28ο ΠΑΝΕΛΛΗΝΙΟ
Πνευμονολογικό ΣΥΝΕΔΡΙΟ
12-15 ΔΕΚΕΜΒΡΙΟΥ 2019 | ATHENS HILTON

16:00-17:30 Στρογγυλή Τράπεζα
Ο ρόλος του εργαστηρίου ύπνου: πέρα από τους ασθενείς με σύνδρομο απνοιών-υποπνοιών

- Ο ρόλος του εργαστηρίου ύπνου σε ασθενείς με νευρομυϊκά νοσήματα
- Ο ρόλος του εργαστηρίου ύπνου σε ασθενείς με σύνδρομο παχυσαρκίας-υποαερισμού
- Ο ρόλος του εργαστηρίου ύπνου σε ασθενείς με καρδιακή ανεπάρκεια
- Μη αναπνευστικές διαταραχές του ύπνου

Ο ρόλος του εργαστηρίου ύπνου σε ασθενείς με καρδιακή ανεπάρκεια

Βλάμη Αικατερίνη

Εργαστήριο Μελέτης Ύπνου
Πανεπιστημιακό Γενικό Νοσοκομείο ΑΤΤΙΚΟΝ

Disorders of the Left Ventricular pump

Systolic vs. diastolic failure

Idiopathic vs. Ischaemic

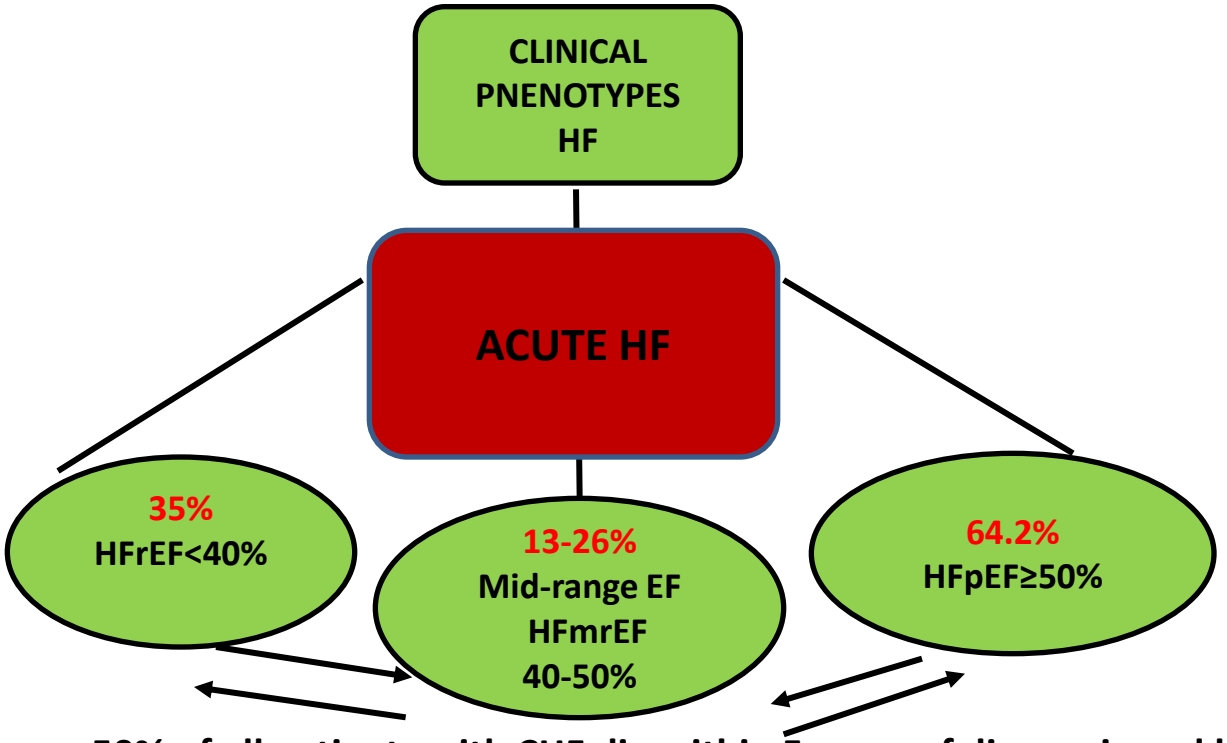
Arrhythmias (Bradycardia, Sick Sinus Syndrome, Atrial Fibrillation, Heart block)

Valvular disorders

End Stage Disease

Congestive Heart Failure

Therapeutic Target ?



Current prognosis is poor: 50% of all patients with CHF die within 5 years of diagnosis and less than 15% survive more than 10 years ***(Rosamond et al, 2007,Tendera, 2005***

26 million patients Worldwide with 1million hospitalizations annually in the United States and Europe ***(Remme et al. 2001; Ambrosy e t al. 2014)***

- **HF affects 1–2% of the adult population in developed countries**
- **In the United States, it is estimated that more than 6.5 million people have HF**
- **The incidence of HF increases along with higher age, and in the age group of 70 years and older more than 10% have the condition**
- **50–80% of the HF population have breathing sleep disorder**
- **HF patients are often unaware of the presence of sleep disorders**
- **The role of sleep lab is very important in HF patients because of the need to inform the cardiologists about this coexistence of this disorder**

Clinical Profile of HF patients

- Insomnia
- Obstructive Sleep apnea/Periodic Breathing
- PLMs
- RLS
- Daytime Sleepiness
- Fatigue
- Nocturnal dyspnea
- Nocturia
- Atrial Fibrilation

Drugs for heart failure

B-Blockers decrease nocturnal production of melatonin

HF patients do not have the same clinical presentation as the typical OSA /CSA CSR patients

Bidirectional

If AHI>15 30% HF have SDB
If AHI>10 80% HF have SDB
OSA in 50% of HFpEF

Depression

Sleep-Disordered Breathing (OSA-CSA)

