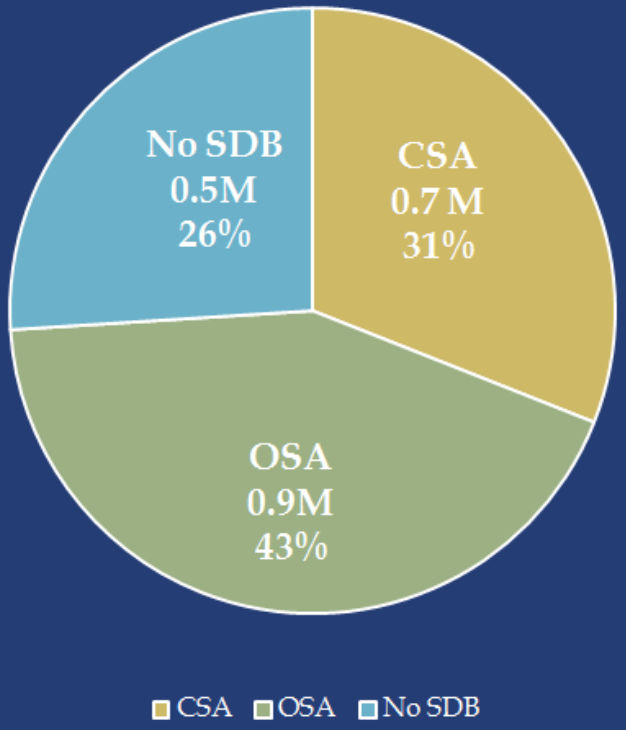
CSA è frequente nei pz HF ed AF

Central Sleep Apnea is Common in Heart Failure and Atrial Fibrillation Patients

United States
Heart Failure Population
5.7 Million



United States
Atrial Fibrillation Population
2.1 Million



Roger et al. Circulation 2011;123:e18-209
Oldenburg et al. Eur J Heart Fail;20079:251-7

2

Bitter et al. Dtsch Arztebl Int 2009;106:164–70

*Courtesy of Prof. E. Gronda (Naples, Sept. **2016**)*

"HF and Sleep Disorders" *(SIC – july 2016)*

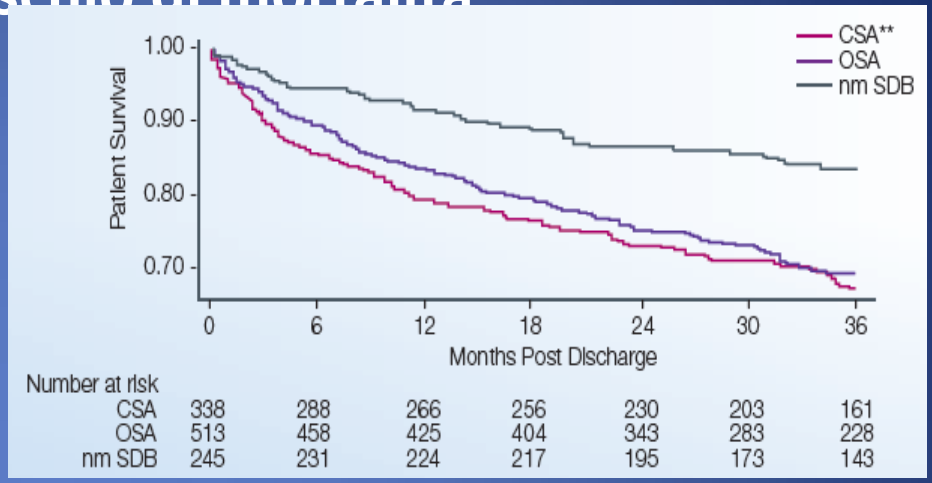
- Growing importance of SBDs in pts with CV diseases, particularly in HF pts.
- **OSA and CSA are common in HF pts** → impact on morbidity and mortality.
- Both OSA/CSA associate with ⇧ sympathetic activation, vagal withdrawal, altered haemodynamic loading conditions, and hypoxaemia.
- OSA strongly associates with AHT (most common risk factor for hypertrophy and failure).
- Intra-thoracic pressure changes associate with OSA → haemod. alterations → V remodeling.
- **HF treatment** can decrease the severity of both OSA and CSA:
  - furosemide, spironolactone
  - exercise training
  - **CRT**
  - eventually heart transplantation

  have shown a **positive effect on OSA and CSA in HF pts**.
- Whether CSA should be treated and, if so, which is the optimal therapy is still debated.
- More evidence available on the beneficial effects of OSA treatment in HF pts.

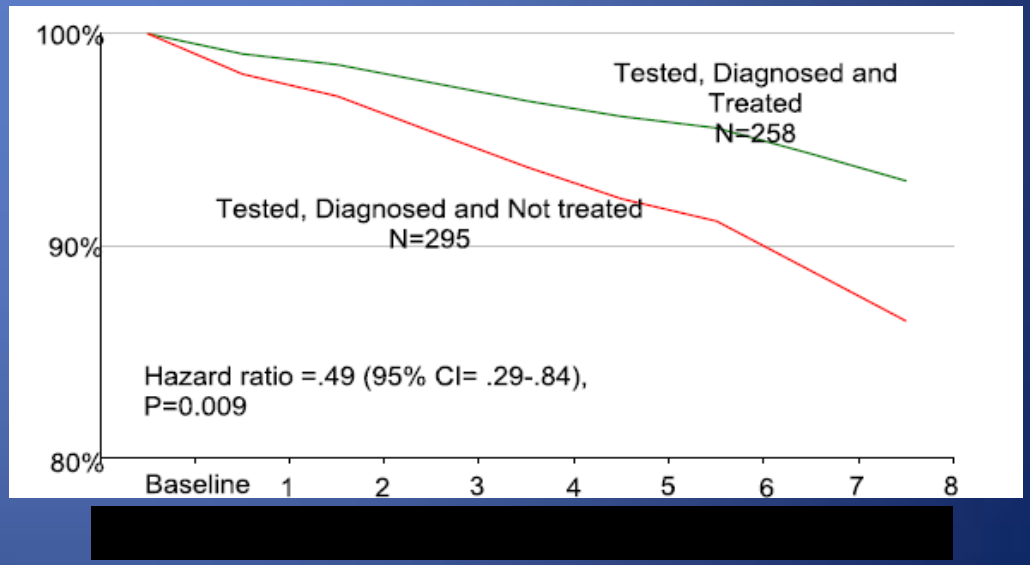
Parati G, Lombardi C et al (SIC Working Group on HF)
*HF and sleep disorders. Nat Rev Cardiol. **2016** Jul;13(7):389-403.*

Pz HF con CSA non trattata → aumentato rischio di mortalità

- Pz HF e CSA non-trattate:
  +60% mortality rate vs.
  pz senza SBDs / SBDs lievi [1-3]



- Pz HF con diagnosi di CSA,
  CSA non trattata:
  +100% mortalità vs.
  pz HF con CSA trattate [4]



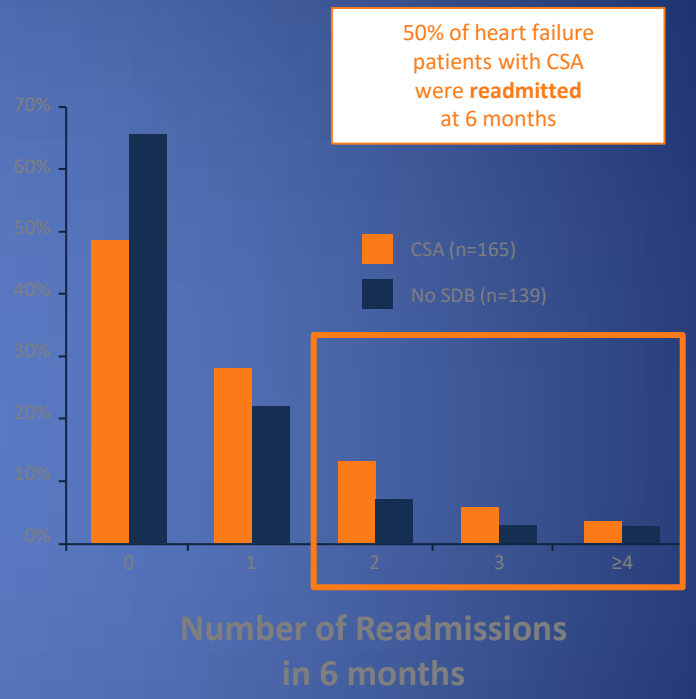
1. S Javaheri, R Shukla, H Zeigler, L Wexler, J Am Coll Cardiol 49, 2028-2034 (2007)
2. JP Bakker, AJ Campbell, AM Neill, Internal Medicine Journal 42, 1264–1268 (2012)
3. R Khayat et al., European Heart Journal (2015), doi:10.1093/eurheartj/ehu522
4. S Javaheri, EB Caref, E Chen, KB Tong, WT Abraham, Am J Respir Crit Care Med 183, 539–546 (2011)

CSA non trattate → aumentato rischio di re-osped. precoce

- **n = 784 pz** ospedalizzati (HF sistolico)

Presenza di CSA si associa ad un
⇧ rischio di RE-OSPEDAL. entro 6M

- **50% dei pz con CSA erano re-osped.**
- 25% dei pz → 2 o più re-ospedal.



*R. Khayat et al. J Card Fail 18, 534–540 (**2012**)*

SAS e HF

RASSEGNA

Apnee notturne e scompenso cardiaco: fisiopatologia, diagnosi e terapia

Cinzia Monda, Oriana Scala, Stefania Paolillo, Gianluigi Savarese, Milena Cecere, Carmen D'Amore, Antonio Parente, Francesca Musella, Susanna Mosca, Pasquale Perrone Filardi

Dipartimento di Medicina Interna, Scienze Cardiovascolari ed Immunologiche, Università degli Studi "Federico II", Napoli

Terapia di resincronizzazione cardiaca

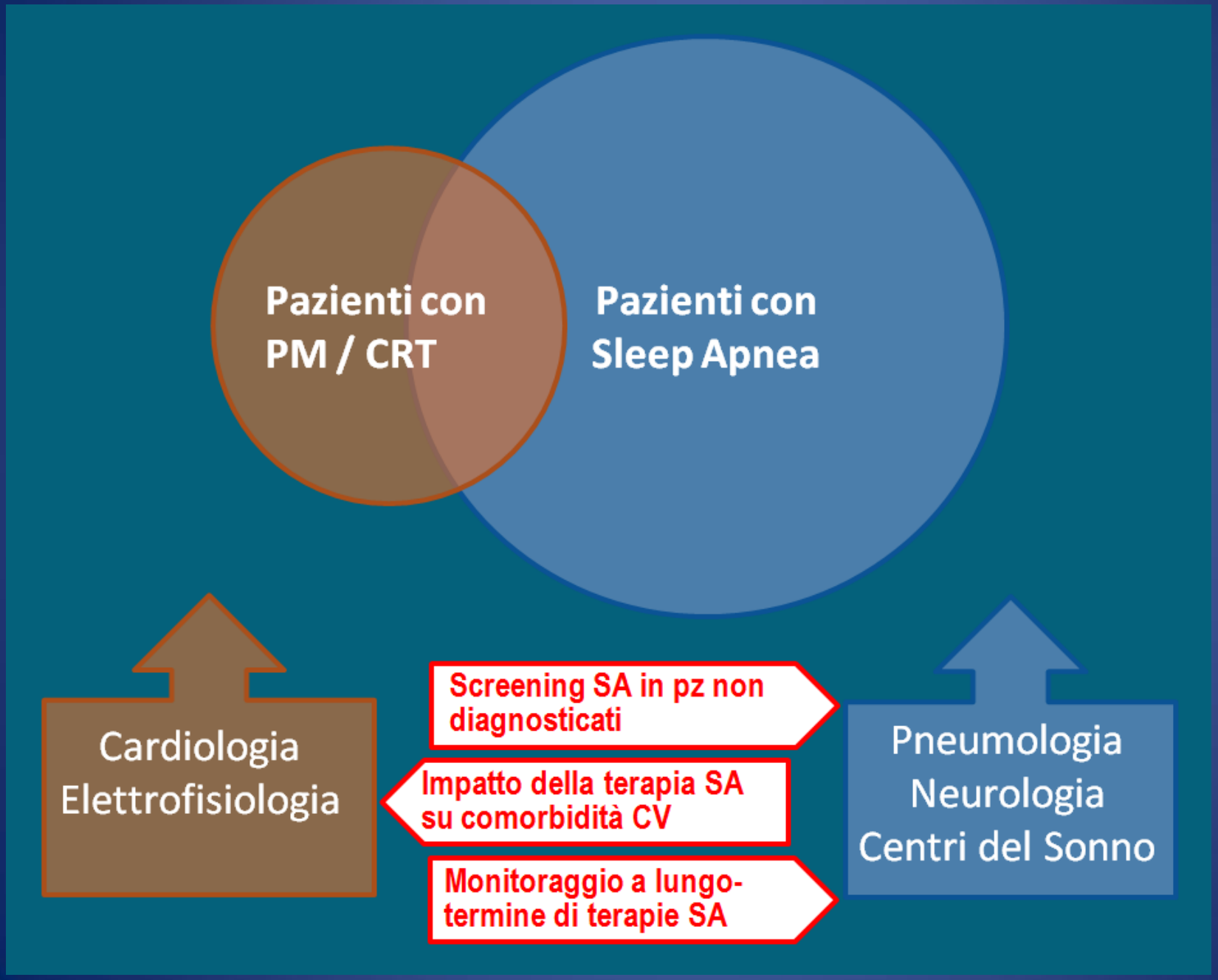
Diversi autori hanno dimostrato un effetto positivo della CRT sui disturbi respiratori durante il sonno in pazienti affetti da scompenso cardiaco. La CRT sembra migliorare la qualità del sonno e ridurre l'AHI nei pazienti con CSA, come dimostrato da Sinha et al.[37] in 14 pazienti in un follow-up di 17 ± 7 settimane. Similmente, lo studio di Oldenburg et al.[38], pubblicato nel 2007, ha dimostrato in 36 pazienti eleggibili per CRT e con CSA, un miglioramento dell'AHI, della saturazione minima e della percentuale di desaturazione notturna dopo 5.3 ± 3 mesi dall'inizio della CRT. Tale dato non è stato, invece, in questo studio, confermato nel sottogruppo di pazienti con OSA. Al contrario, Stanchina et al.[39] hanno riportato in 13 pazienti in programma per CRT e con diagnosi di OSA, una riduzione dell'AHI medio in associazione ad un aumento della frazione di eiezione e al tempo di circolazione, quale misura indiretta della portata cardiaca. Il miglioramento dei disturbi del sonno dipende, in questi pazienti, da una risposta positiva sia di tipo clinico che emodinamico alla CRT e tali risultati aprono nuove prospettive terapeutiche per i pazienti affetti da SA. L'analisi dei disturbi del sonno potrebbe, inoltre, nel futuro, essere utilizzata come ulteriore strumento per la valutazione dell'efficacia della CRT.

insufficienza cardiaca. L'individuazione della presenza di apnee notturne in tali pazienti è di grande importanza per intraprendere modifiche dello stile di vita e percorsi terapeutici in grado di determinare un miglioramento della qualità di vita, nonché un rallentamento della progressione dell'insufficienza cardiaca congestizia.