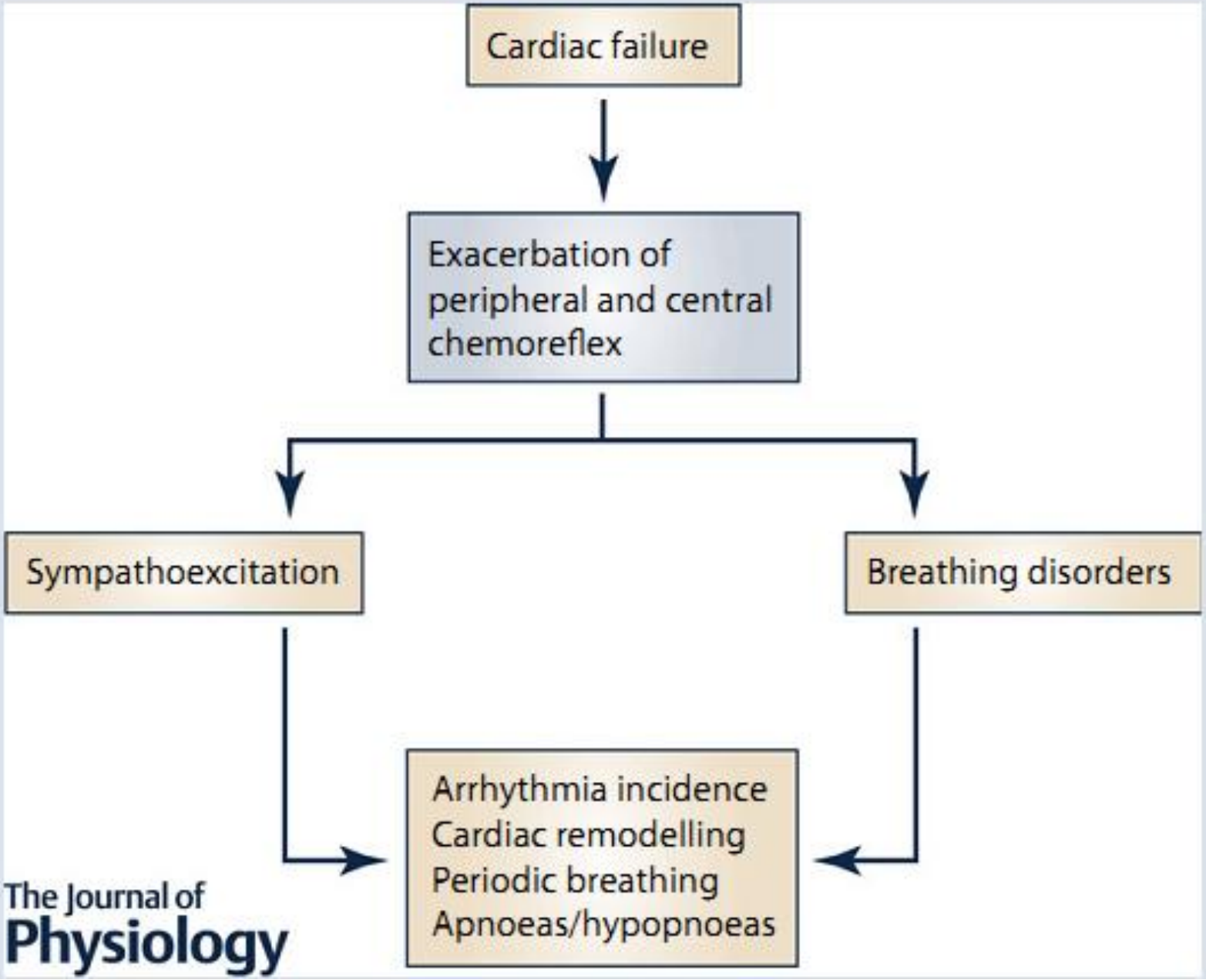
Low Sleep Quality

Insomnia 23%-73%

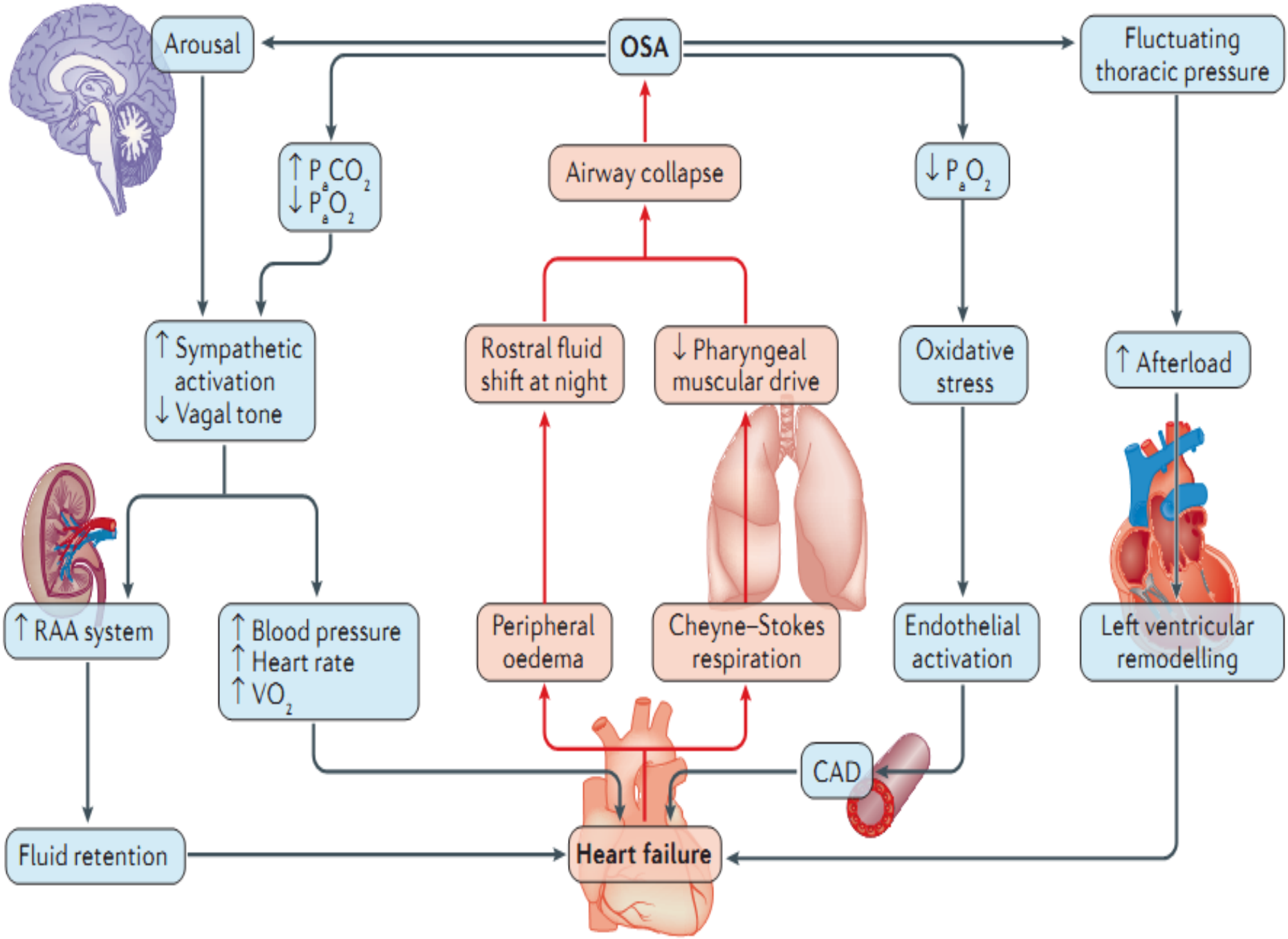
Short Sleep Time

RLS 8%-13%

PLMs 37%


Cardiac failure
Exacerbation of peripheral and central chemoreflex
Sympathoexcitation
Breathing disorders
Arrhythmia incidence
Cardiac remodelling
Periodic breathing
Apnoeas/hypopnoeas
The Journal of Physiology

HF- SLEEP APNEA


Arousal
OSA
Fluctuating thoracic pressure
↑ P_aCO_2
↓ P_aO_2
Airway collapse
↓ P_aO_2
↑ Sympathetic activation
↓ Vagal tone
Rostral fluid shift at night
↓ Pharyngeal muscular drive
Oxidative stress
↑ Afterload
↑ RAA system
↑ Blood pressure
↑ Heart rate
↑ VO_2
Peripheral oedema
Cheyne–Stokes respiration
Endothelial activation
Left ventricular remodelling
CAD
Fluid retention
Heart failure

Arousal

CSA

Apnoea threshold

P_aO_2 and P_aCO_2 oscillation

Respiratory centre alterations

↑ Sympathetic activation
↓ Vagal tone

Cardiovascular sympathetic neuron cyclic activation

Breathing Near ImPossible

↓ P_aCO_2

↑ P_aCO_2 sensitivity

↑ RAA system

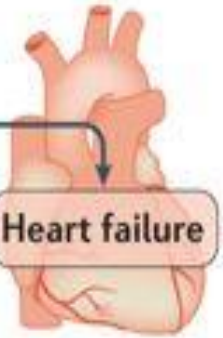
Blood pressure, heart rate, and VO_2 oscillation

↑ Ventilatory rate

↑ Stretch receptor stimulation

↑ Pulmonary venous pressure

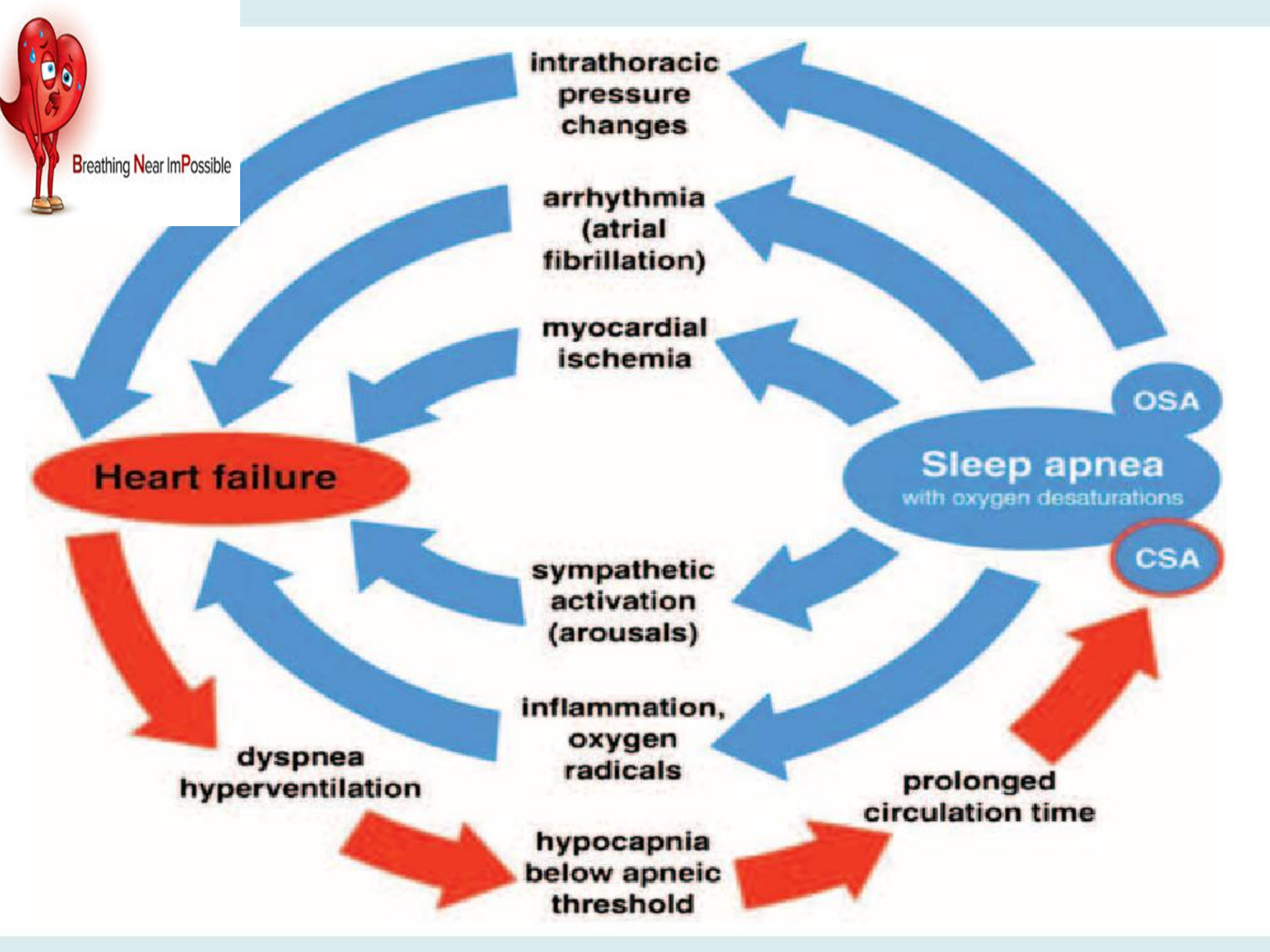
Left ventricular remodelling



Fluid retention

Heart failure

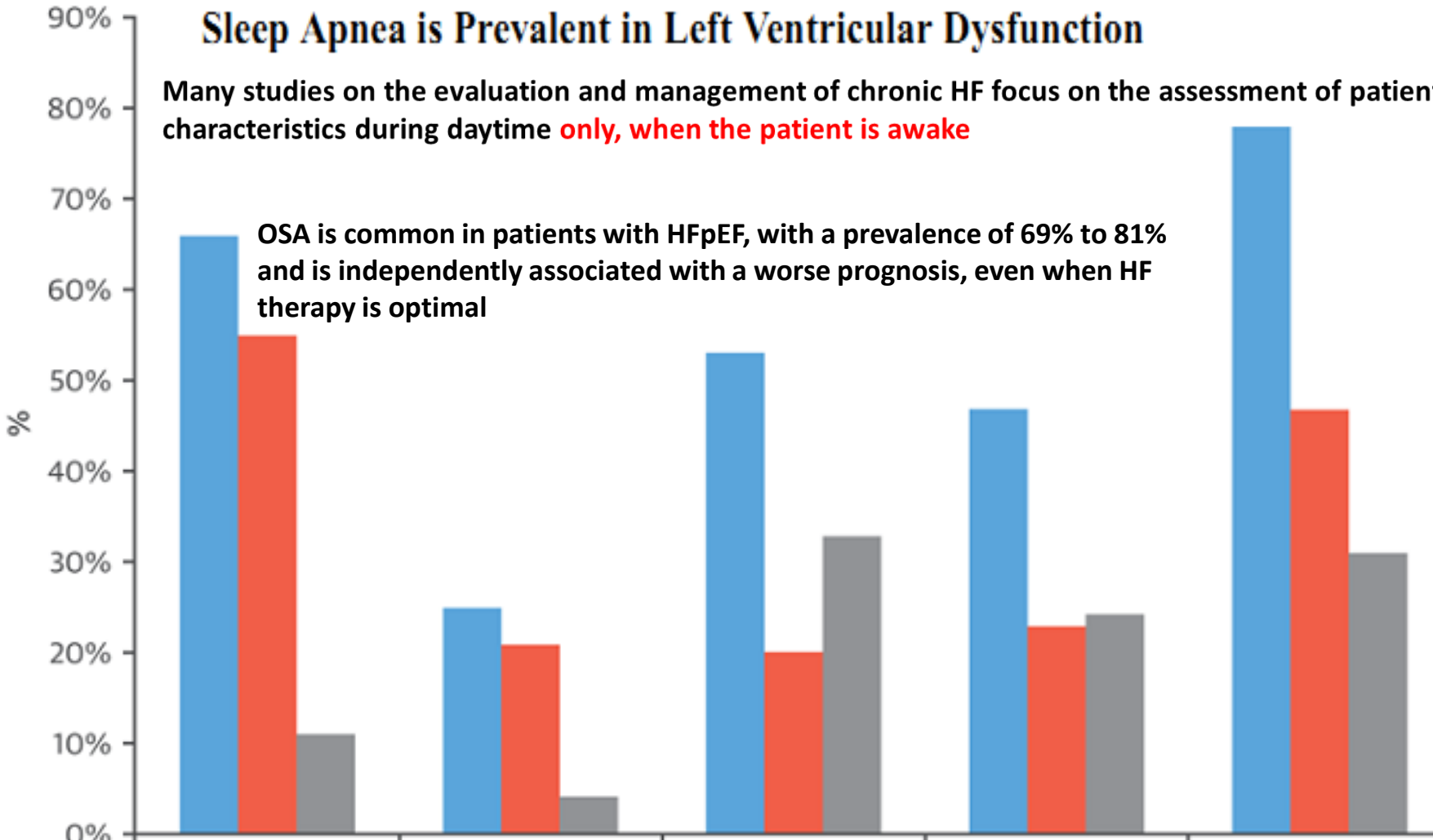
Pulmonary congestion


Breathing Near ImPossible
intrathoracic pressure changes
arrhythmia (atrial fibrillation)
myocardial ischemia
OSA
Heart failure
Sleep apnea
with oxygen desaturations
CSA
sympathetic activation (arousals)
inflammation, oxygen radicals
dyspnea hyperventilation
prolonged circulation time
hypocapnia below apneic threshold