Terapia HF deve dipendere ANCHE dalla valutazione del profilo apnoico del pz HF

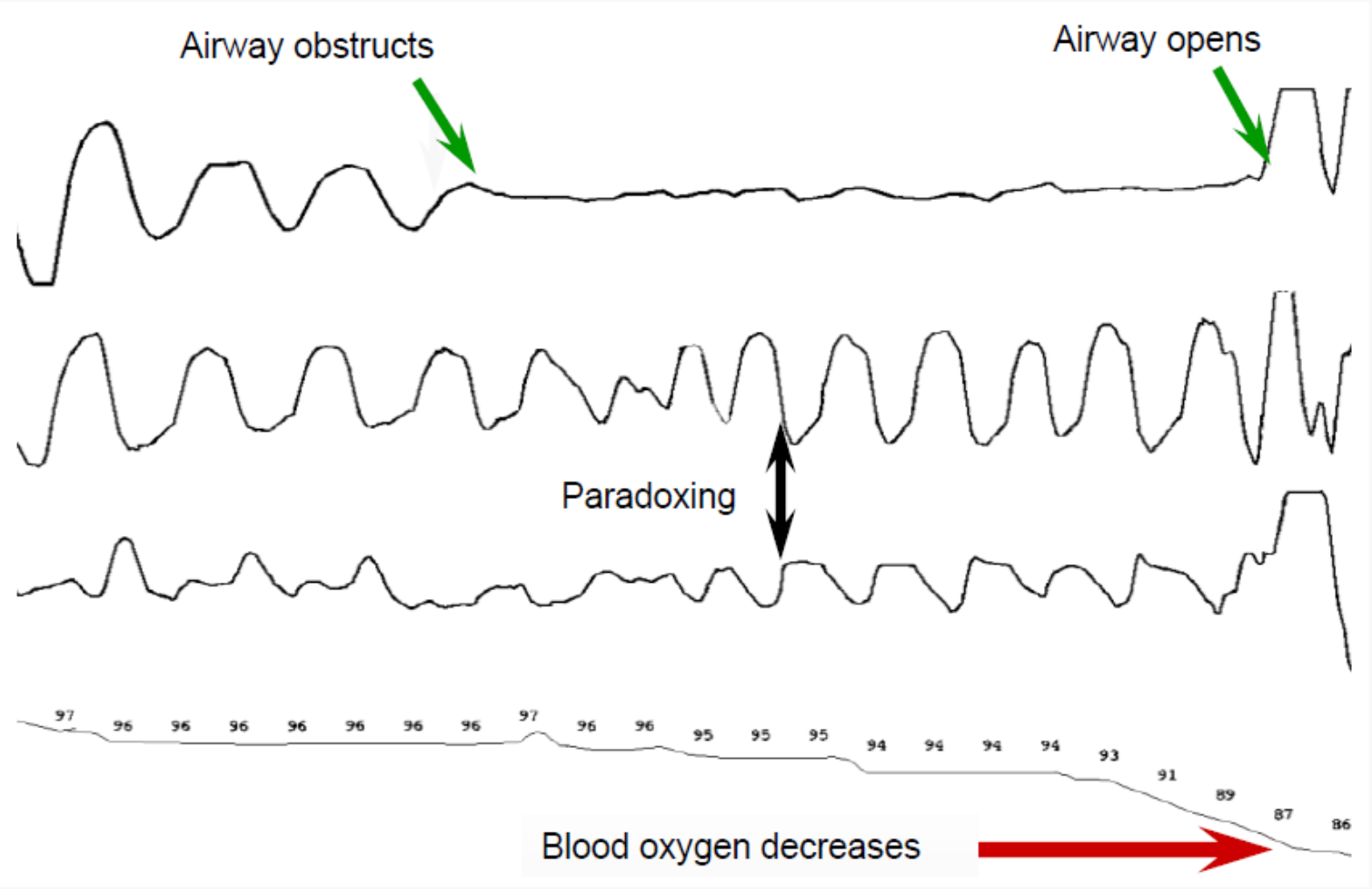
Monda C, Scala O et al. G Ital Cardiol ***2010***

Cuore ⇔ Sonno: nuovi modelli di gestione clinica?



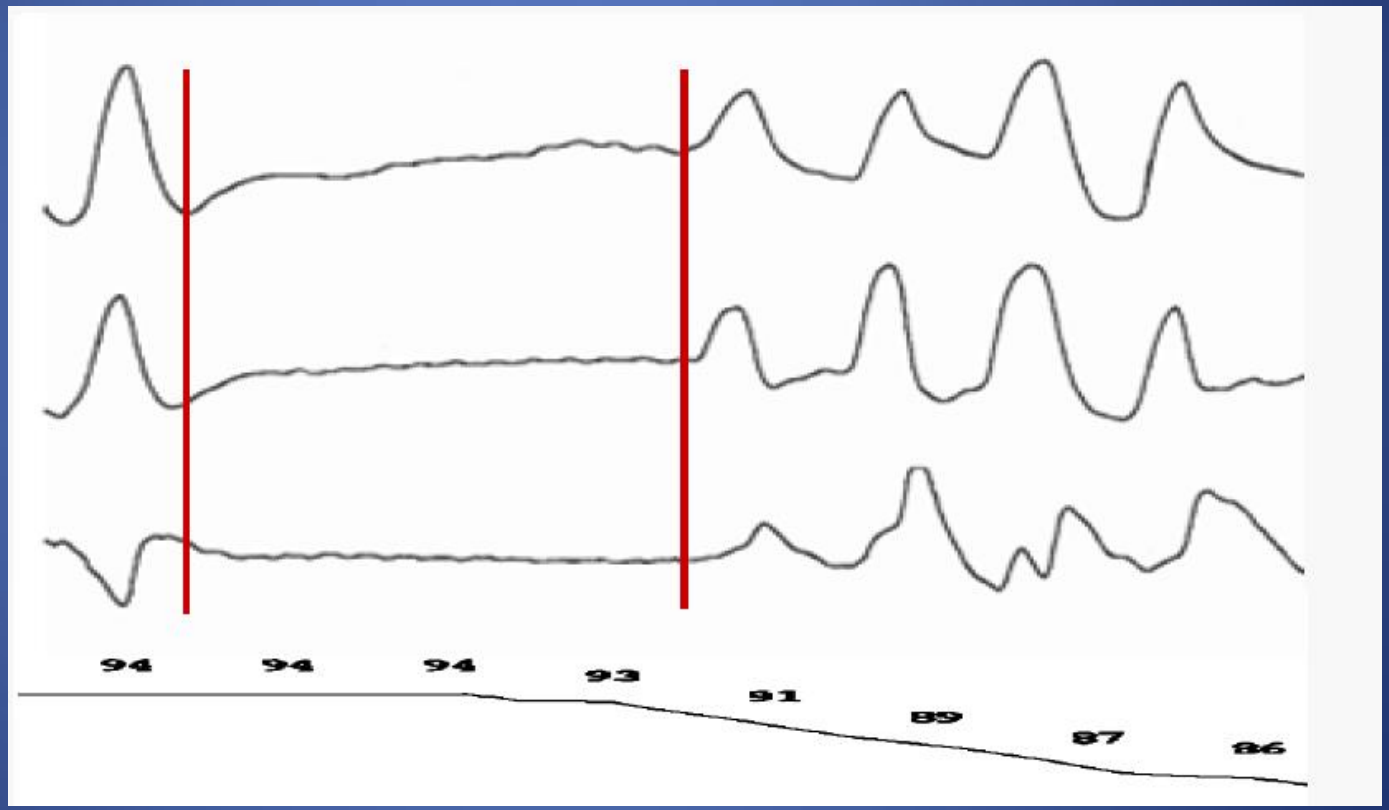
Apnea/Ipopnea Ostruttiva

OSA

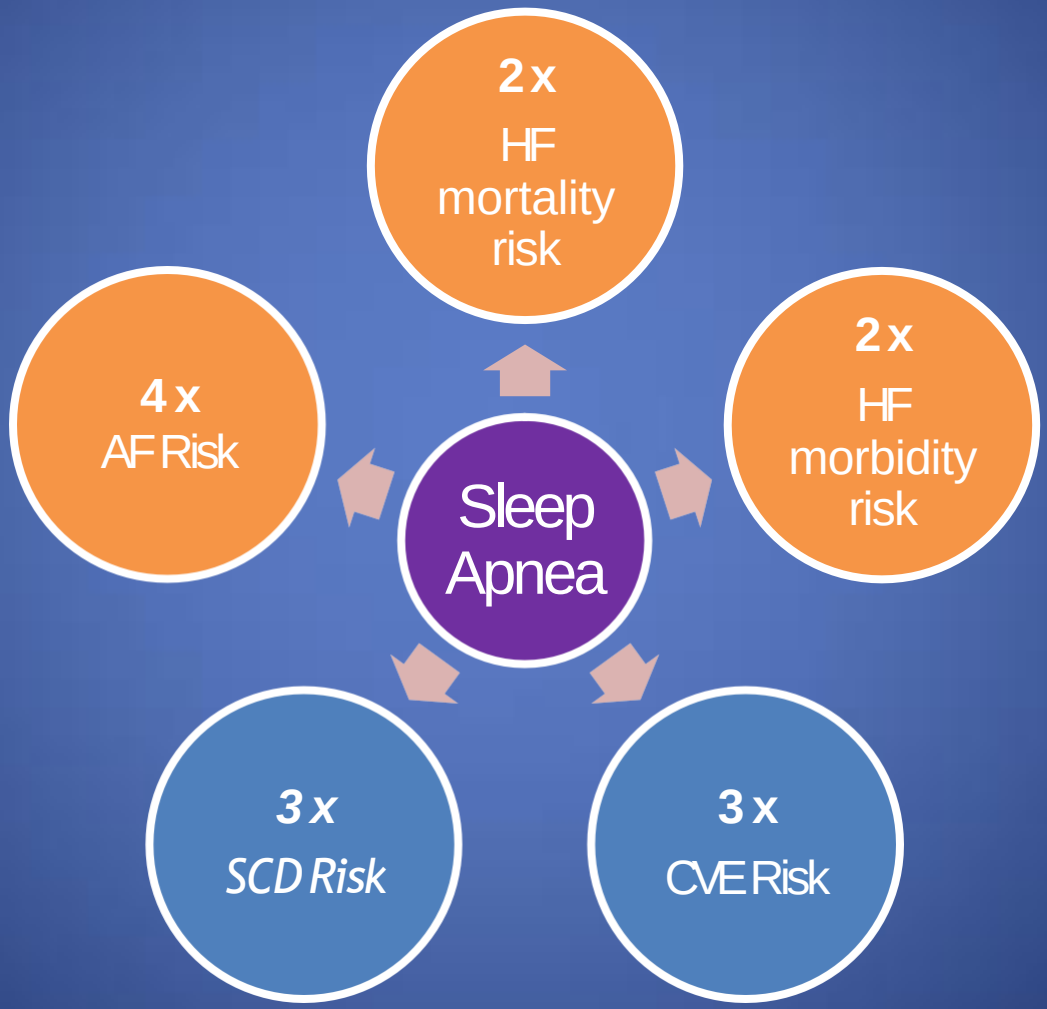


Apnea/Ipopnea Centrale

CSA



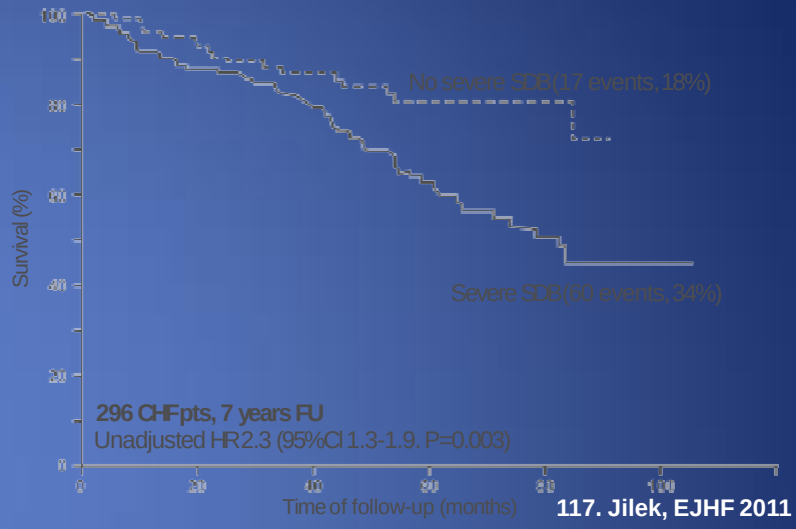
Sleep Apnea e conseguenze cardiovascolari



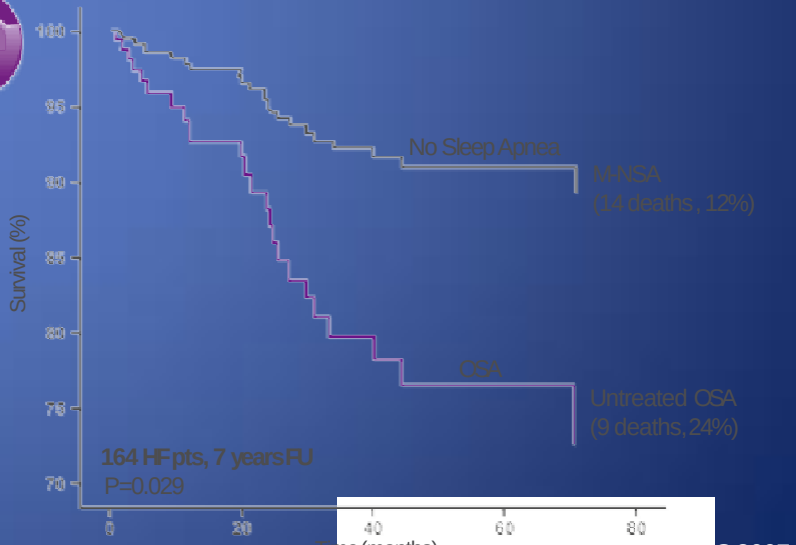
2012 Clinical update

Conseguenze cardiovascolari delle apnee notturne

- **Mortalità per Scompenso**
  - La **mortalità per HF aumenta di 2 volte**
  - Peggioramento della sopravvivenza nei pazienti con HF con apnea notturna non trattata rispetto ai pazienti con apnea notturna lieve o assente (76% vs. 88%).
  - **Sopravvivenza maggiore** per i pazienti con apnea notturna trattata.
- **Complicanze per HF**
  - OSA può portare ad un peggioramento dello scompenso e refrattarietà alla terapia
  - OSA aumenta le complicanze dello scompenso di 2.2 volte.
- **Eventi cardiovascolari**
  - La Sleep Apnea Ostruttiva severa aumenta il rischio di eventi cardiovascolari fatali di 3 volte



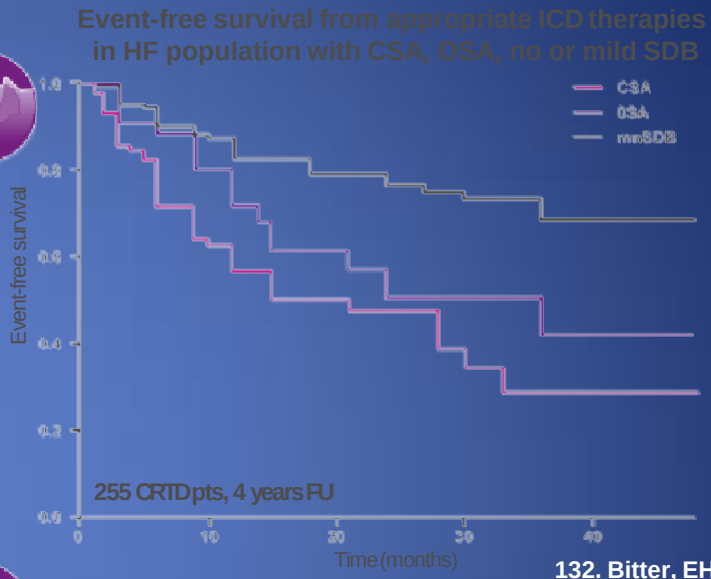
117. Jilek, EJHF 2011



C 2007

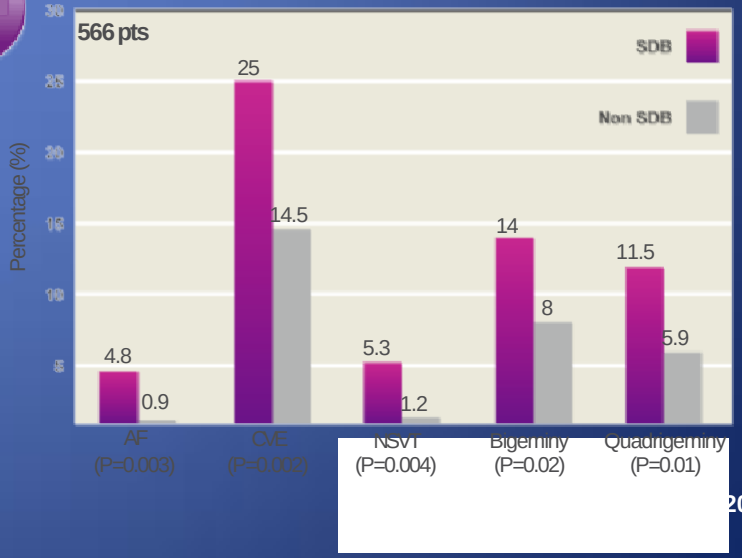
Conseguenze cardiovascolari dell'Apnea Notturna