Sleep Apnea is Prevalent in Left Ventricular Dysfunction

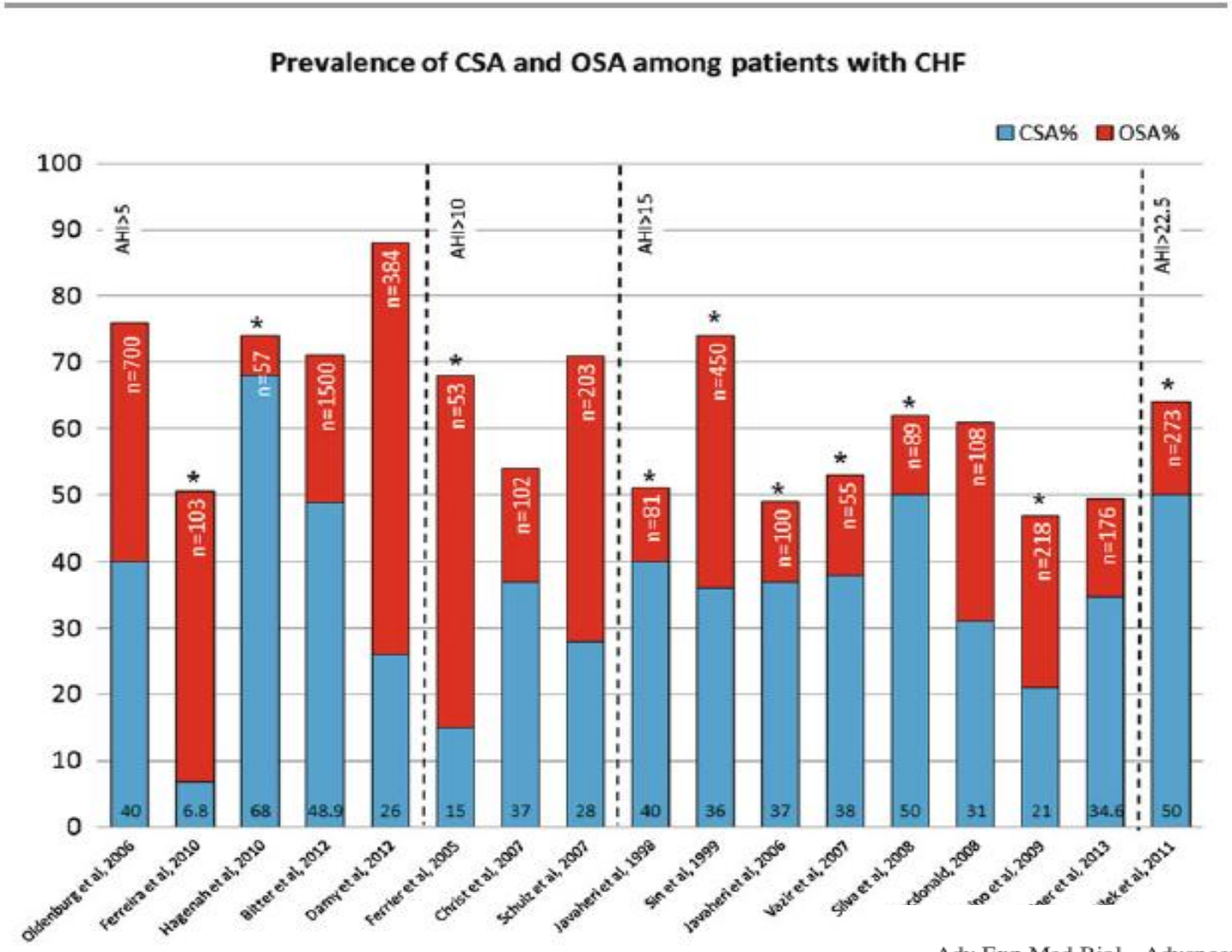
Many studies on the evaluation and management of chronic HF focus on the assessment of patien characteristics during daytime only, when the patient is awake

OSA is common in patients with HFpEF, with a prevalence of 69% to 81% and is independently associated with a worse prognosis, even when HF therapy is optimal

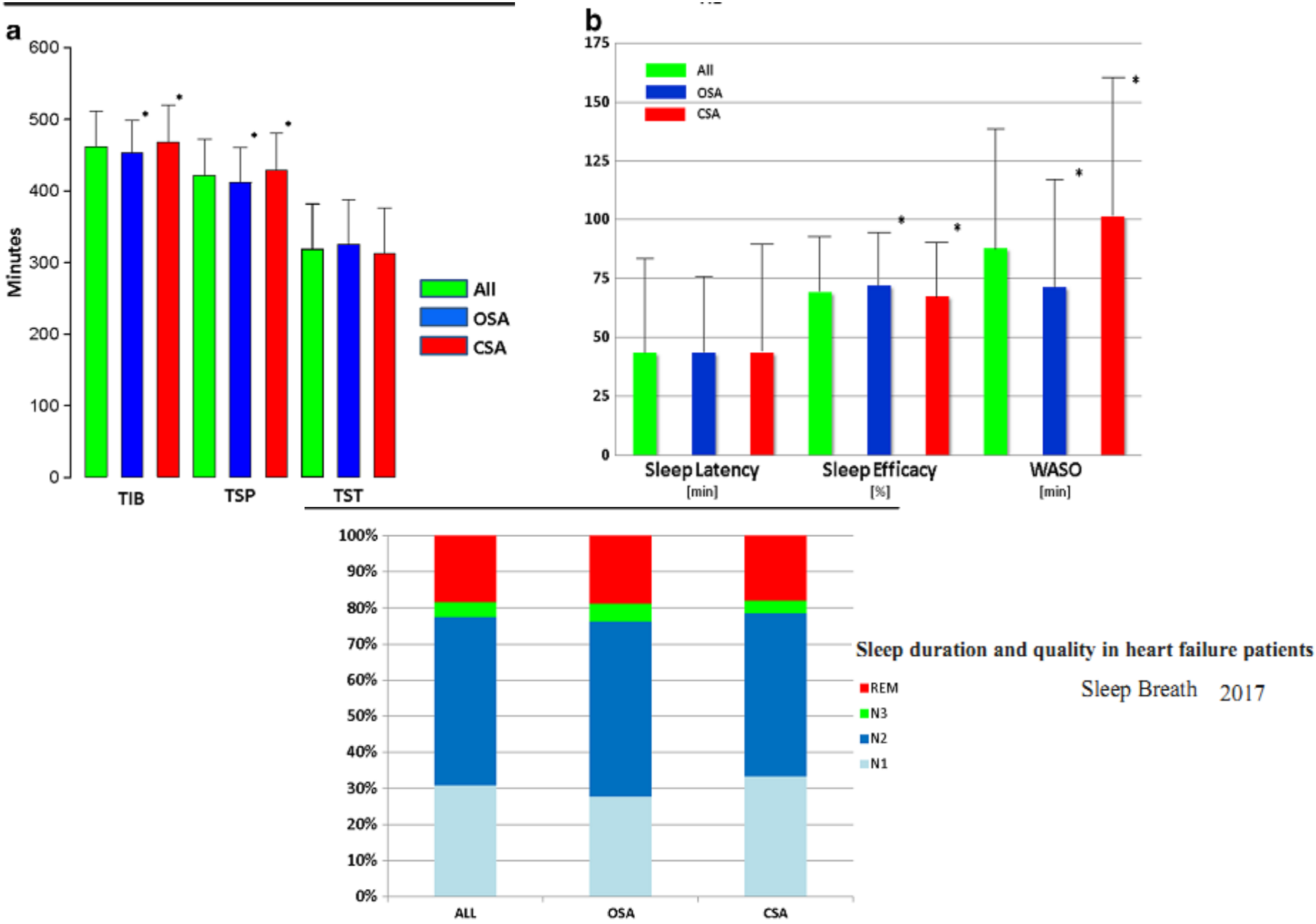


	LVSD Asymptomatic	LVDD Asymptomatic	HFrEF	HFpEF	ADHF
AHI > 15/h	66%	25%	53%	47%	78%
OSA	55%	21%	20%	23%	47%
CSA	11%	4%	33%	24%	31%

In HFrEF, there is an association between the presence of CSA and an increased risk of ventricular arrhythmias



Adv Exp Med Biol - Advances in Internal Medicine
DOI 10.1007/5584_2018_146

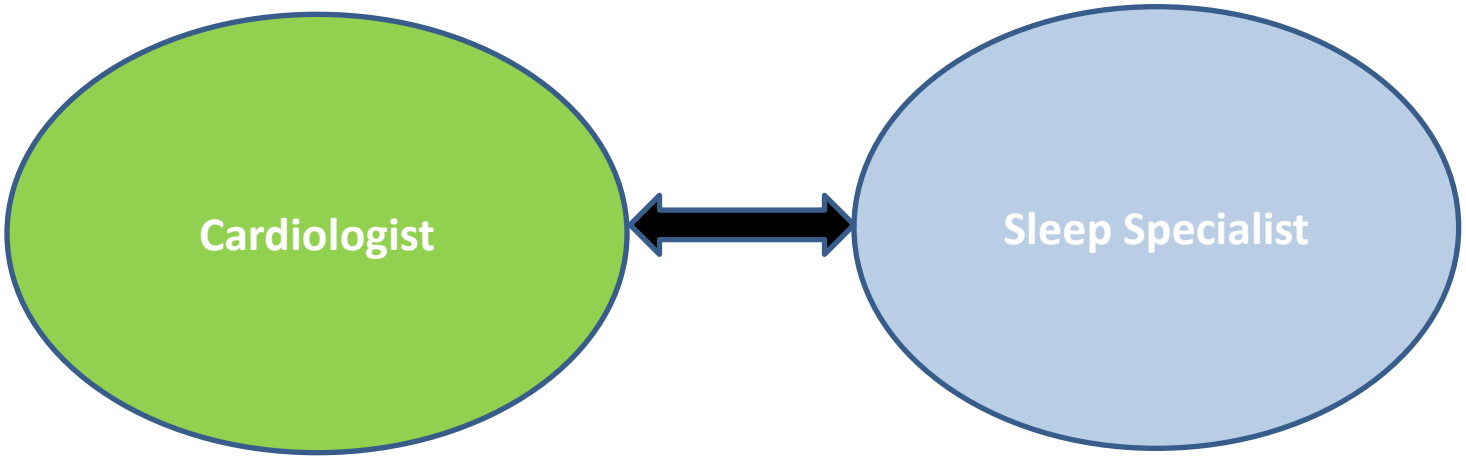


Sleep duration and quality in heart failure patients

Sleep Breath 2017

Fig. 3 Sleep stages in patients with heart failure and reduced ejection fraction, overall and by type of sleep-disordered breathing (*OSA* obstructive sleep apnea and *CSA* central sleep apnea). *REM* rapid eye movement

Cardiologists should be concerned with the possibility that their patient's cardiac condition might be caused or aggravated by Sleep Apnea



Patients with HF have a moderate or high probability of OSA, screening all AF and heart failure patients with home sleep apnea testing might prove to have the highest utility