- **Morte Improvvisa**
  - La Sleep Apnea **aumenta il rischio di TV/FV & terapie ICD di 2-3 volte.**



132. Bitter, EHJ 2011

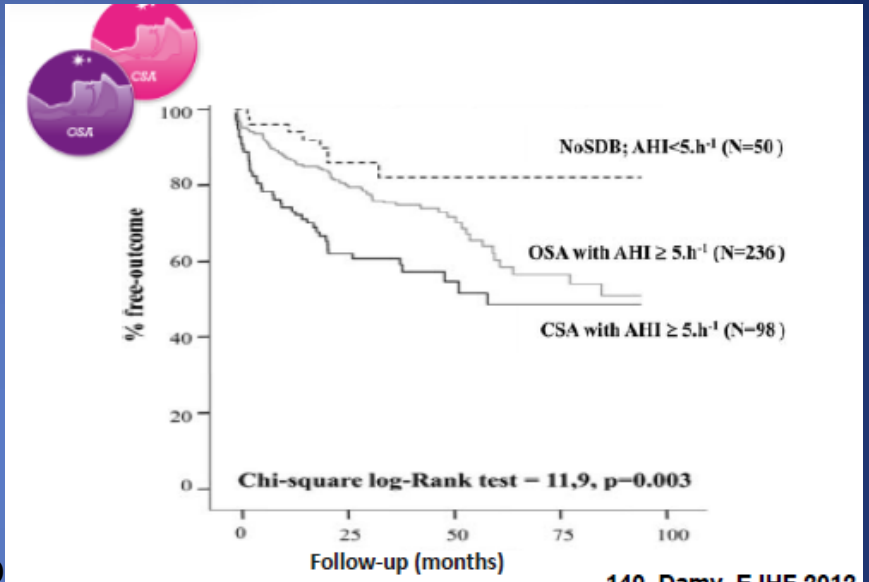
- **Fibrillazione Atriale**
  - La Sleep Apnea è un predittore indipendente di **nuovi episodi di FA**, e può essere una causa dello sviluppo dell'**FA**
  - La Sleep Apnea aumenta la probabilità di **FA ricorrenti dopo cardioversione** (dal 42% all' 82%).
  - **La ricomparsa si riduce dopo terapia CPAP.**



2006

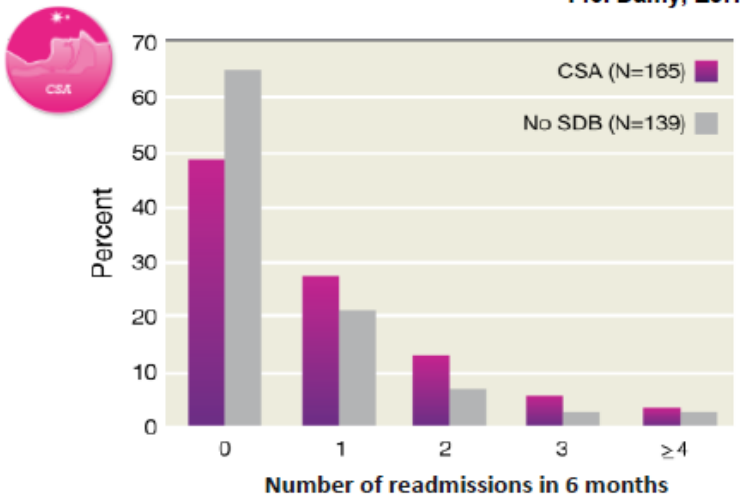
Conseguenze cardiovascolari dell'Apnea Notturna – un aggiornamento dagli studi del 2012

- **Mortalità e peggioramento dello Scompenso**
  - OSA e CSA mostrano una **prognosi sfavorevole** nei pazienti con CHF rispetto ai pazienti senza SDB, **considerando morte, trapianto cardiaco** o impianto di un dispositivo di assistenza ventricolare (graph)
  - **CPAP** per SDB severa **incrementa l'outcomes nei pazienti Scompensati** (HR = 0.56, p = 0.031)



140. Damy, EJHF 2012

- **Rischio di riammisione cardiaca nello Scompenso**
  - Il fattore di rischio indipendente da CSA per riammissioni cardiache di sei mesi nei pazienti con HF (rischio aumentato del 53% vs pazienti senza SDB, p = 0.03).
  - CSA durante il ricovero per scompenso predice quindi un incremento significativo delle complicanze.



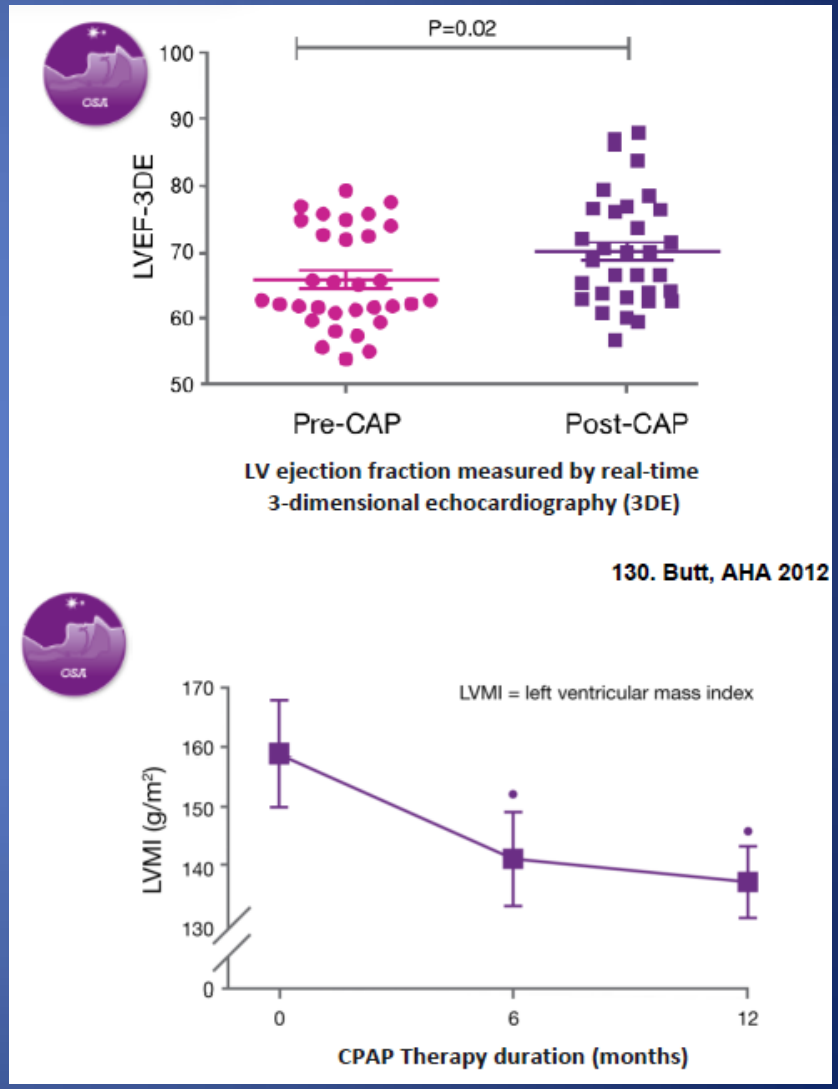
127. Khayat, JCF 2012

2012 Clinical update

Conseguenze cardiovascolari dell'Apnea Notturna – un aggiornamento dagli studi del 2012

- **Funzione cardiaca nei pazienti con scompenso**
  - I cambiamenti strutturali e funzionali del Ventricolo Sinistro nei pazienti OSA sono **comparabili con quelli dell'ipertensione**.
  - **La terapia CPAP incrementa significativamente la frazione di eiezione LV e riduce lo spessore delle pareti posteriori nei pazienti in** OSA ($p \leq 0.05$)

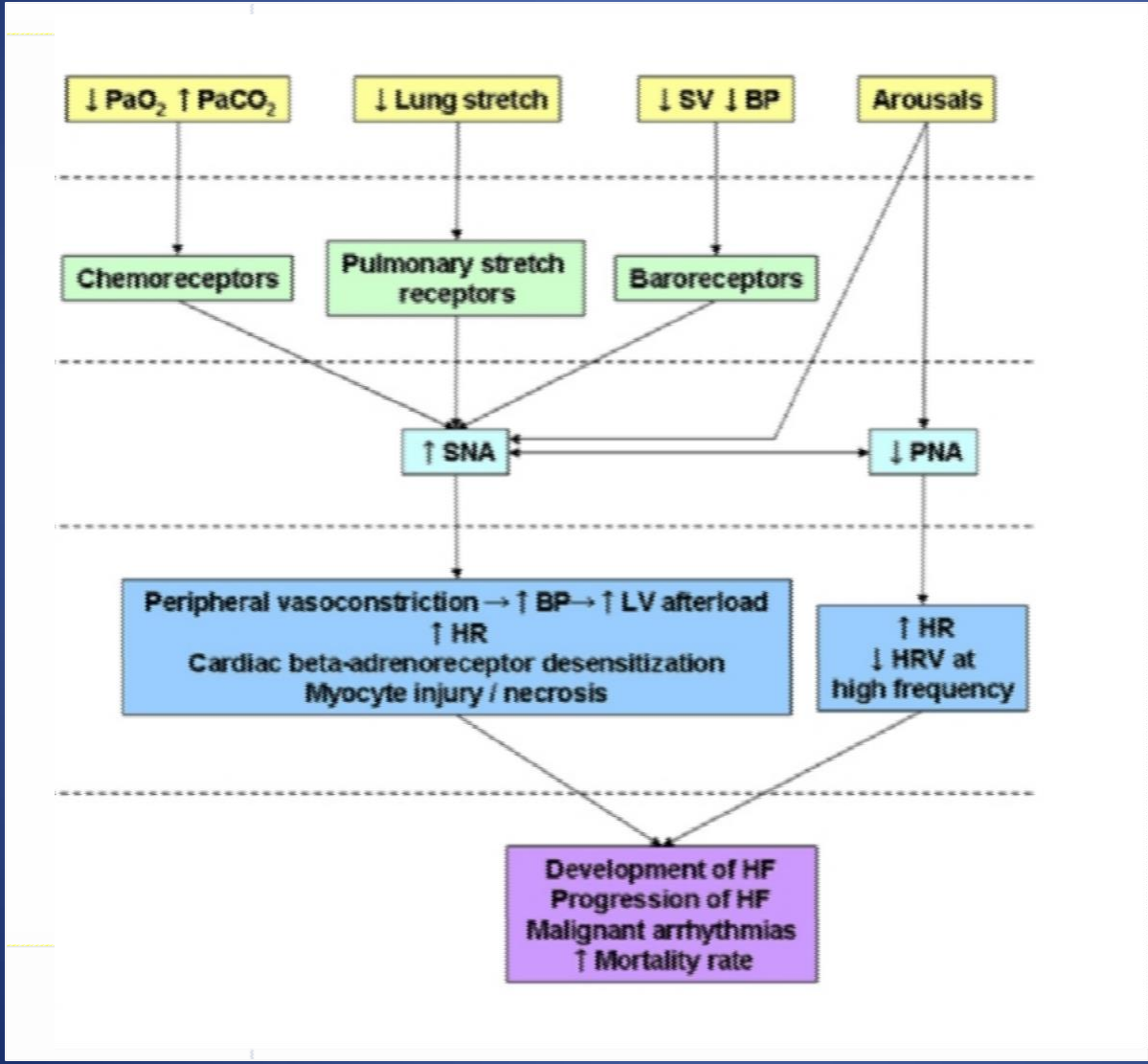
- **Rimodellamento cardiaco nei pazienti scompensati**
  - Nei pazienti con OSA entrambe le anomalie **sistoliche e diastoliche possono essere invertite con la terapia CPAP** entro 3-6 di terapia
  - La massa del Ventricolo Sinistro si è ridotta significativamente con sei mesi di terapia ed è continuata a migliorare ad un anno.



2012 Clinical update

Effetti della Sleep Apnea Ostruttiva OSA: Aritmie, Scompenso, Mortalità

OSA



OSA

Sensor Activated

Autonomic imbalance

Effect on CV system

Negative clinical outcome

Kasai, J Am Coll Cardiol 2011;57:119–27

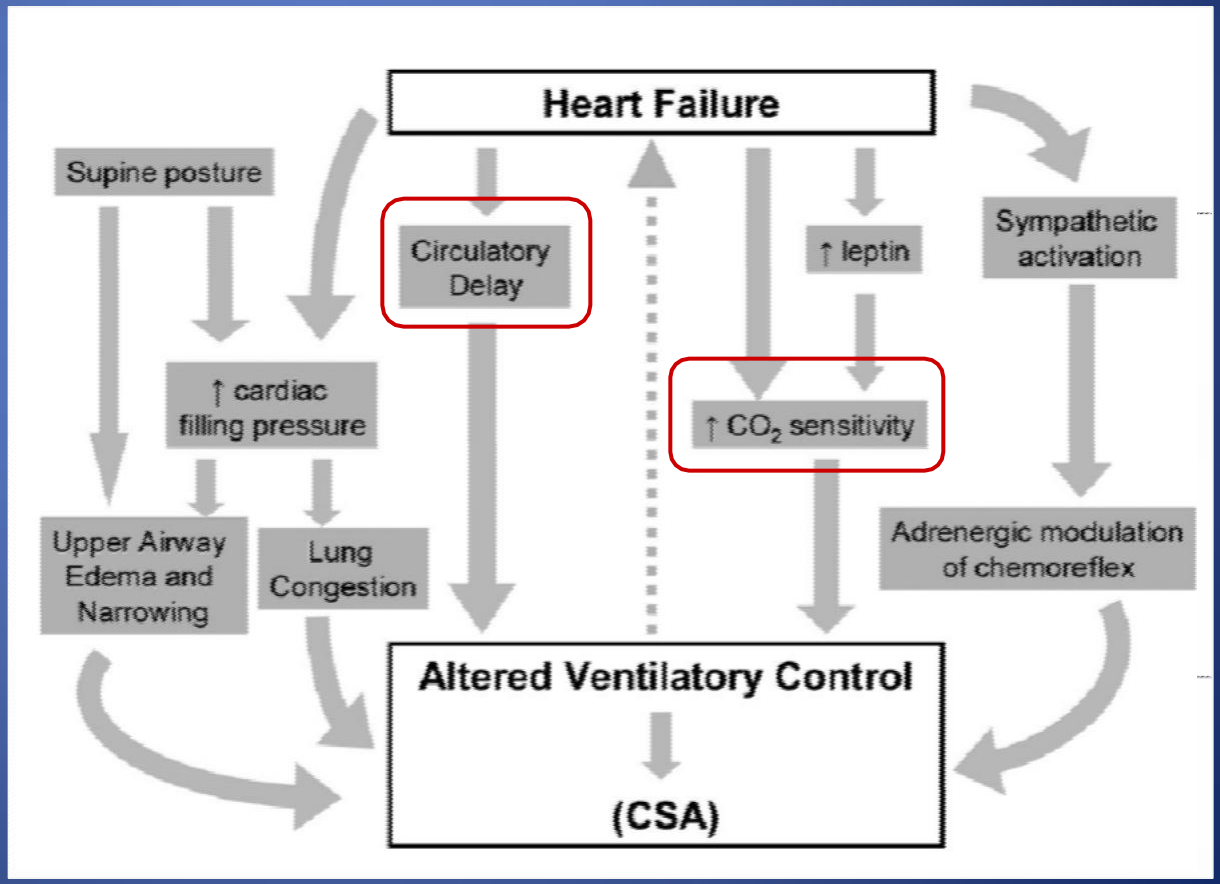
Sleep Apnea Centrale ed interazione con lo scompenso