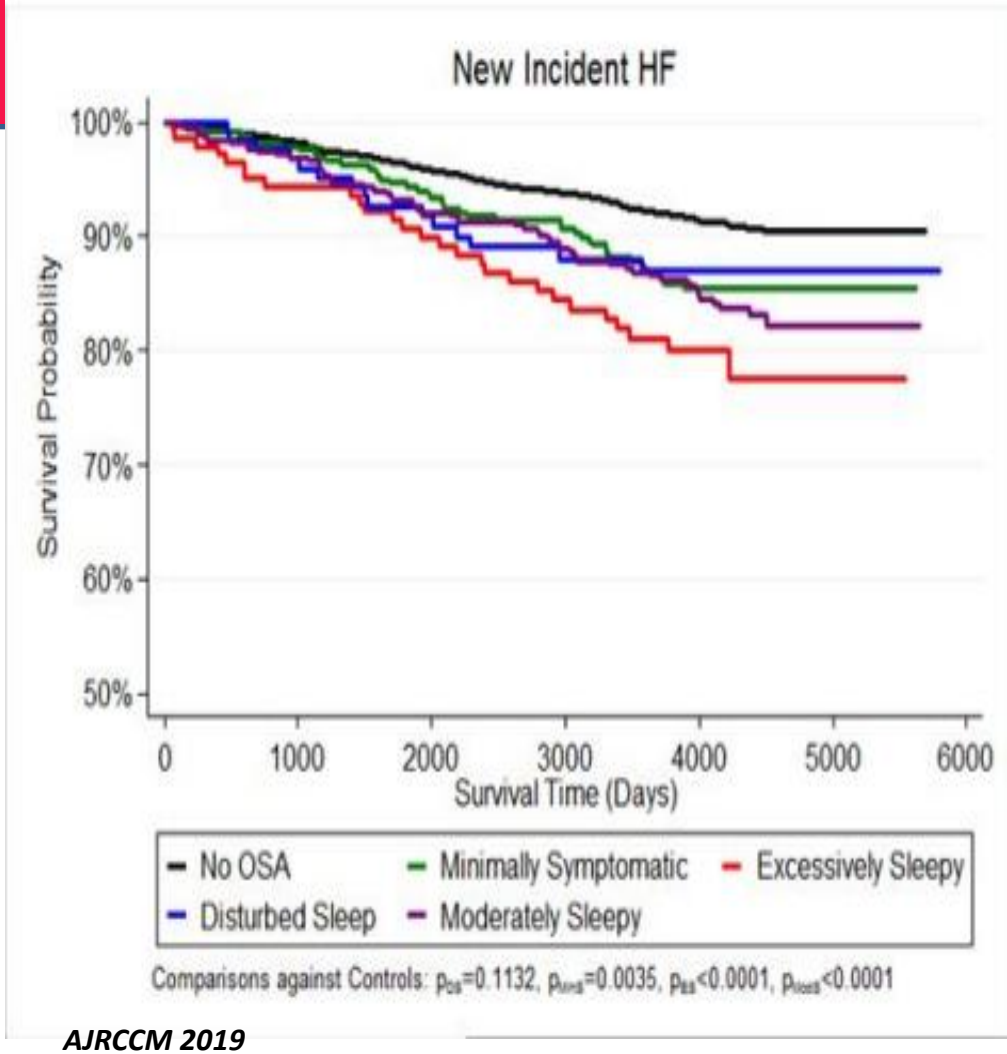
Clinical symptom-based questionnaires have been proposed to help identify patients who should be formally assessed for Sleep Apnea, but these tools have been proven to have disappointing utility in HF

Sleep Apnea Heterogeneity, Phenotypes, and Cardiovascular Risk

Symptom Subtypes of Obstructive Sleep Apnea Predict Incidence of Cardiovascular Outcomes

Clinical Symptoms Subtypes of Sleep Apnea

PSG metrics
AHI
Oxygen Desaturation
Arousal Index
Heart Rate Variability



AJRCCM 2019

Sleep Apnea Heterogeneity, Phenotypes, and Cardiovascular Risk

- Symptoms
- Physiologic traits linked to disease pathogenesis
- Polysomnographic expression of this Breathing Sleep Disorder (e.g., severity o f hypoxemia and sleep architectural changes)
- AHI is not the best predictor o f OSA-related morbidity, and the field is now questioning the use of the AHI as the primary diagnostic or prognostic criterion for patients with sleep-disordered breathing

- REM sleep apnea and hypoxic burden significantly increase cardiovascular risk in patients with sleep apnea

- Various health outcomes may be related to sleep apnea through distinct pathophysiologic pathways that differentially reflect responses to hypoxemia, arousal, and sleep state

NEW PSG INDICES

Hypoxic Burden

A measure for enhanced prediction of OSA related cardiovascular mortality

The hypoxic burden of sleep apnoea predicts cardiovascular disease-related mortality: the Osteoporotic Fractures in Men Study
and the Sleep Heart Health Study

European Heart Journal 2018

Obstruction Severity

Stronger relationship with increase mortality rate than AHI, especially among severe OSA patients

Muraja-Murro A et al The severity of individual obstruction events is related to increased mortality rate in severe obstructive sleep apnea J Sleep Res 2013

Adjusted-AHI

was further shown to be an independent risk factor for all-cause mortality and non-fatal cardiovascular events

Leppanen T et al RemLogic plug-in enables clinical application of AHI adjusted for severity of individual Obstruction events. J Med Eng Technol 2016

ESC European Society of Cardiology

European Heart Journal (2018) **0**, 1–10
doi:10.1093/eurheartj/ehy624

CLINICAL RESEARCH
Prevention and epidemiology

The hypoxic burden of sleep apnoea predicts cardiovascular disease-related mortality: the Osteoporotic Fractures in Men Study and the Sleep Heart Health Study

Ali Azarbarzin[1]*, Scott A. Sands[1], Katie L. Stone[2,3], Luigi Taranto-Montemurro[1], Ludovico Messineo[1], Philip I. Terrill[4], Sonia Ancoli-Israel[5,6], Kristine Ensrud[7], Shaun Purcell[1,8], David P. White[1], Susan Redline[1], and Andrew Wellman[1]

JCSM
Journal of Clinical Sleep Medicine

J Clin Sleep Med. 2019;

SCIENTIFIC INVESTIGATIONS

Severity of Desaturations Reflects OSA-Related Daytime Sleepiness Better Than AHI

Samu Kainulainen, MSc[1,2,3]; Juha Töyräs, PhD[1,2,4]; Arie Oksenberg, PhD[5]; Henri Korkalainen, MSc[1,2]; Sandra Sefa, MSc[2]; Antti Kulkas, PhD[1,3]; Timo Leppänen, PhD[1,2]

Hypoxic Burden Predicts Incident Heart Failure in Adults with Sleep Apnea: The Sleep Heart Health Study

A. Azarbarzin, S. A. Sands, L. Taranto Montemurro, D. Vena, T. Sofer, S. Kim, D. P. White, D. Wellman, S. S. Redline; Division of Sleep and Circadian Disorders, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, United States.

Corresponding author's email: aazarbarzin@bwh.harvard.edu

Rationale: We recently showed that greater obstructive sleep apnea (OSA)-associated hypoxic burden confers greater risk of cardiovascular (CV) mortality independent of OSA severity (apnea-hypopnea index, AHI) and other known confounders (Azarbarzin et al., 2018). Here we assessed whether elevated hypoxic burden is associated with incident heart failure and compared it with apnea-hypopnea index (AHI). Methods: The sample was derived from the Sleep Heart Health Study (SHHS), which included 5036 middle-aged and older adults (53.4% women), age: 63.9±11.2 years. The outcome was incident congestive heart failure. The hypoxic burden was determined by measuring the respiratory event-associated area under the desaturation curve from pre-event baseline. Baseline polysomnography was manually annotated for conventional parameters, including AHI (hypopneas associated with ≥3% oxygen desaturation), and percent time with oxygen saturation below 90% (T90). Several Cox proportional hazards regression models were used to calculate the hazard ratios after adjusting for age, BMI, race, gender, smoking status, and comorbidities, including COPD, diabetes, hypertension, cardiovascular disease, and prevalent heart failure (Figure 1). Hypoxic burden, AHI, and T90 were natural log-transformed and then modeled. Results: Over the follow-up period (10.2±3.5 years), 618 (12.2%) individuals experienced incident heart failure. The mean (±SD) AHI and hypoxic burden were 13.7±14.8 events/hour and 50.5±57.8 %min/hour (Hypoxic burden of 50%min/hour is equivalent to 10 minutes of 5% desaturation below baseline every hour). The hypoxic burden predicted increased risk of incident heart failure in this sample in both minimally and fully adjusted models (Figure 1). In the fully adjusted, for every two-fold increase in the hypoxic burden, the risk of incident heart failure increased by 14.3%. In contrast, the association between AHI and incident

European Heart Journal (2012) 33, 1787–1847
doi:10.1093/eurheartj/ehs104

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

The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC

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.

European Heart Journal (2012) 33, 1787–1847
doi:10.1093/eurheartj/ehs104

ESC GUIDELINES

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2016

Heart failure and sleep disorders

May 2016

Gianfranco Parati[1–3], Carolina Lombardi[1,2], Francesco Castagna[1,2,4], Paola Mattaliano[1,2], Pasquale Perrone Filardi[5] and Piergiuseppe Agostoni[6,7] on behalf of the Italian Society of Cardiology (SIC) Working Group on Heart Failure

NATURE REVIEWS | CARDIOLOGY

Box 2 | Epidemiology of sleep-disordered breathing

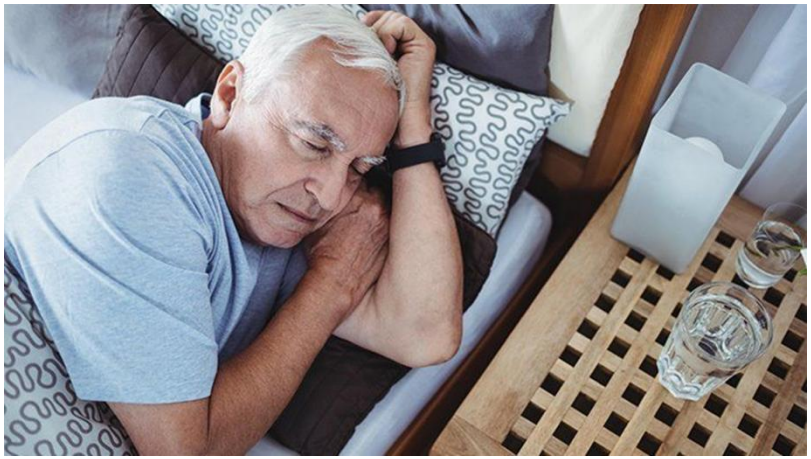
Prevalence of sleep disorders in patients with heart failure compared with the general population

Obstructive sleep apnoea[20,21,26,27]:
11–38% versus 2–26%

Central sleep apnoea/Cheyne–Stokes respiration[26–28,30–33,194]:
28–82% versus <5%

Chronic insomnia[2]:
33% versus 10–15%

- Full Polysomnography
- Unattended Polysomnography
- Home Sleep Testing
- Cardiorespiratory monitoring during sleep
- Nocturnal Oximetry
- Bedsided tesing during hospital staying
- Titration of the positive upper airway devices



?Splitnight in HF because of different attitude of HF patients at the beginning of sleep and the end of sleep

AHI, ODI, T90, Desaturation burden, Arousal index, Sleep Efficiency, WASO, Heart Rate Variability

Follow-up the response of patients with CHF to standard treatments and alternative treatments (CPAP or oxygen)

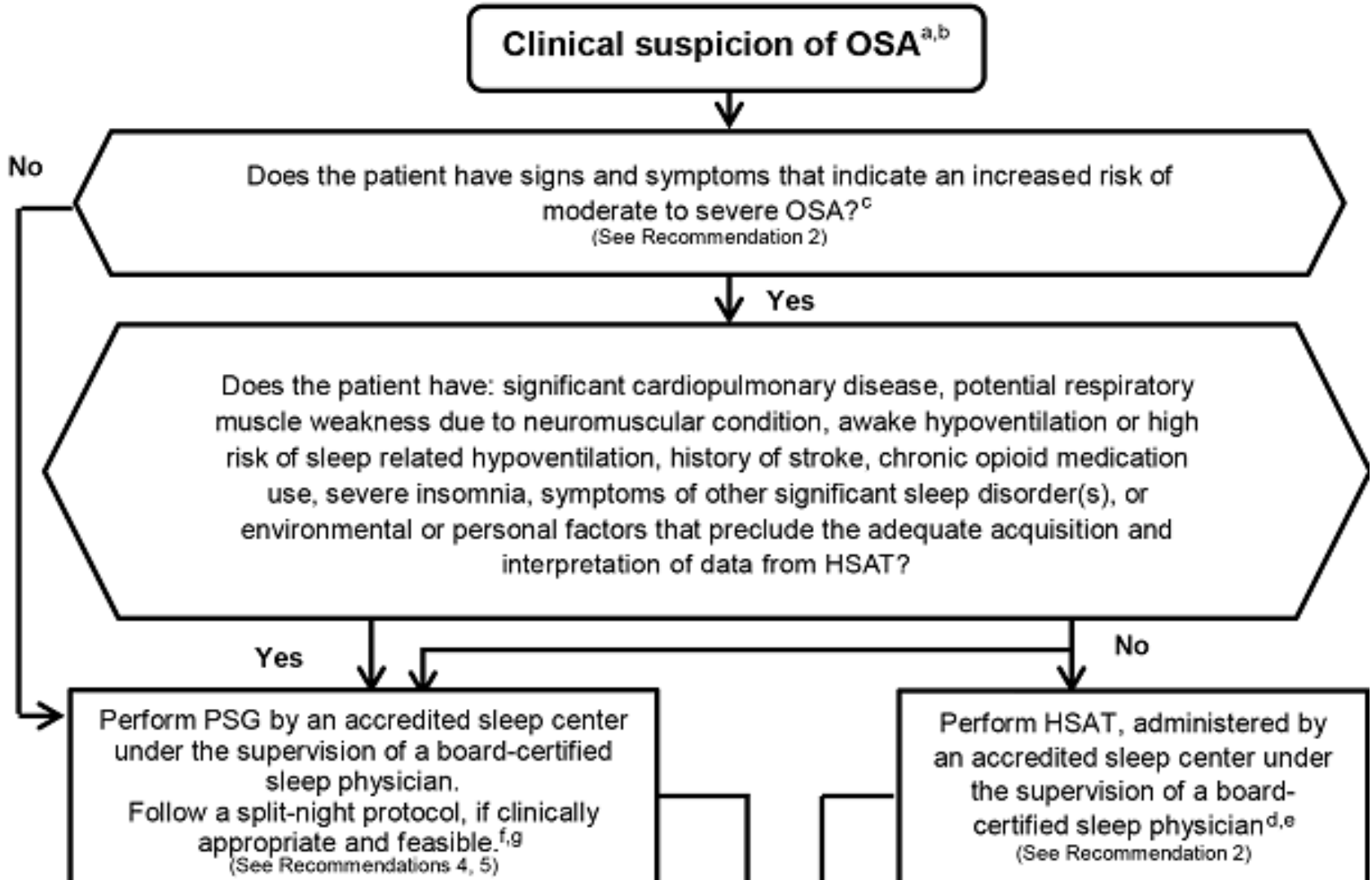
PSG should be used to assess the response after atrial pacing in patients with CHF and sleep apnea (possibly via improved chronotropic performance)

Polysomnogaphy is the best test to investigate symptoms of orthopnea and paroxysmal nocturnal dyspnea, particularly when there is doubt as to the degree of cardiac failure.

SPECIAL ARTICLES

Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea: An American Academy of Sleep Medicine Clinical Practice Guideline

Figure 2—Clinical algorithm for implementation of clinical practice guidelines.



Home Sleep Apnea Testing for the Diagnosis of Obstructive Sleep Apnea in Adults

Journal of Clinical Sleep Medicine, Vol. 13, No. 3, 2017

Recommendation 2: We recommend that polysomnography, or home sleep apnea testing with a technically adequate device, be used for the diagnosis of OSA in uncomplicated adult patients presenting with signs and symptoms that indicate an increased risk of moderate to severe OSA. (STRONG)

Recommendation 3: We recommend that if a single home sleep apnea test is negative, inconclusive or technically inadequate, polysomnography be performed for the diagnosis of OSA. (STRONG)

Uncomplicated patient = **Conditions that place the patient at increased risk of non-obstructive sleep-disordered breathing (e.g., central sleep apnea, hypoventilation and sleep related hypoxemia). Examples of these conditions include significant cardiopulmonary disease**

JCSM
Journal of Clinical Sleep Medicine

Journal of Clinical Sleep Medicine, Vol. 1, No. 1, 2005

PRO/CON DEBATE

Routine Polysomnography is Indicated in Congestive Heart Failure

Matthew T. Naughton, M.D.

Monash University and Alfred Hospital, Melbourne, Victoria, Australia

In summary, routine polysomnography is required in patients with CHF in order to classify presence and type of SDB, plus response to treatment.

ELSEVIER

Canadian Journal of Cardiology 31 (2015) 935–939

Point/Counterpoint

Should All Congestive Heart Failure Patients Have a Routine Sleep Apnea Screening? Pro

Frédéric Sériès, MD

Should All Congestive Heart Failure Patients Have a Routine Sleep Apnea Screening? Con

Yanru Li, MD[a], Lori B. Daniels, MD, MAS, FACC[b], Patrick J. Strollo Jr., MD, FCCP, FAASM[c], and Atul Malhotra, MD[d]

Can J Cardiol. 2015

Is There a Need to Routinely Assess for the Presence of

Pro

- **Non typical symptoms, difficult to distinguish from nonspecific symptoms such as fatigue in HF**

- **Comorbid conditions such as refractory hypertension, absence of arterial pressure nocturnal dipping , atrial fibrillation, diastolic dysfunction, and hypocapnia are associated with an increase in the risk of SDB but are not sufficient to establish a diagnosis on their own**

- **Before heart transplantation**

- **Follow-up the response of patients with CHF to treatments which include both standard to the extravagant (biventricular pacing, transplantation, left ventricular assist devices) and alternative treatments (positive airway pressure or oxygen)**

ELSEVIER

Canadian Journal of Cardiology 31 (2015) 935–939

Point/Counterpoint

Should All Congestive Heart Failure Patients Have a Routine Sleep Apnea Screening? Pro

Frédéric Sériès, MD

Table 1. Main rationales that justify the for the need to identify the presence of sleep disturbances in CHF patients

SDB-associated risks in CHF patients	• Ventricular arythmia[1,7,8] • Increase in cardiac readmission in a cardiology clinical unit[2] • Reduced life expectancy[3-6,9]
Benefits of treatment of SDB in CHF patients	• Improvement in left ventricular ejection fraction[12] • Improvement in mortality[14] • Decrease in the rate of hospital readmission or consultation to emergency department after a cardiac event[13]

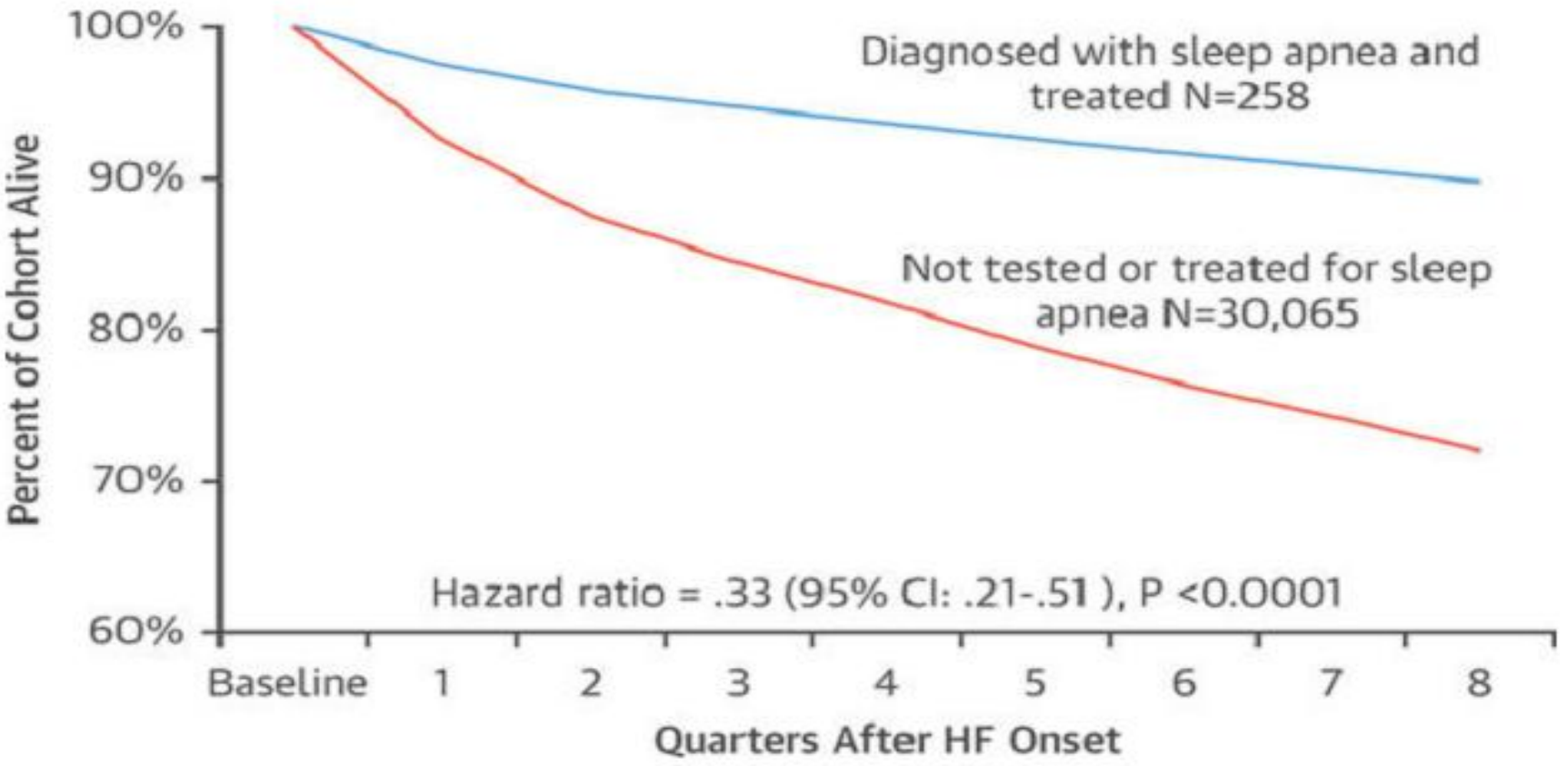
CHF, congestive heart failure; SDB, sleep-disordered breathing.

Is There a Need to Routinely Assess for the Presence of SDB in Congestive HF?