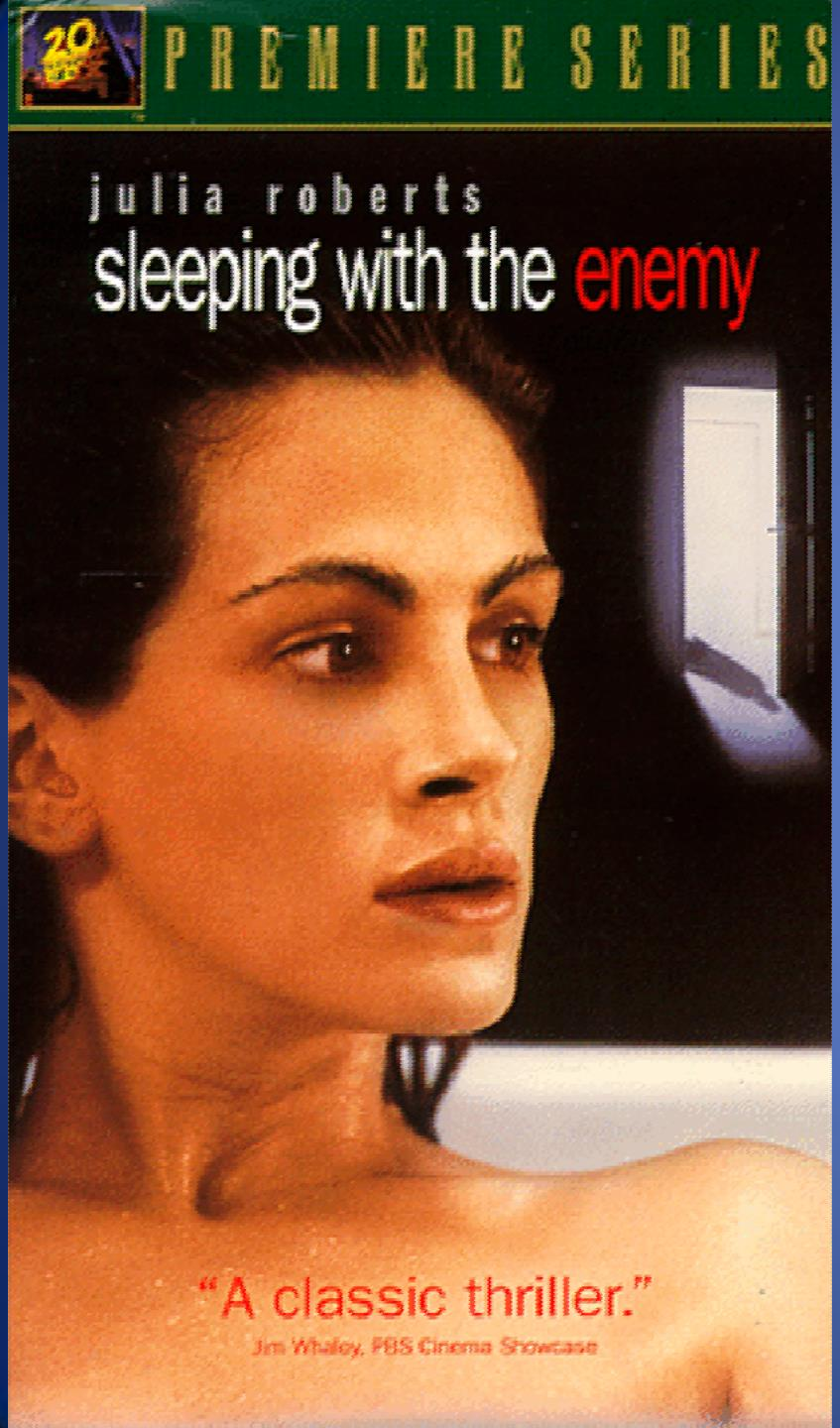
- La Sleep Apnea Centrale è caratterizzata da cessazioni ripetitive della respirazione durante il sonno derivante dalla perdita di ventilazione
- Nei pazienti con HF, la CSA si ritiene che derivi da una combinazione di:

CSA

increased CO2 sensitivity

prolonged circulation time (Circulatory Delay)

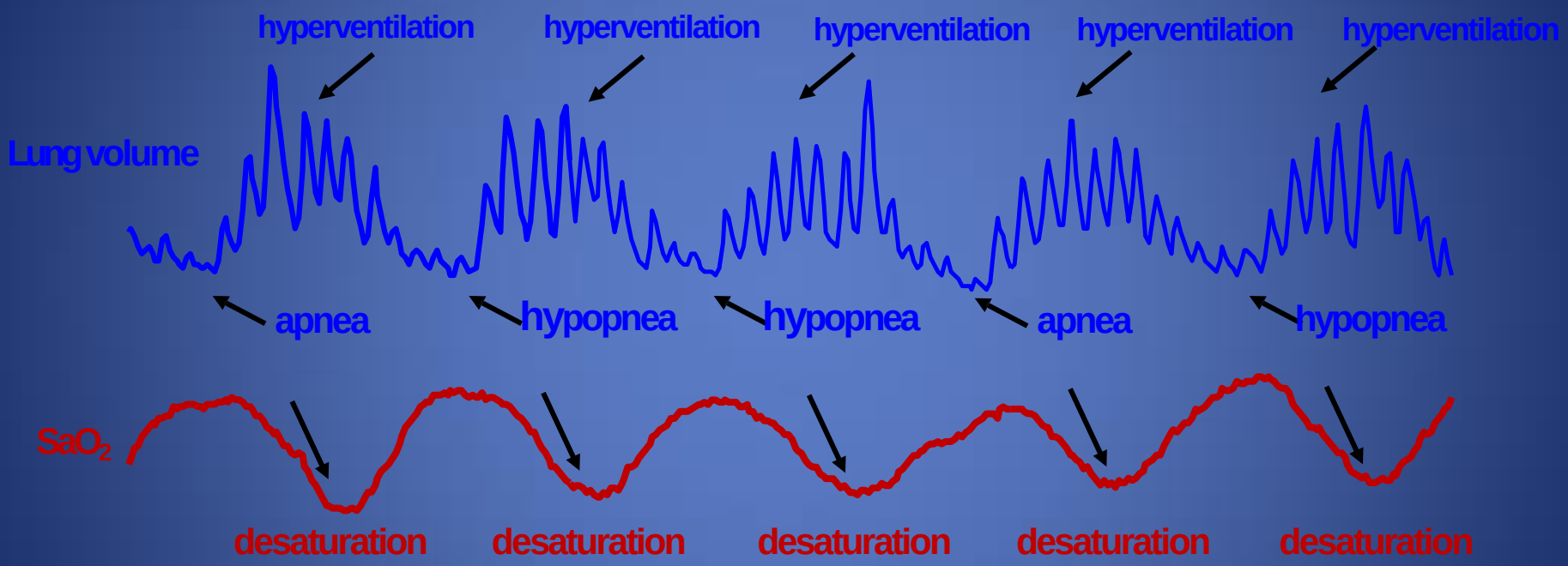




Respirazione Disordinata nel sonno

Respirazione Disordinata nel Sonno

Attacchi ricorrenti di Overshoots e Undershoots Ventilatori



Apnea: cessazione del flusso di aria per più di 10 sec

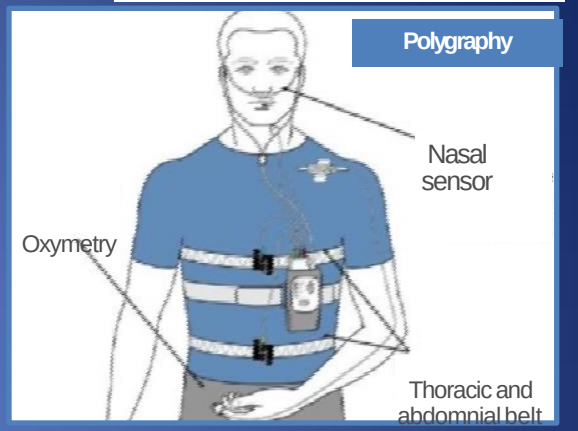
Ipopnea: riduzione del flusso di aria per più del 50% rispetto al normale, di solito in associazione con una riduzione di SaO2

Diagnosi della Sleep Apnea

- **Diagnosi della Sleep Apnea:**
  - **Poligrafia (PG)**: registra il numero di eventi per ora
  - **Polisonnografia (PSG)**: definisce il tipo di evento (apnea Ipopnea, ostruttiva o centrale). PSG è l'esame diagnostico di riferimento.
  - PSG= PG+ (EEG/EOG/EMG)

- **Apnea/Hypopnea Index (AHI) = Numero di apnee + Ipopnee per ora (di sonno)**
  - 5 ≤ AHI< 15 Sleep Apnea lieve
  - 15 ≤ AHI< 30 Sleep Apnea moderata
  - AHI≥ 30 Sleep Apnea severa

  - **Diagnosis of SAS is confirmed for AHI ≥ 5**



American Academy of Sleep Medicine Task Force (Sleep 1999;22:667-689):
EEG = Electro EncephaloGram , EOG = ElectroOculoGram,
EMG = Electro MioGram

Conclusioni

- La Sleep Apnea è :
  - molto presente nei pazienti CRM e con Scompenso
  - una patologia importante
  - associata ad un aumento del rischio di FA, SCD nei pazienti con ICD e CRT
  - associata ad un aumentpo del rischio di mortalità e peggioramento dello scompenso
  - fortemente non diagnosticata
- Le conseguenze della Sleep Apnea possono essere invertite con terapie appropriate

Patients at High Risk for Central Sleep Apnea

- ✓ **Primary risk factors for Central Sleep Apnea**
  - ✓ Recent heart failure hospitalization
  - ✓ Chronic fatigue
  - ✓ Nocturia (> 2 per night)
  - ✓ Atrial fibrillation
  - ✓ Ventricular arrhythmias
  - ✓ Witnessed apneas
- ✓ **Additional risk factors (secondary)**
  - ✓ Male
  - ✓ Elderly
  - ✓ Lean
  - ✓ Decreased exercise tolerance
  - ✓ Low ejection fraction
    - » Paroxysmal nocturnal dyspnea (PND)
    - » Stroke
    - » Carotid stenosis
    - » Diabetes mellitus

Sleep apnoea in heart failure - summary

1. Present as OSA or CSA (specific for HF syndrome)
2. Prevalent (affects more than 50% HF pts),
   but still under-recognized among cardiologists
3. Diagnosis possible in the everyday cardiology practice
4. Ominous pathophysiological and clinical consequences
   (progression of the disease, increased M&M)
5. Potential therapeutic target in HF

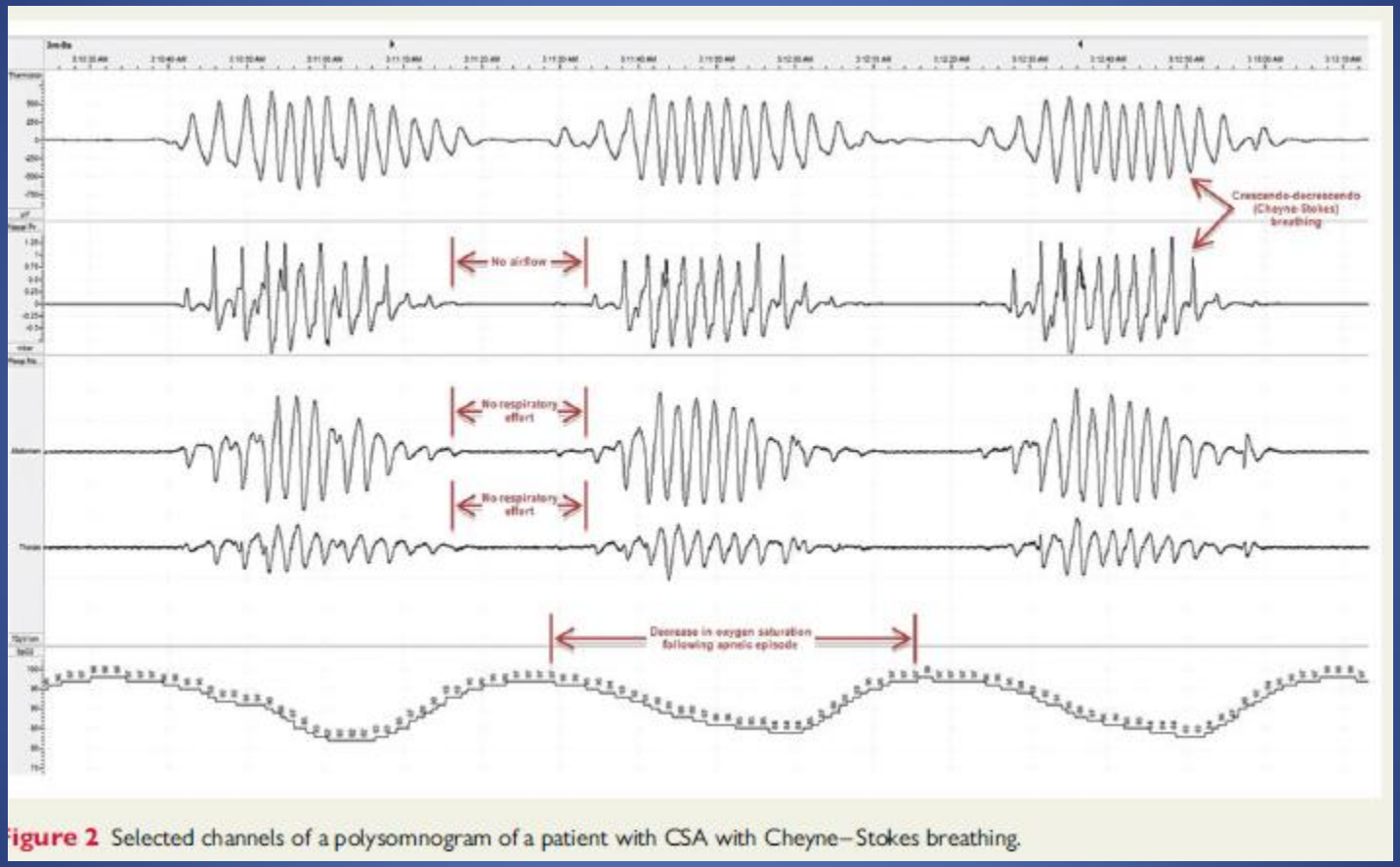


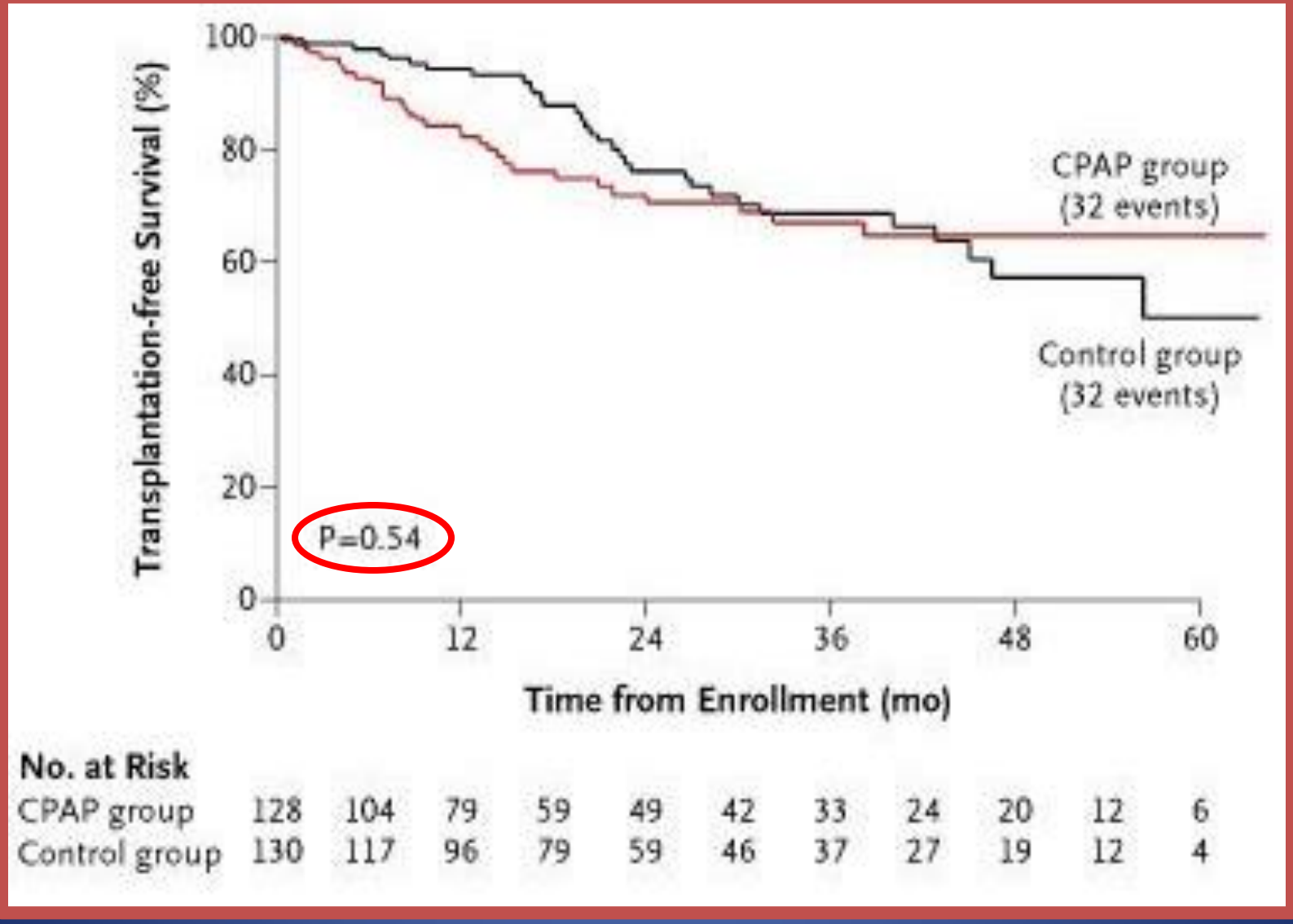
Figure 2 Selected channels of a polysomnogram of a patient with CSA with Cheyne–Stokes breathing.