Con

- **Use of routine screening for SDB include cost considerations and poor adherence of CHF patients to positive pressure therapy**
- **Accute ill HF do not need screening for SDB but only treatment with positive airway devices**
- **Portable sleep monitoring is increasing in popularity for the diagnosis of SDB in patients with HF (*Woehrle H, et al. Determining the prevalence and predictors of sleep disordered breathing in patients with chronic heart failure: rationale and design of the SCHLA-HF registry. BMC Cardiovasc Disord. 2014)***
- **A careful history can help with case-finding and potentially reduce the need for screening of truly asymptomatic individuals with HF**
- **Data suggest that breathing abnormalities might be related to inadequate medical therapy rather than an independent issue requiring intervention (*Solin et al. Influence of pulmonary capillary wedge pressure on central apnea in heart failure. Circulation. 1999)***
- **Diagnosis of OSA or CSA do not change management in HF patients**

Am J Respir Crit Care Med. 2011



11. Comparative Survival of 258 HF Patients Treated for Sleep Apnea and 30,000 Not Tested for Sleep Apnea

In the largest observational study of about 30,000 Medicare beneficiaries newly diagnosed with HF, treatment of SDB was associated with decreased readmission, health care cost, and mortality

Common clinical characteristics and diagnosis of obstructive sleep apnoea

Obstructive sleep apnoea
Clinical characteristics
• Unexplained daytime somnolence[195]
• Abnormal sleep noises[196] (gasping, choking, loud apnoeas) with respiratory effort witnessed by bed partners
• Fatigue[195]
• Resistant arterial hypertension[45]
• Cardiac rhythm abnormalities[197]
• Obesity/high waist and neck circumference[198]
• Narrow oropharynx[199]
• Heart failure symptoms, in particular peripheral oedema[200]

Obstructive sleep apnoea	*Diagnosis*
• ≥5 predominantly obstructive respiratory events (obstructive and mixed apnoeas, hypopnoeas, or respiratory effort related arousals) per hour of sleep, and at least one of the following:
• Sleepiness, nonrestorative sleep, fatigue, or insomnia symptoms
• Waking up with breath holding, gasping, or choking
• Habitual snoring, breathing interruptions, or both noted by a bed partner
• Presence of hypertension, mood disorder, cognitive dysfunction, coronary artery disease, stroke, congestive heart failure, atrial fibrillation, or type 2 diabetes mellitus
Or:
• ≥15 predominantly obstructive respiratory events (apnoeas, hypopnoeas, or respiratory effort related arousals) per hour of sleep — even in absence of the associated symptoms or comorbidities

Common clinical characteristics and diagnosis of central sleep apnoea

The principal risk factors for CSA/Cheyne–Stokes respiration in patients with HF identified in cross sectional studies are male sex, advanced age, hypocapnia, atrial fibrillation, or presence of a pacemaker, but not obesity

Central sleep apnoea

Clinical characteristics

- Rarely daytime somnolence[129]
- Repetitive sleep apnoeas without abnormal noises, and without respiratory effort[193]
- Poor quality of sleep[201]
- Possible association with periodic breathing during exercise[118]
- Cardiac rhythm abnormalities[197]
- Heart failure symptoms, in particular peripheral oedema[200]

Central sleep apnoea

Diagnosis

- ≥5 central apnoeas and/or central hypopnoeas per hour of sleep; the number of central apnoeas and/or central hypopnoeas needs to be >50% of the total number of apnoeas and hypopnoeas
- Cheyne–Stokes breathing ventilation pattern; in the absence of this element and of daytime or nocturnal hypoventilation, the disorder is considered primary central sleep apnoea

And:

- At least one of the following: sleepiness, difficulty initiating or maintaining sleep, frequent awakenings, or nonrestorative sleep; awakening with shortness of breath; snoring, witnessed apnoea

Or:

- Presence of atrial fibrillation or flutter, congestive heart failure, or a neurological disorder

And:

- The disorder is not better explained by another current sleep disorder, medication use, or substance use disorder

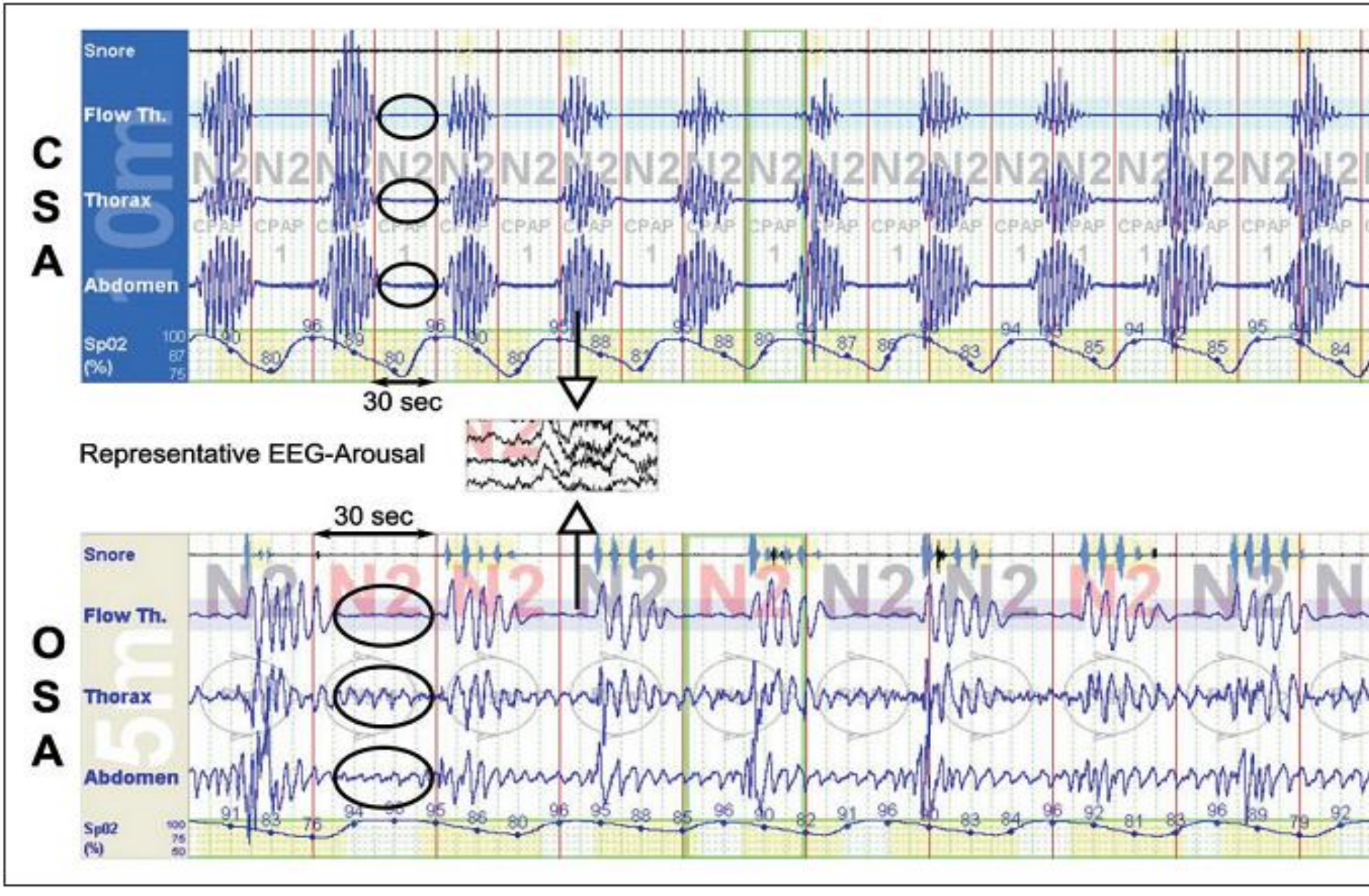
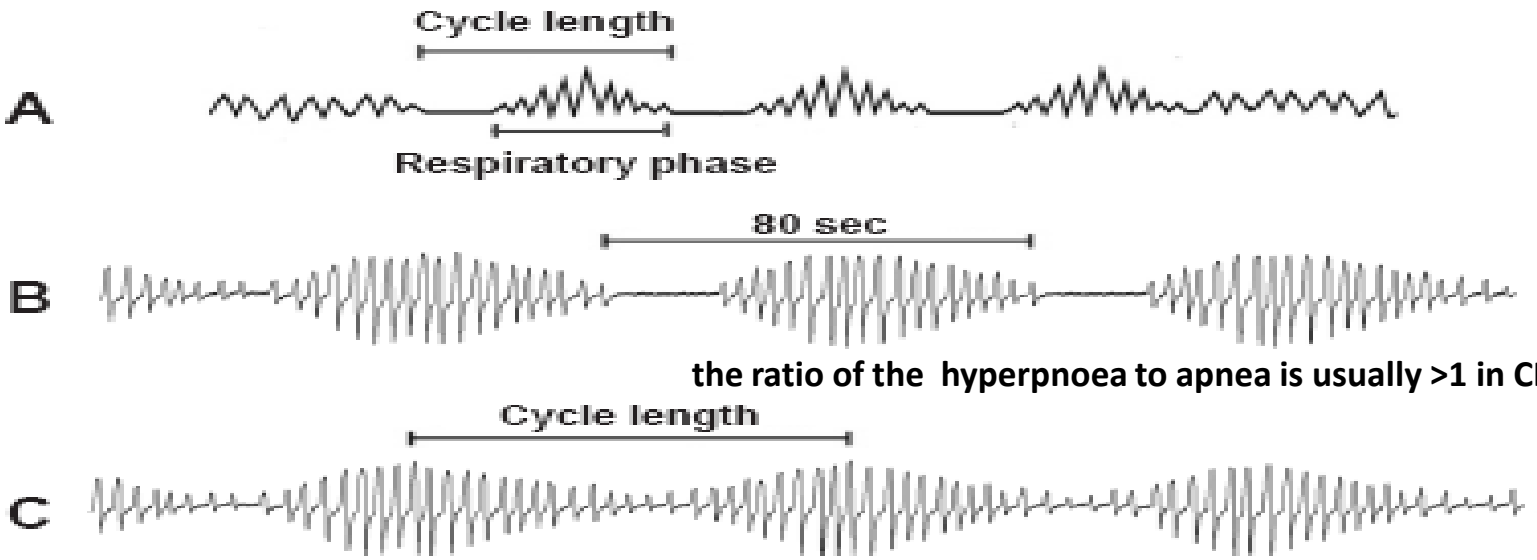


Figure 4. Tracings showing the different features of CSA–CSR (top panel) versus OSA (bottom panel). Unlike in OSA, in CS phases of hyperventilation alternate with central apnoeas and are characterised by cessation of airflow in the absence of as compensatory breathing efforts during the apnoea. Plus, unlike in OSA, in CSA–CSR, arousals are not closely linked to the en apnoea.

Cheyne Stokes Respiration

Figure 8



the ratio of the hyperpnoea to apnea is usually >1 in CHF

(A) Schematic of Cheyne-Stokes breathing (airflow shown) with a minimum of 3 consecutive central apneas (effort not shown) separated by a crescendo-decrescendo pattern of breathing. **(B)** Cheyne-Stokes breathing with central apneas (only airflow shown) with a long cycle time of 80 seconds. **(C)** Cheyne-Stokes breathing with central hypopneas (airflow shown). Although respiratory effort is not shown, these are central hypopneas with no evidence of airflow limitation (no flattening). As it is difficult to identify a beginning or end of the hypopnea, cycle time is defined as the time from one zenith in airflow during the respiratory phase to the next zenith in airflow.

PAP -HF

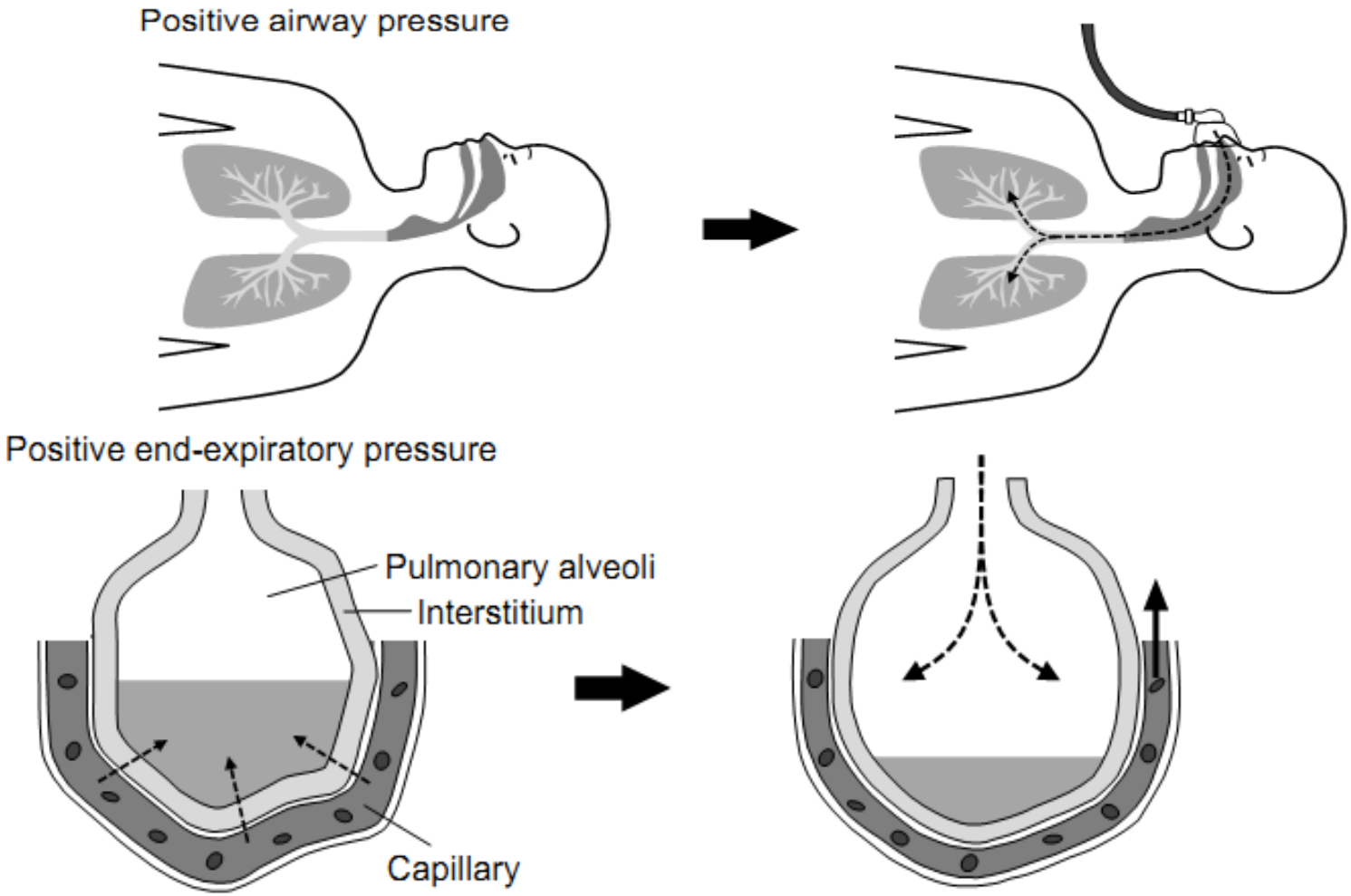


Fig. 3. Effect of positive airway pressure
Upper panels : Positive airway pressure widens an upper airway and pulmonary alveoli.
Lower panels : Positive end-expiratory pressure expands pulmonary alveoli, decreases pulmonary fluid and improves congestion and gas exchange in patients with heart failure.

Table 4 Actions of continuous positive airway pressure in CHF

Scenario	Acute pulmonary oedema	OSA	CSA-CSR
Upper airway			
Pneumatic splinting	+	+++	+
Pulmonary			
Overcome negative ITP	+	+++	+
Increase lung volume	++	++	++
Prevent alveolar collapse	+++	+	++
Improve VQ matching	+++	+	++
Reduce pulmonary vasoconstriction	+++	+	++
Assist inspiratory muscles	+++	+	++

Table 4 Actions of continuous positive airway pressure in CHF

Scenario	Acute pulmonary oedema	OSA	CSA-CSR
Cardiac			
Afterload reduction			
Less negative ITP	+	+++	+
Fall in systemic BP	+	++	++
Reduced LV diameter	+	++	++
Preload reduction	++	+	+

Current and potential treatments for sleep-disordered breathing

Treatment	Evidence
Obstructive sleep apnoea	
Noninvasive positive airway pressure: • Continuous positive airway pressure • Bilevel positive airway pressure	Strong evidence
Weight loss	Strong evidence provided by large interventional and observational studies
Mandibular advancement devices	Small studies, controversial evidence
Uvulopalatopharyngoplasty and laser assisted uvulopalatoplasty	Small studies
Furosemide and spironolactone	Preliminary results
Hypoglossal nerve stimulation	Preliminary results
Cardiac pacing	Potential treatment, but negative results have been obtained

HF-OSA-CPAP?

- **RCTs involving patients with HF and OSA treated with CPAP showed an improvement in left ventricular systolic function and reductions in blood pressure, heart rate, and sympathetic nerve activity (*Kaneko, Y. et al. Cardiovascular effects of continuous positive airway pressure in patients with heart failure and obstructive sleep apnea. N. Engl. J. Med.2003, Mansfield, D. R. et al. Controlled trial of continuous positive airway pressure in obstructive sleep apnea and heart failure. Am. J. Respir. Crit. Care Med. 2004)***

- **2 observational studies show that CPAP treatment lowers mortality and improves hospitalization free survival in patients with HF, particularly in compliant patients (use CPAP 4.9 h) (*Kasai, T. et al. Prognosis of patients with heart failure and obstructive sleep apnea treated with continuous positive airway pressure. Chest 2008)***

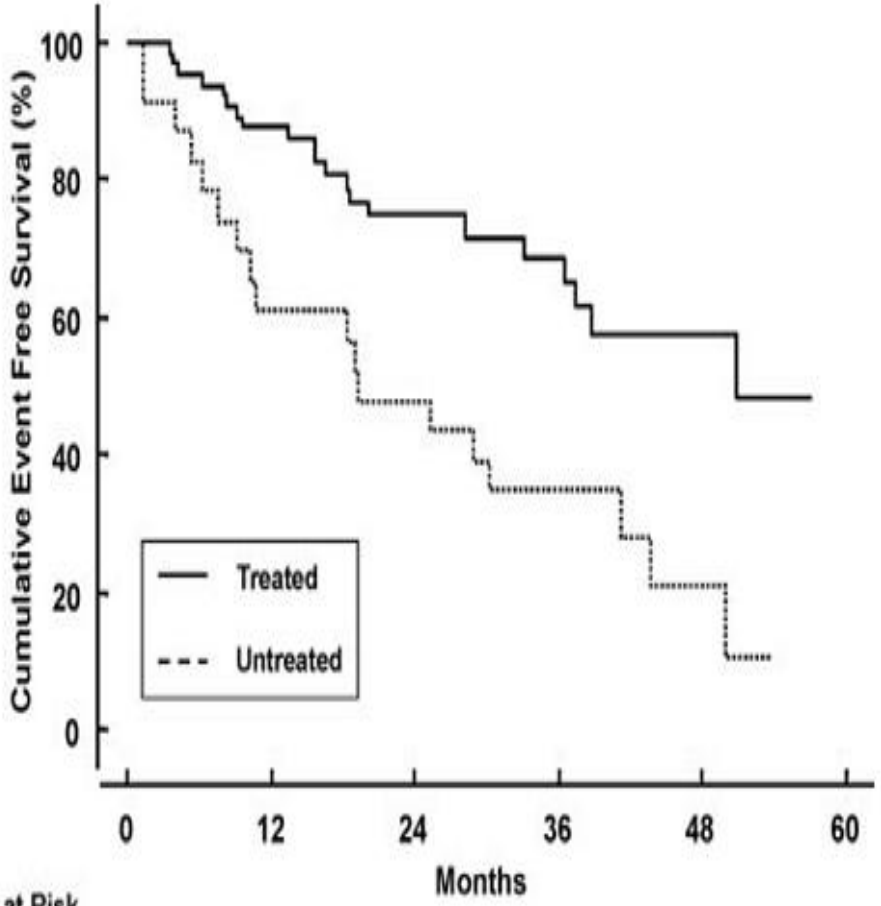
- **Until now, there is no RCT to evaluate the effects on mortality of CPAP treatment for OSA in HF**

- **AHA/ACC Foundation considers CPAP in HF as being investigational because this treatment option is not supported by RCTs data**

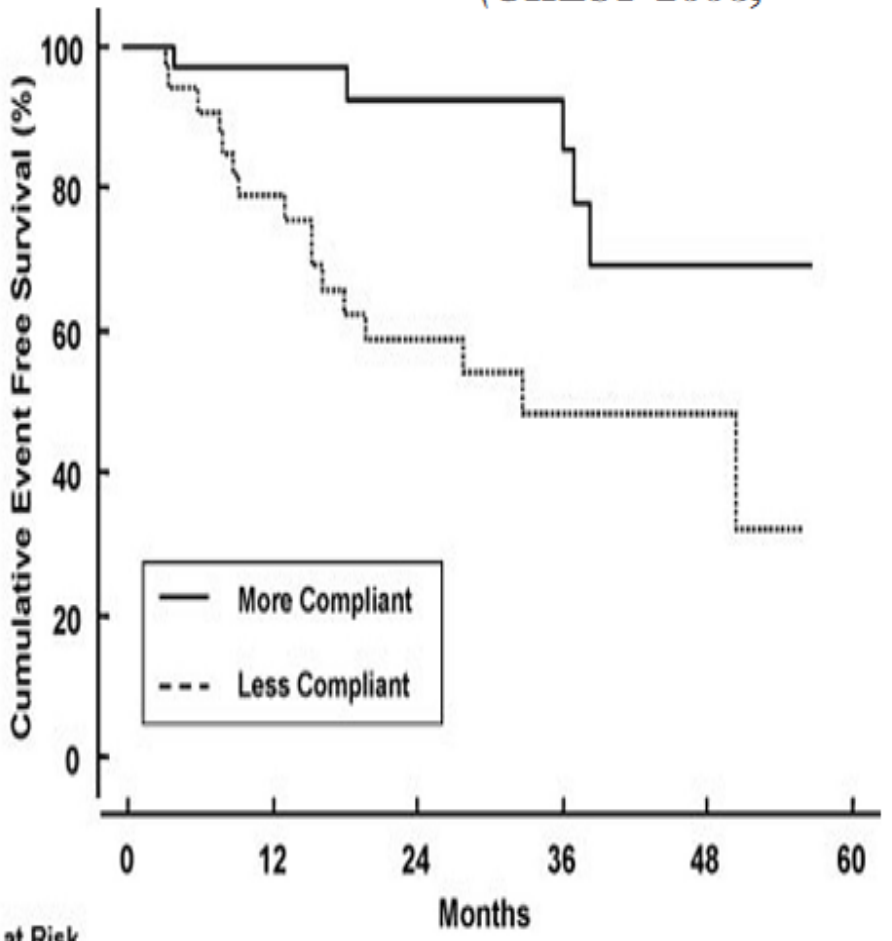
Based on the available evidence, it is reasonable to recommend PAP therapy for the improvement of symptoms in patients with OSA but not for protection against vascular disease or death. It is possible that an enhanced evidence base able to better explore effects in patient subgroups might identify protective effects of PAP treatment for some patient subsets