Snoring
Snoring
Snoring
Snoring
Snoring
OSA (41.70s)
OSA (25.60s)
OSA (36.10s)
OSA (21.10s)
OSA
OSA (21.10s)
Desaturation (38.67s) [14]
Desaturation (28.67s) [12]
Desaturation (29.67s) [14]
Desaturation (39.67s) [17]
CSA (9.16s)
CSA (10.75s)
CSA (10.15s)
CSA (15.10s)
No effort
No effort
No effort
No effort
No effort
No effort
No effort
No effort
Desaturation (20.33s) [11]
Desaturation (17.00s) [9]
Desaturation (24.00s) [11]
Desaturation (21.00s) [9]

Canadian Continuous Positive Airway Pressure for Patients with Central Sleep Apnea and Heart Failure Trial (CANPAP)

- Randomized, controlled clinical trial involving 258 HF patients with CSA (mean LVEF= 24.5)
- Hypothesis: Does continuous positive airway pressure (CPAP) improve both survival without heart transplantation and cardiovascular function
- Randomized 128 CPAP/130 Control
- Endpoints
  - Transplant-free survival
  - EF
  - Exercise capacity
  - Quality of life
  - Neurohormonal changes

Heart-Transplantation-Free Survival

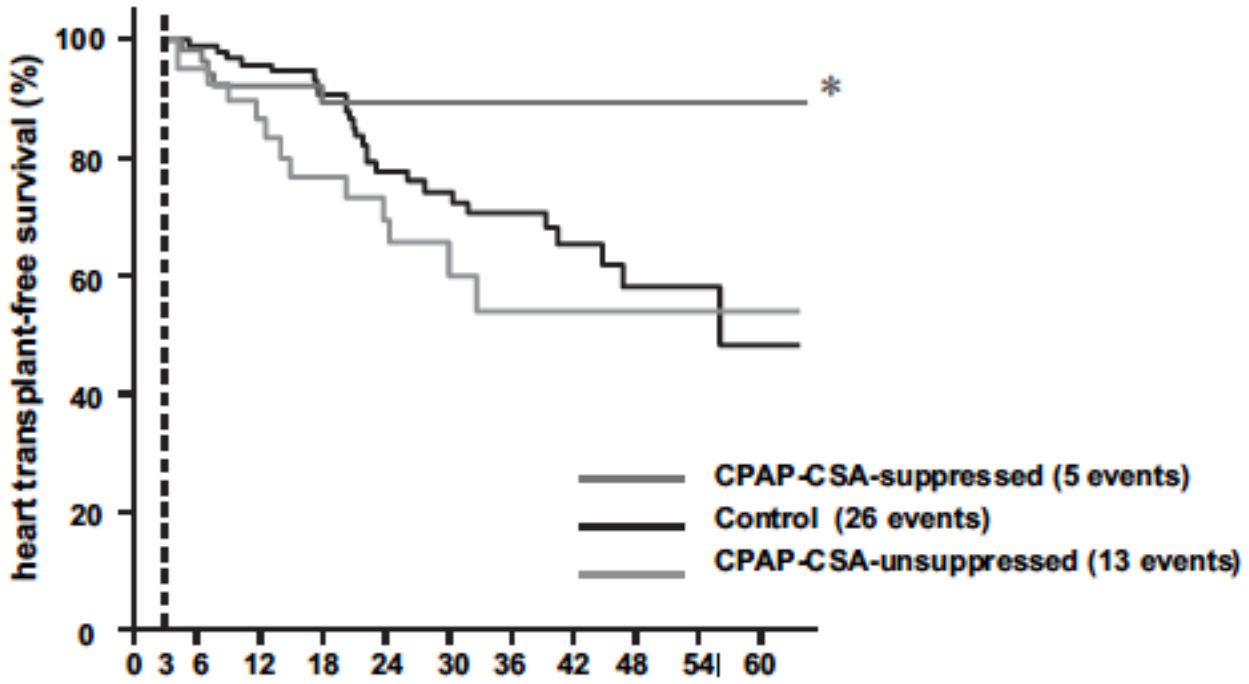


Bradley T et al. N Engl J Med 2005;353:2025-2033

The NEW ENGLAND JOURNAL of MEDICINE

CANPAP trial : early suppression of CSA by CPAP to an AHI below 15/hr may improve LVEF and transplant-free survival

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



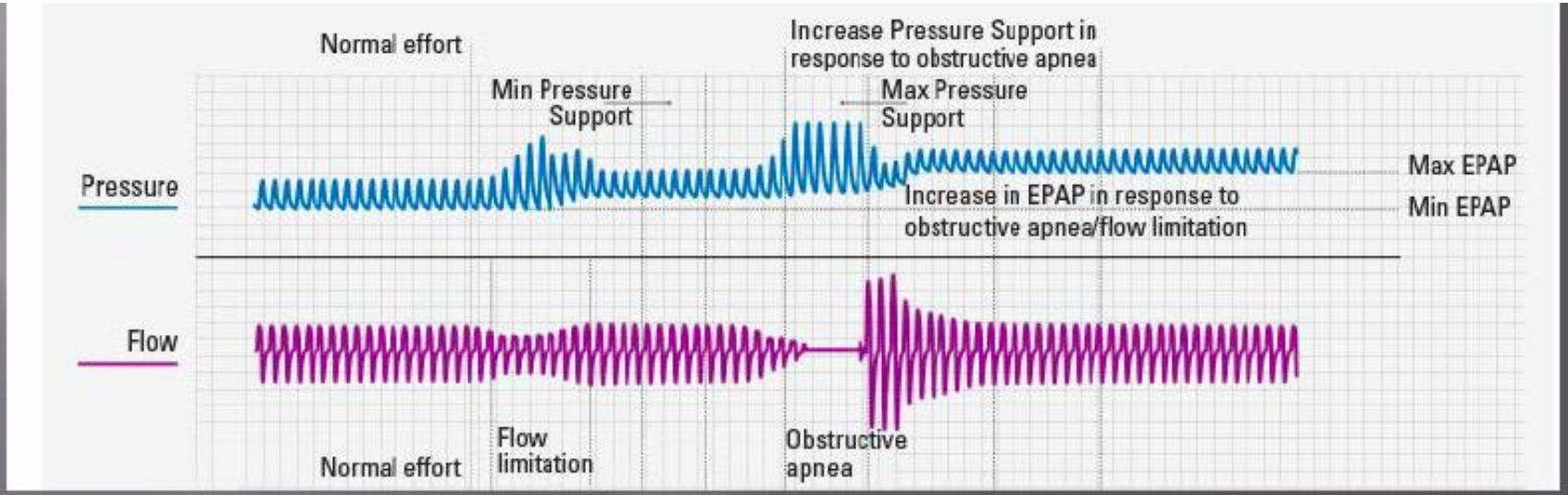
number at risk

CPAP-CSA-suppressed (n=57)	51	38	31	27	23	21	15	11	7	3
Control (n=110)	99	83	71	50	41	33	22	15	9	3
CPAP-CSA-unsuppressed (n=43)	36	27	22	18	12	9	6	6	4	2

Adaptive Servoventilation

Stabilises breathing and maintains upper airway open.

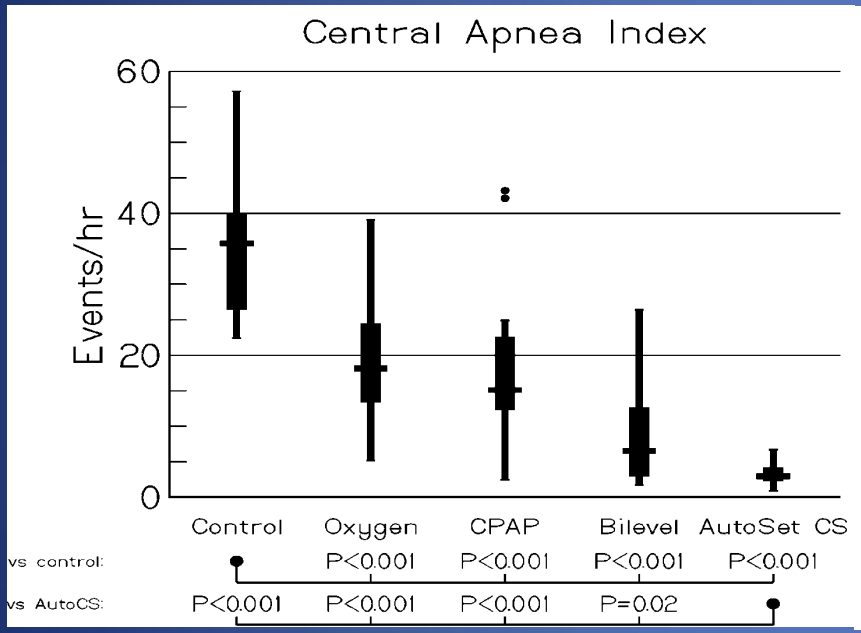
Continually adjusting inspiratory and expiratory pressure with variable, on-demand, back up rate.

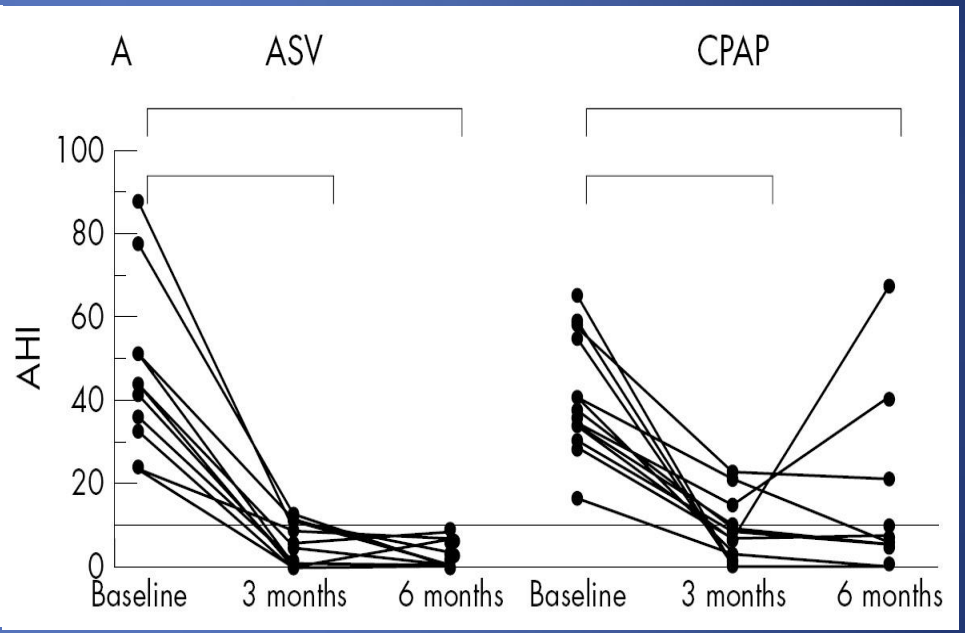


Allam, J.S., et al. Chest, 2007. 132(6): 1839-46.

SERVE-HF: Background (3)

- **ASV is more effective than CPAP for treating CSA/CSR**





- **HF patients comply better with ASV vs CPAP therapy**
- **Patients prefer ASV over both CPAP and bilevel PAP**

Teschler et al. AJRCCM 2001; Philippe et al. Heart 2006; Kasai et al. Circ Heart Fail 2010.

SERVE-HF: Baseline

	Control (n=659)	ASV (n=666)
Age, years	69.3±10.4	69.6±9.5
Male	90.0%	89.9%
NYHA class III or IV, n (%)	70.3%	70.5%
LVEF, %	32.5±8.0	32.2±7.9
Ischaemic HF aetiology, n (%)	57.0%	59.7%
Implanted device, n (%)	55.2%	54.5%
eGFR, mL/min/1.73m^2	59.3±20.8	57.8±21.1
Six-minute walk distance, m	337.9±127.5	334.0±126.4
ACEI/ARB, n (%)	91.5%	92.0%
β-blockers, n (%)	92.7%	91.9%
Antiarrhythmics, n (%)	13.5%	19.2%

p=0.005

Cowie et al. NEJM 2015, 1 Sep [Epub ahead of print].

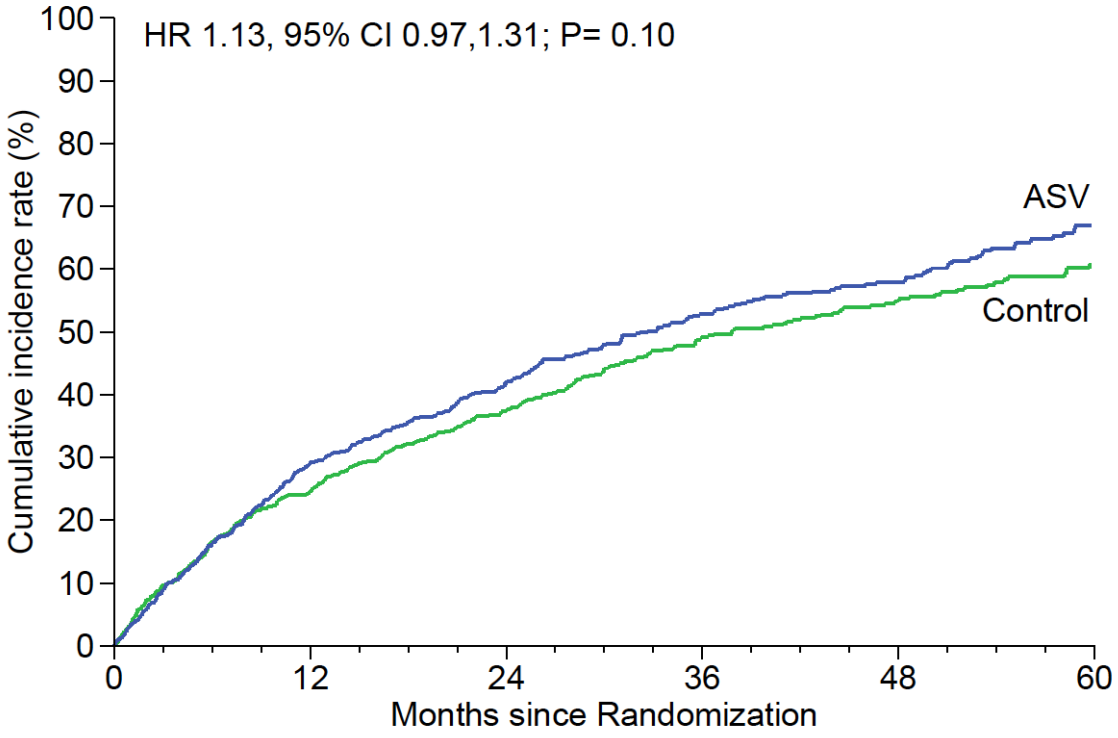
Baseline Respiratory Characteristics

	Control (n=659)	ASV (n=666)
AHI, /h	31.7±13.2	31.2±12.7
cAI/total AHI, %	46.5±30.0	44.6±28.9
cAHI/total AHI, %	81.8±15.7	80.8±15.5
Desaturation index (3%), /h	32.8±19.0	32.1±17.7
Average SaO_2, %	92.8±2.5	92.8±2.3
Minimum SaO_2, %	80.3±7.5	80.7±7.0
Time with SaO_2 <90%, min	55.7±73.9	50.5±68.2
Epworth Sleepiness Scale score	7.1±4.6	7.0±4.3

Cowie et al. NEJM 2015;373:1095-105.

Primary Endpoint Neutral

Time to first event of all-cause death, life-saving cardiovascular intervention, or unplanned hospitalization for worsening chronic HF

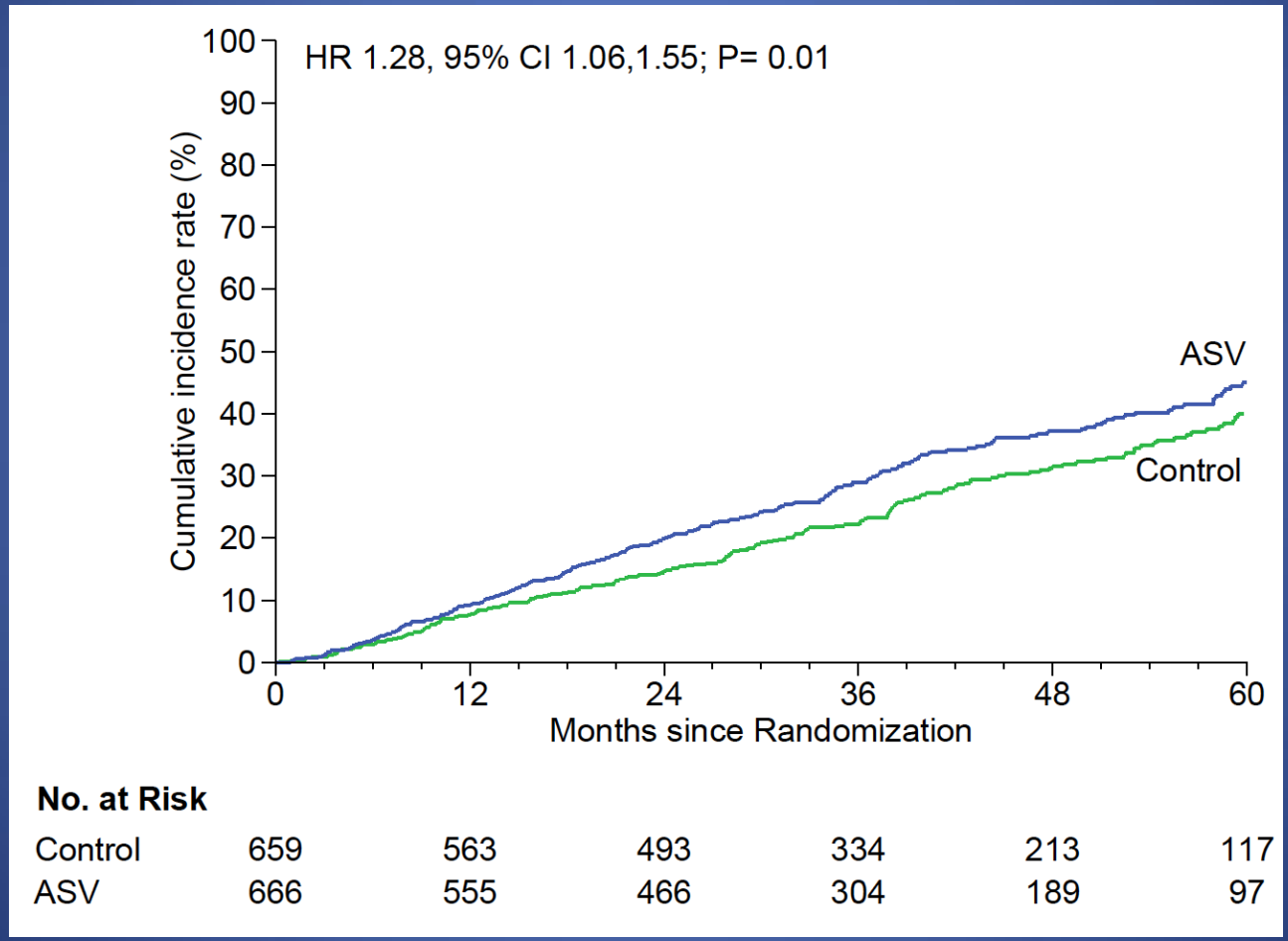


No. at Risk

Control	659	463	365	222	136	77
ASV	666	435	341	197	122	52

Cowie et al. NEJM 2015, 1 Sep [Epub ahead of print].

All-Cause Death

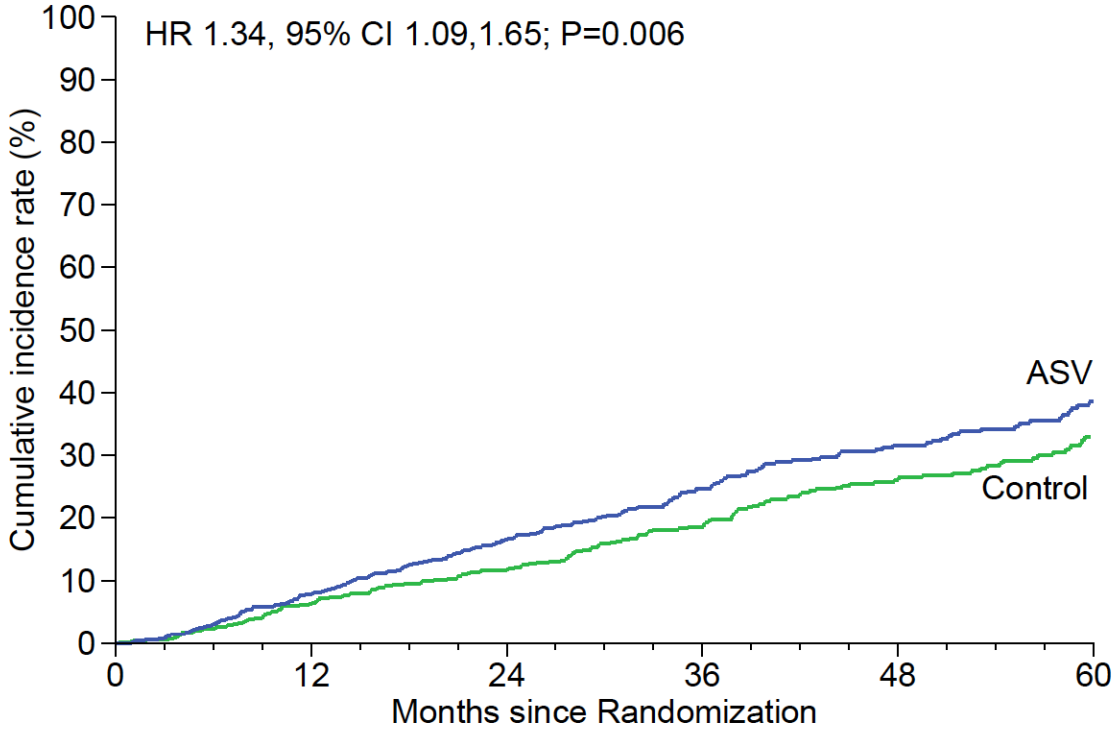


No. at Risk

Control	659	563	493	334	213	117
ASV	666	555	466	304	189	97

Cowie et al. NEJM 2015, 1 Sep [Epub ahead of print].

Cardiovascular Death

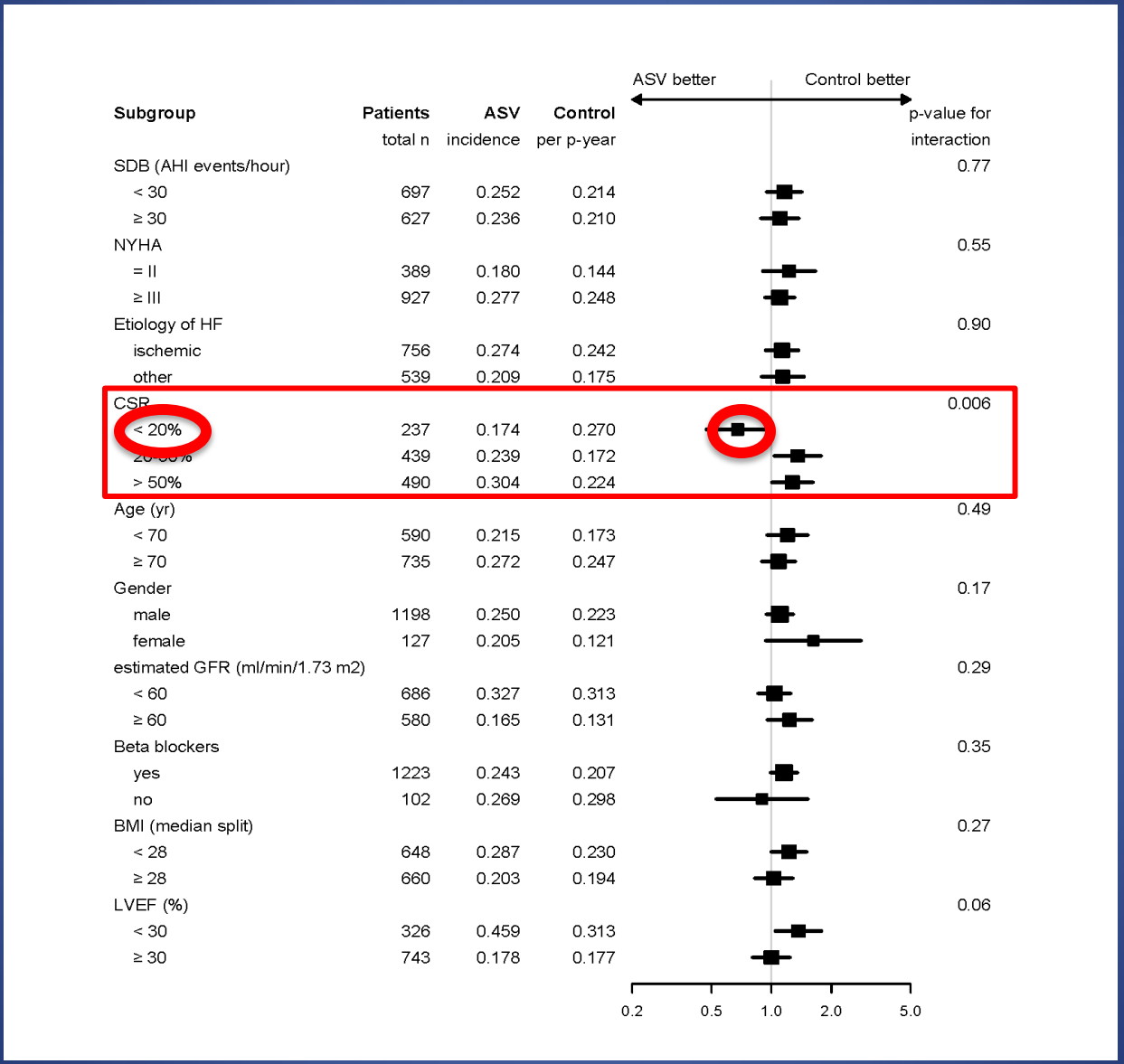


No. at Risk

Control	659	563	493	334	213	117
ASV	666	555	466	304	189	97

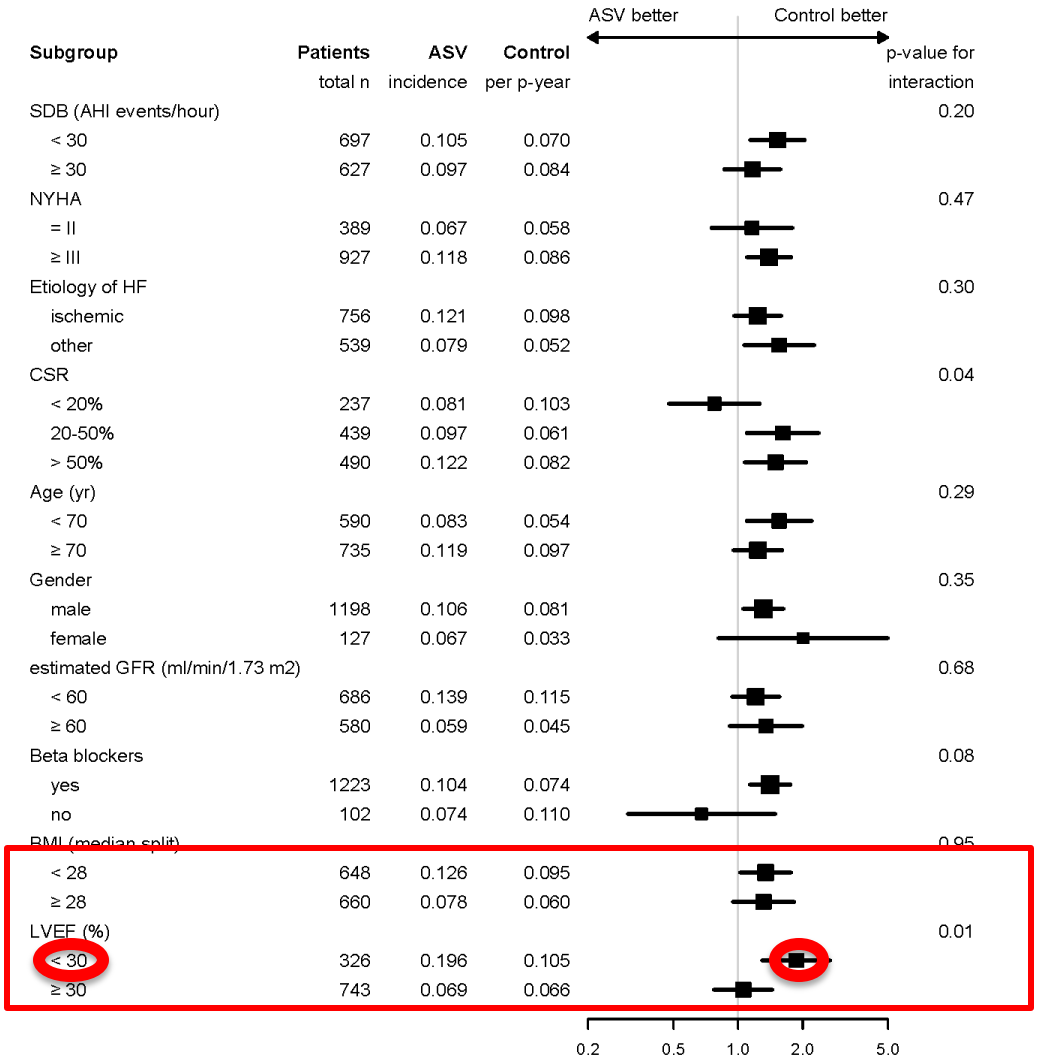
Cowie et al. NEJM 2015, 1 Sep [Epub ahead of print].

Subgroup Analysis: 1° Endpoint



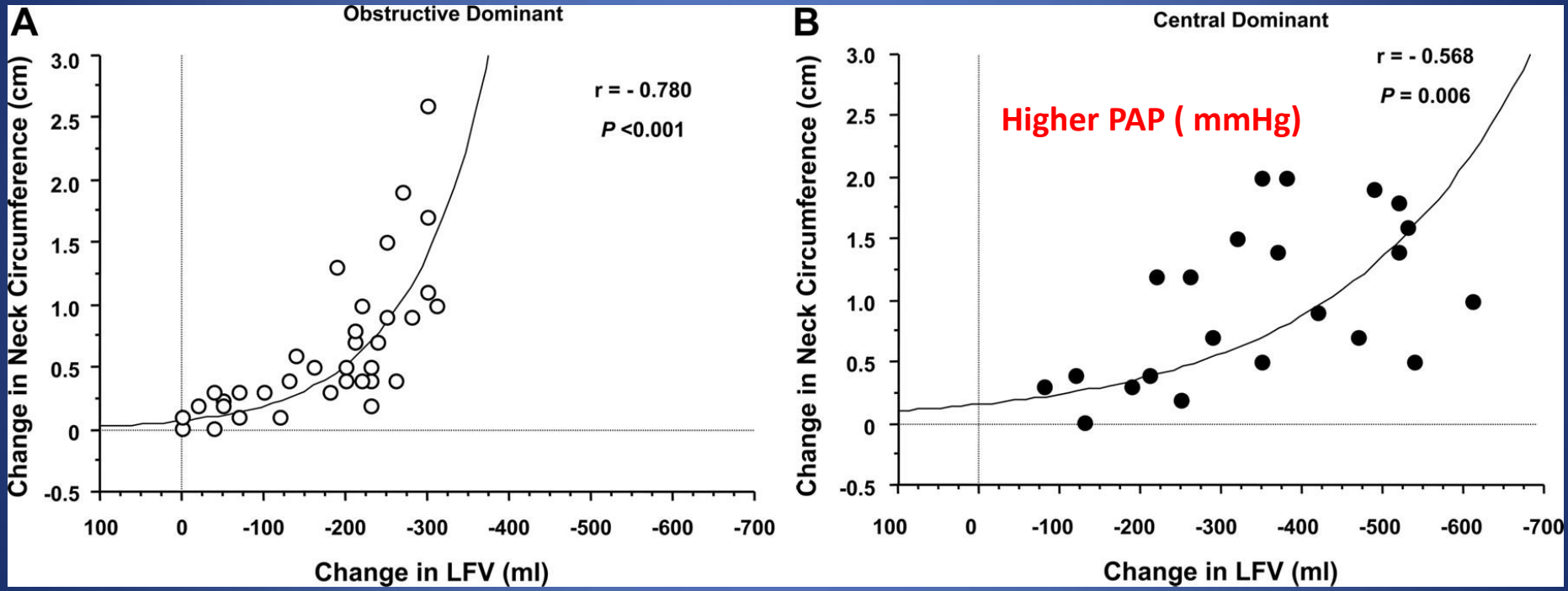
Cowie et al. NEJM 2015, 1 Sep [Epub ahead of print].

Subgroup Analysis: CV Death



Cowie et al. NEJM 2015, 1 Sep [Epub ahead of print].

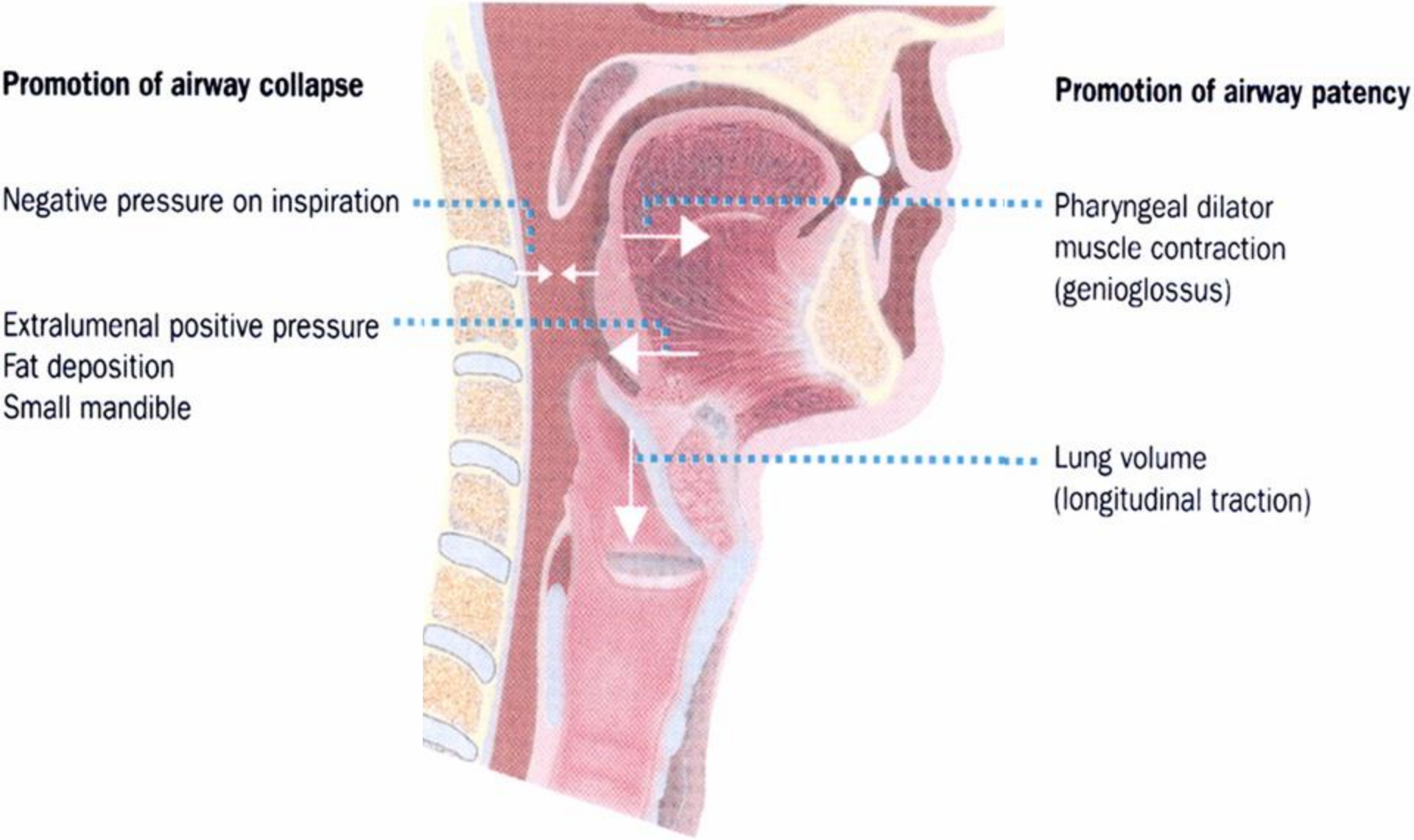
Inverse exponential relationships between overnight changes in neck circumference and LFV in the obstructive- (A) and central-dominant (B) groups



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

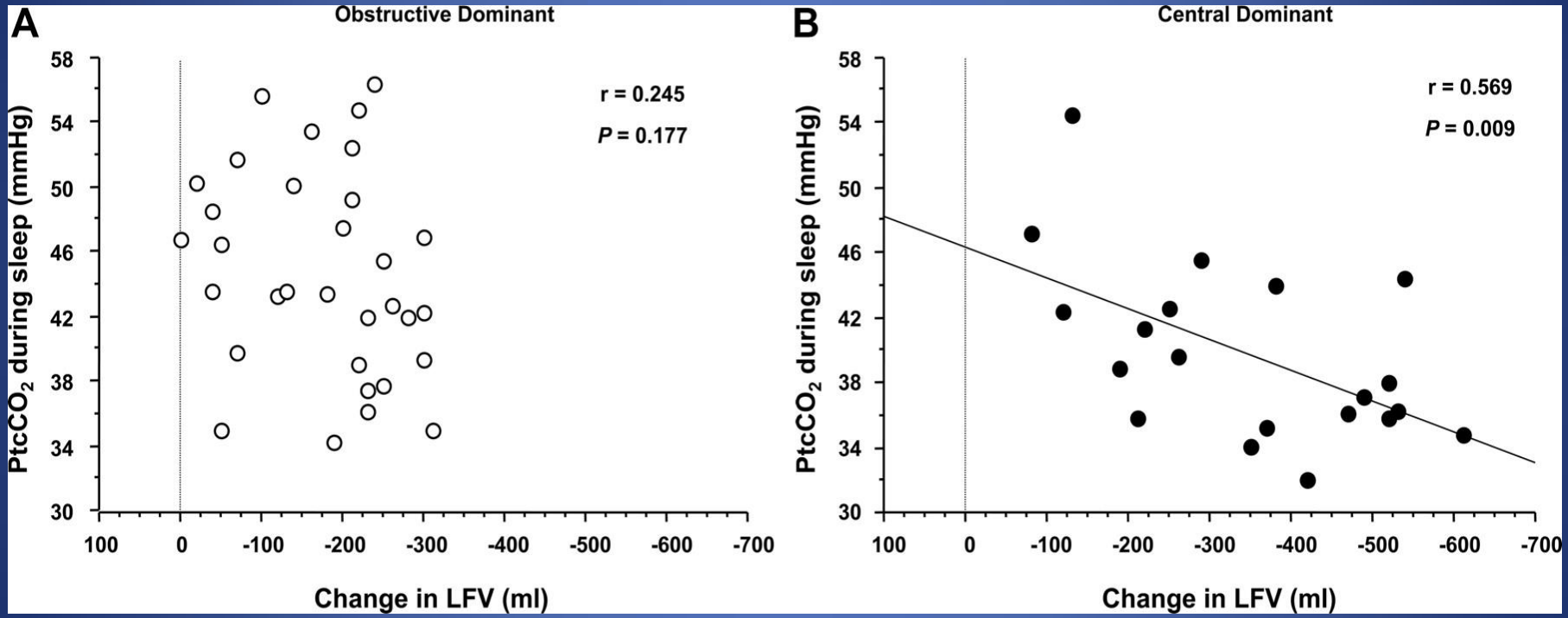
American Heart Association

Mechanism of OSA in the General Population



White AJRCC 2005

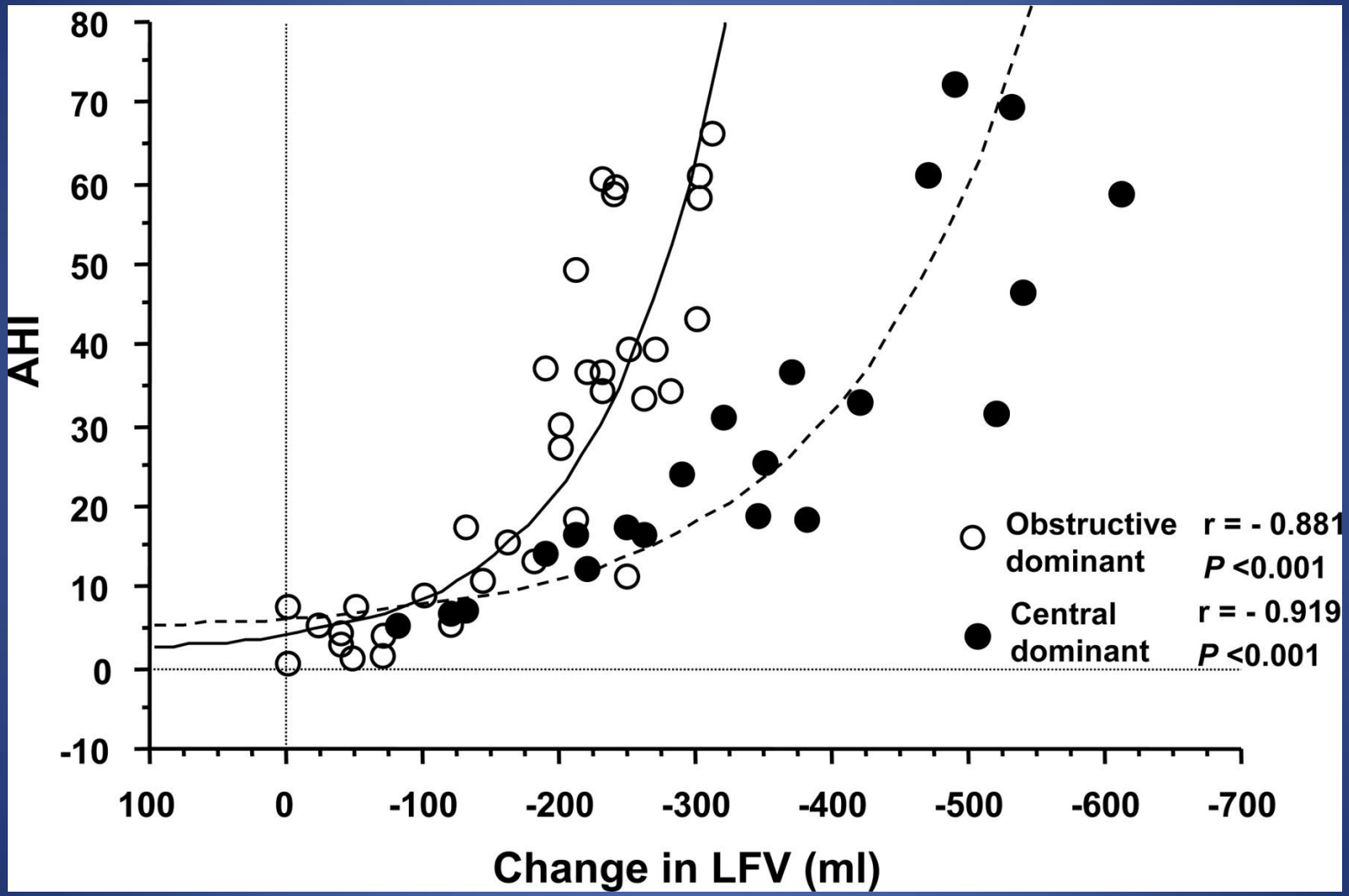
In the obstructive-dominant group, there was no significant correlation between mean Ptcco2 during sleep and overnight change in LFV (n=32; A).



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

American Heart Association

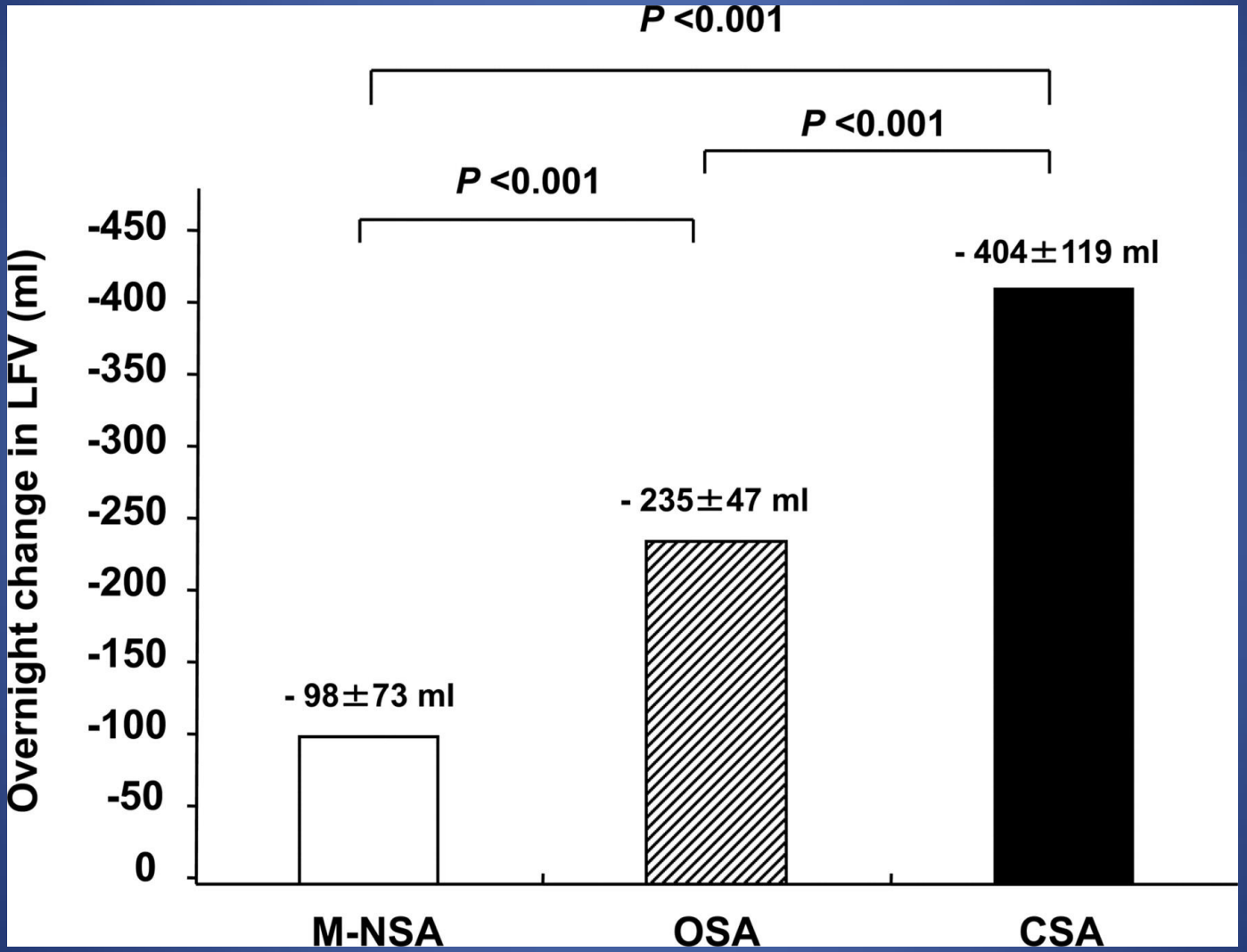
Relationship between change in LFV and AHI in the obstructive- and central-dominant groups.



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

American Heart Association

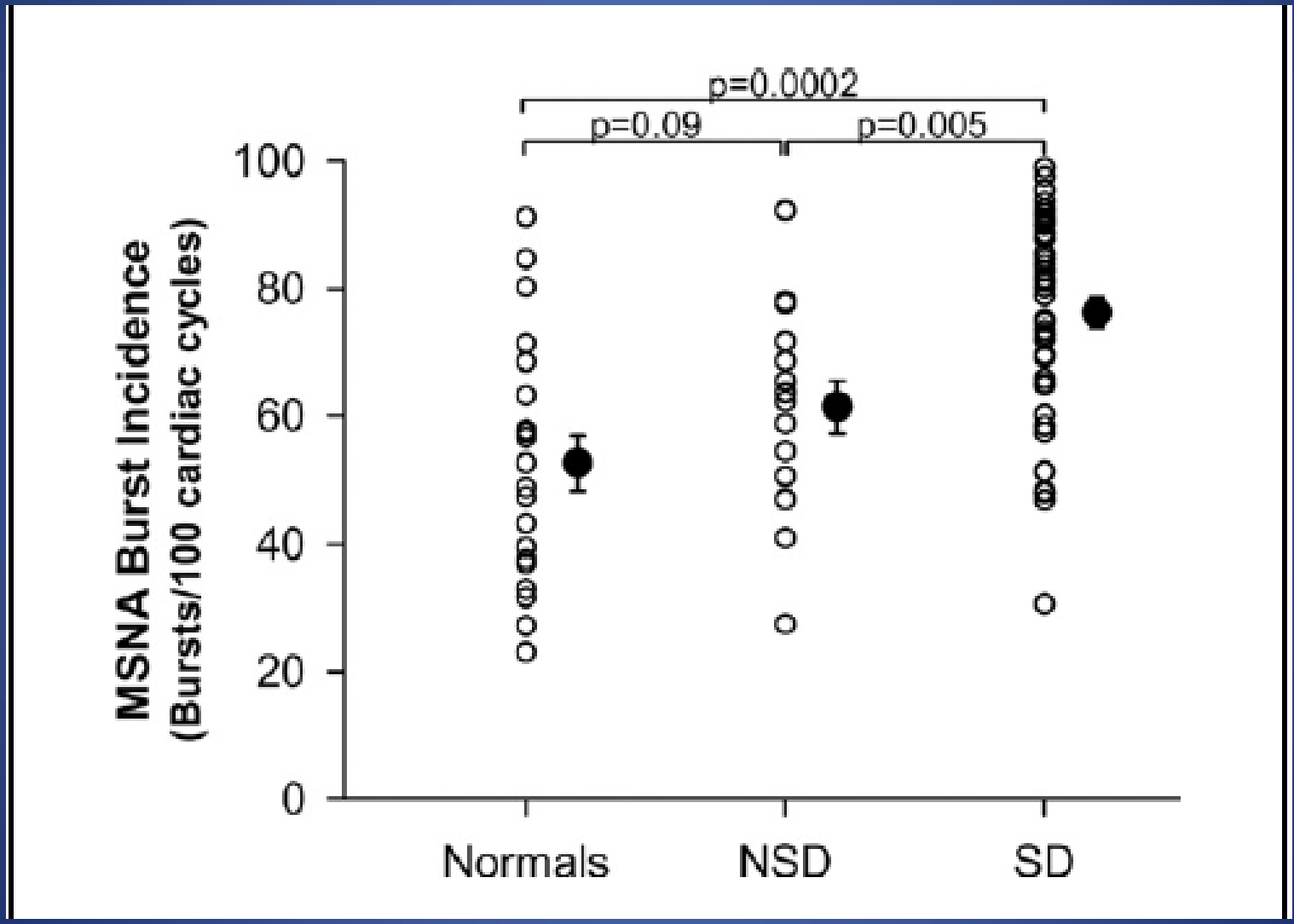
Demonstration of a progressively greater reduction in LFV from patients with mild to no sleep apnea (M-NSA) (AHI <15; n=19) to OSA (AHI ≥15; n=21) to CSA (AHI ≥15; n=17).



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

American Heart Association

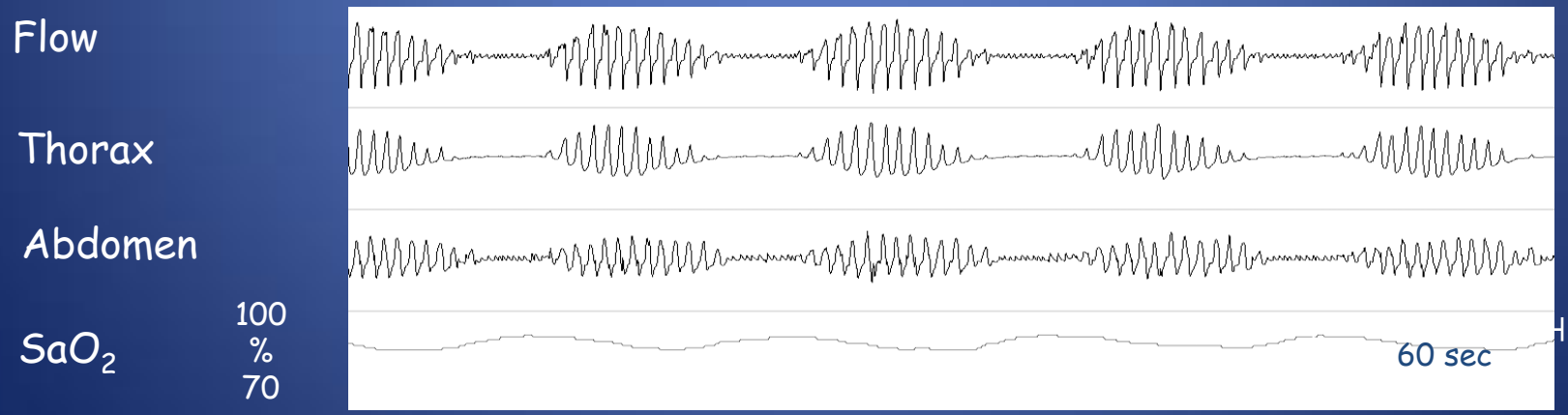
Muscle Sympathetic Burst Incidence at Rest in Subjects With and Without HF



Floras JACC 2009

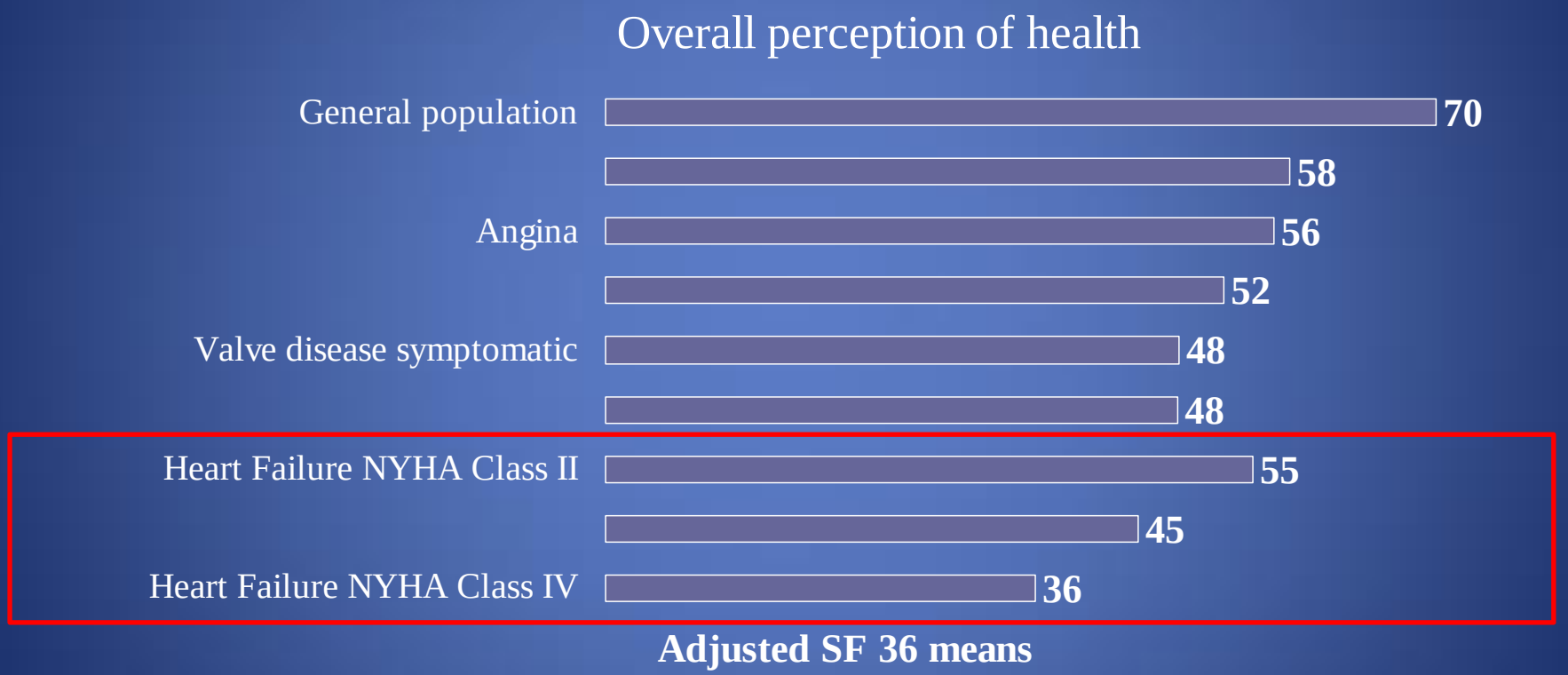
Clinical Definitions

- ***Central sleep apnoea (CSA):***
  - ≥10 second cessation of airflow, without effort
    - Dysregulation of respiratory control (lack of drive to breathe during sleep)
    - Repetitive periods of reduced ventilation
    - May manifest at CSR (central apnoeas alternating with periods of crescendo-decrescendo respiratory tidal volume)
- **Causes *increases sympathetic nervous system activity, greater cardiac electrical instability*, low frequency oscillations in heart rate and blood pressure**



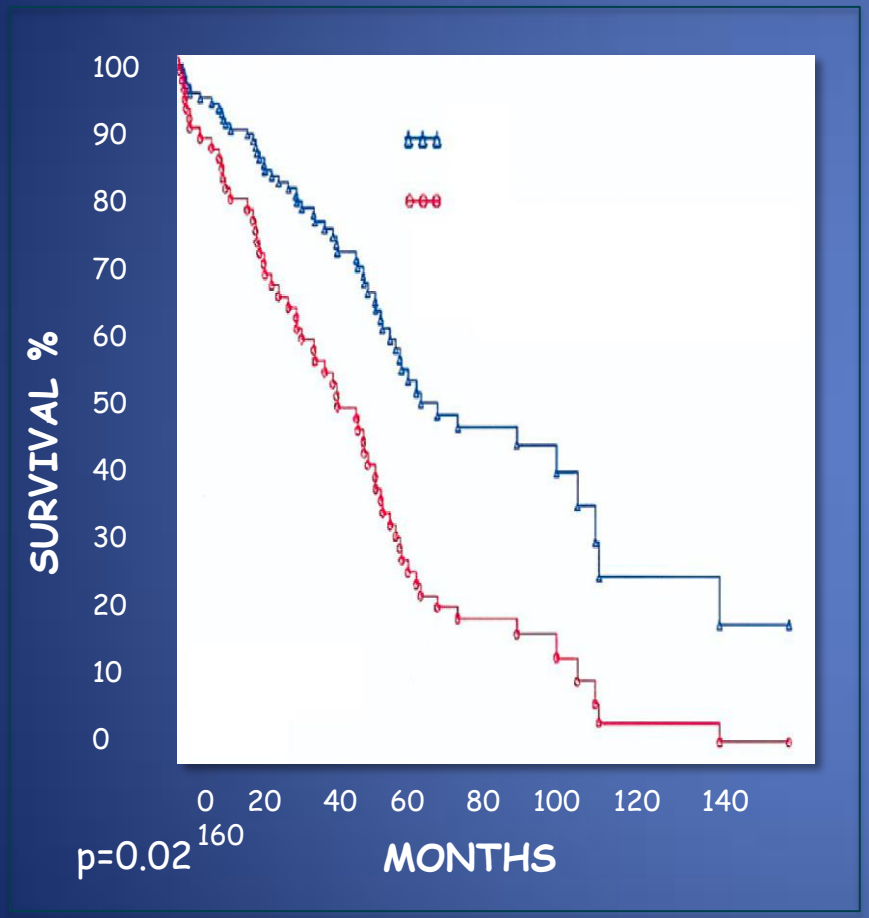
Cowie et al. Eur Cardiol Rev 2015.

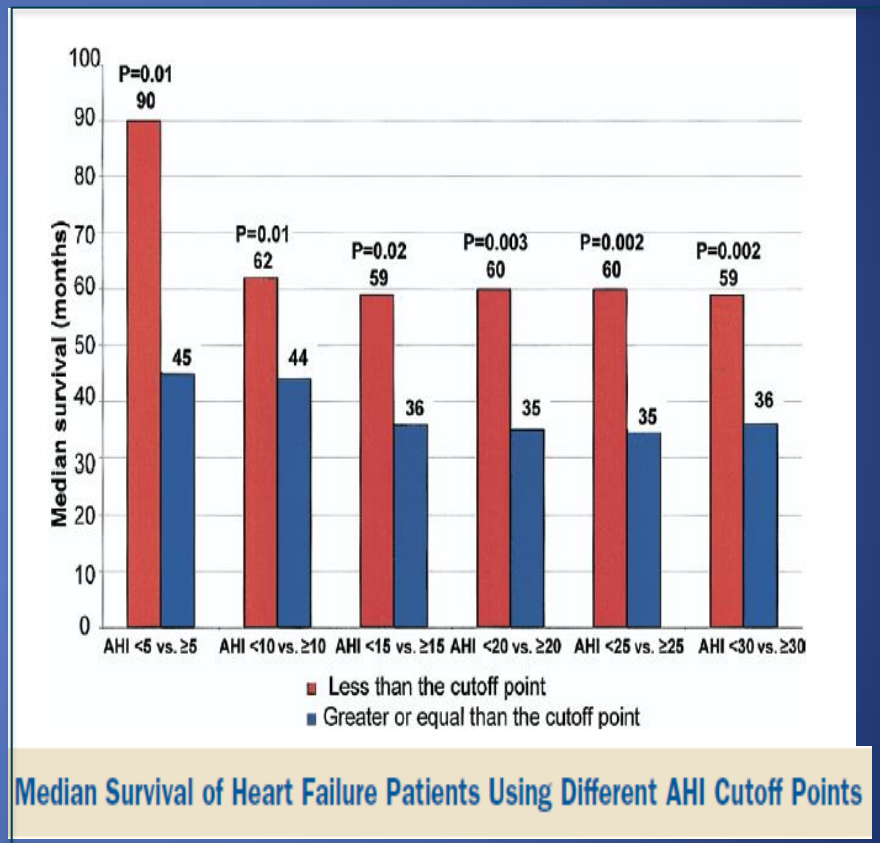
Qualita' di vita percepita



Hobbs FDR, et al. Eur Heart J 2002;23:1867-1876

CSA Significantly Increases Mortality in HF Patients





Median Survival of Heart Failure Patients Using Different AHI Cutoff Points

Javaheri, et. al.: JACC 49(20):2028-34, 2007