Prognosis of Patients With Heart Failure and Obstructive Sleep Apnea Treated With Continuous Positive Airway Pressure*

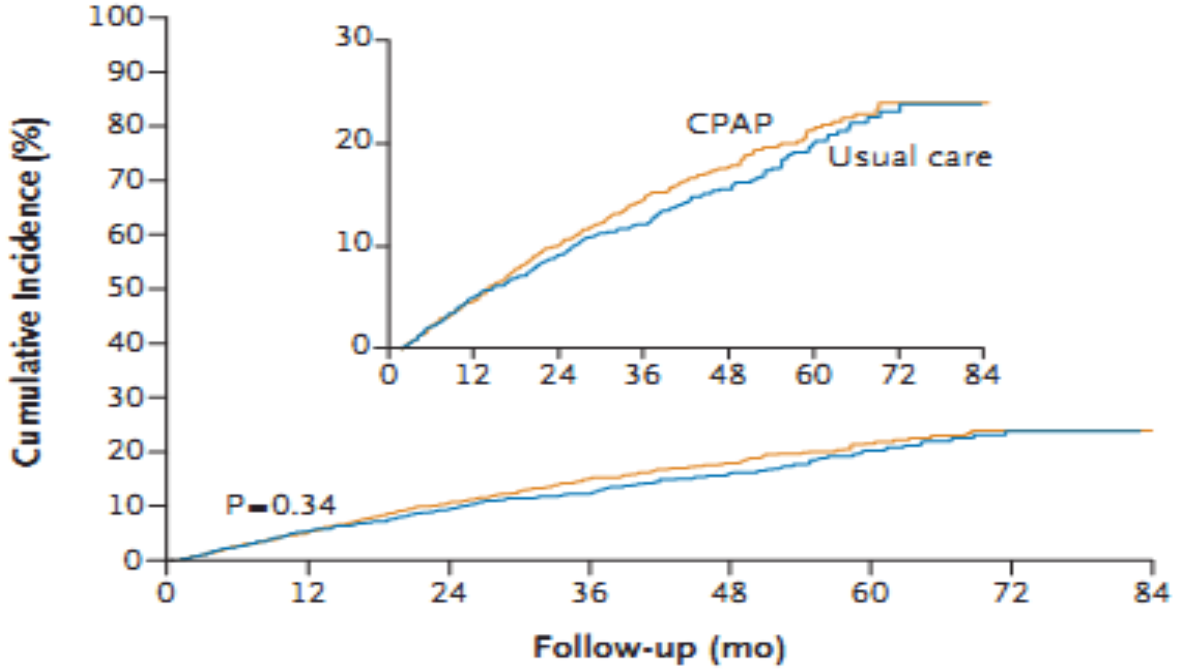
(CHEST 2008;



Numbers at Risk					
Treated	65	56	27	20	7
Untreated	23	14	11	6	2



s at Risk					
mpliant	32	30	14	12	4
mpliant	33	26	13	7	3



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

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

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

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 SEPTEMBER 8, 2016 VOL. 375 NO. 10

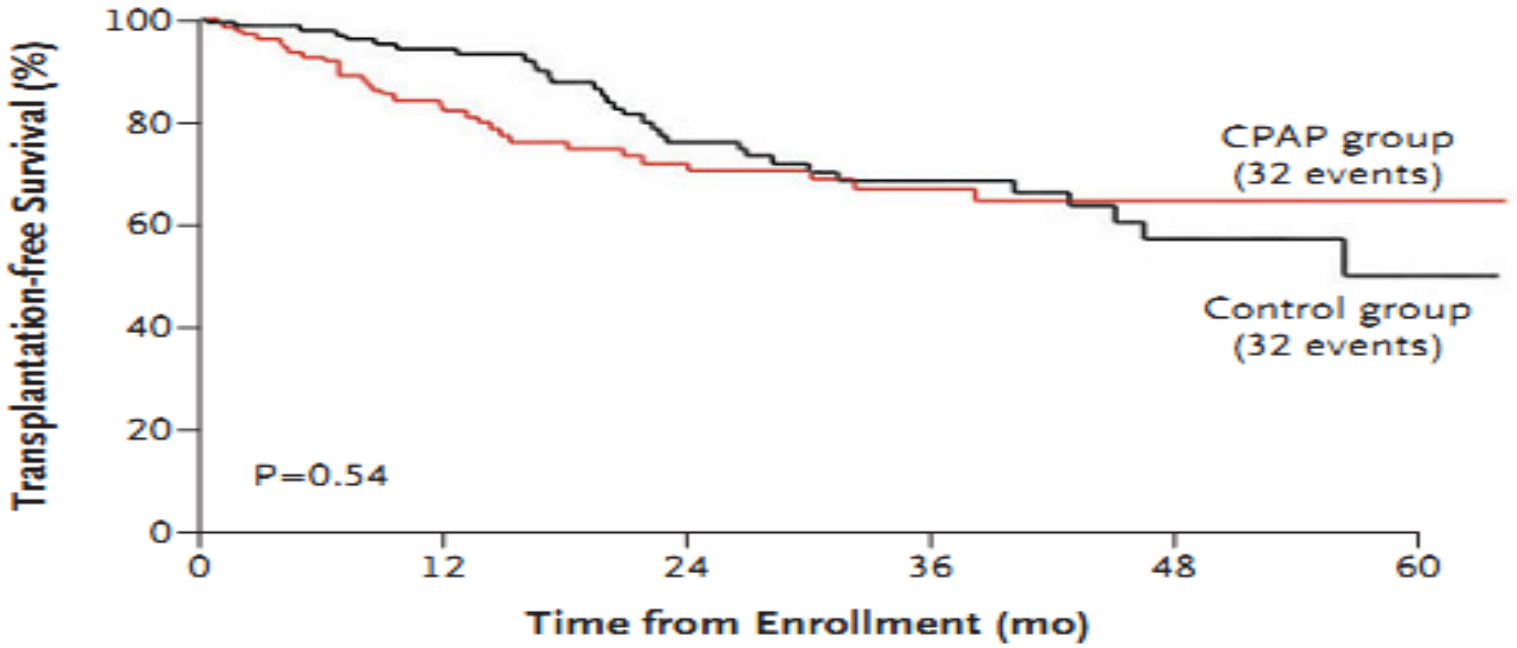
Current and potential treatments for sleep-disordered breathing

Central sleep apnoea	Evidence
Noninvasive positive airway pressure:	
• Continuous positive airway pressure	• Partly controversial evidence from small studies
• Bilevel positive airway pressure	• Partly controversial evidence from small studies
• Adaptive pressure support servo-ventilation	• Still under investigation
Acetazolamide and theophylline	Small observational studies
Supplemental O_2	Controversial evidence
Phrenic nerve stimulation	Pilot studies, efficacy to be proven
Cardiac pacing	Small studies, more evidence needed

- **CSA in HF should trigger attention to determine whether more aggressive therapy is required to combat the CHF**
- **Sleeping upright or laterally**
- **Greater afterload reduction (vasodilators), preload reduction with diuretics such as acetazolamide, inotropes, surgery (coronary artery graft surgery, valvular repair or replacement), rhythm correction, pacemakers [atrial overdrive, biventricular, left ventricular assist device or even heart transplantation,**

HF-CSA-PAP???

- **CPAP responders HF patients – non CPAP responders HF patients**
- **CANPAP trial : HF and CSA at 3 months, the CPAP group showed a reduction in the AHI, increase of EF and mean Oxygen Saturation but no differences were found in the overall death (*Bradley, T. D. et al. Continuous positive airway pressure for central sleep apnea and heart failure. N. Engl. J. Med. 2005*)**
- **A post-hoc analysis showed a decrease in mortality in patients in whom CPAP resulted in amelioration of CSA (CPAP responders *(Arzt, M. et al. Suppression of central sleep apnea by continuous positive airway pressure and transplant-free survival in heart failure: a post hoc analysis of the CANPAP for Patients with Central Sleep Apnea and Heart Failure Circulation 2007)***



No. at Risk

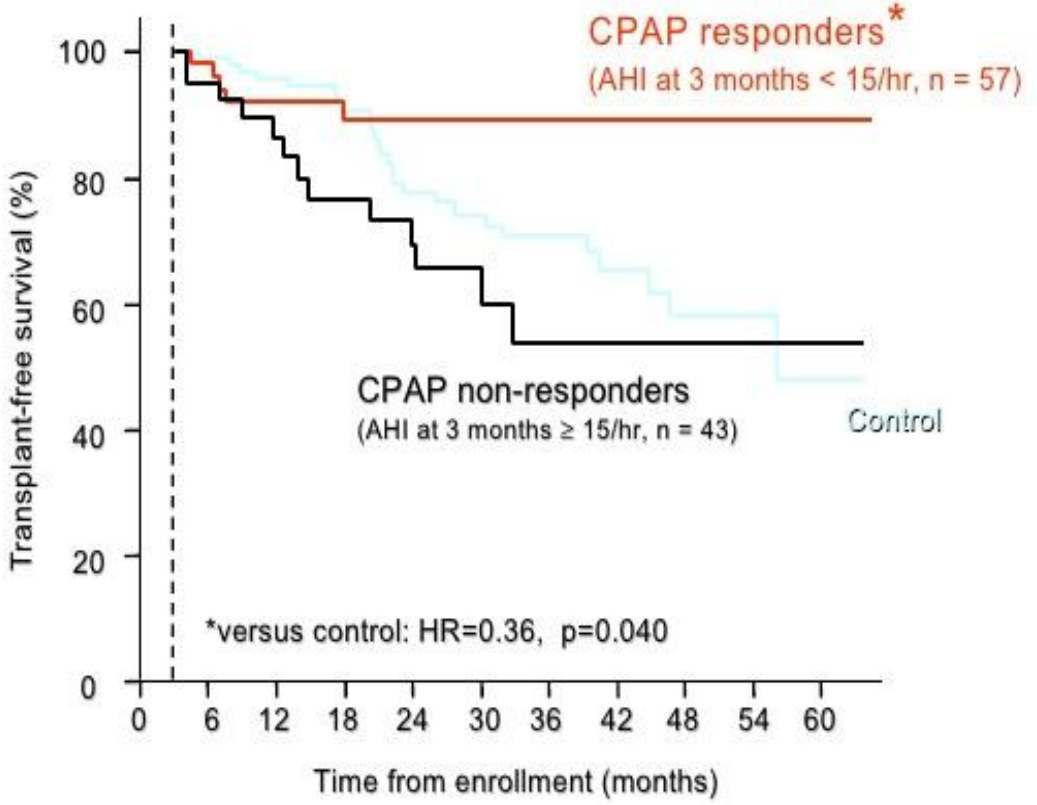
CPAP group	128	104	79	59	49	42	33	24	20	12	6
Control group	130	117	96	79	59	46	37	27	19	12	4

Figure 3. Heart-Transplantation–free Survival.

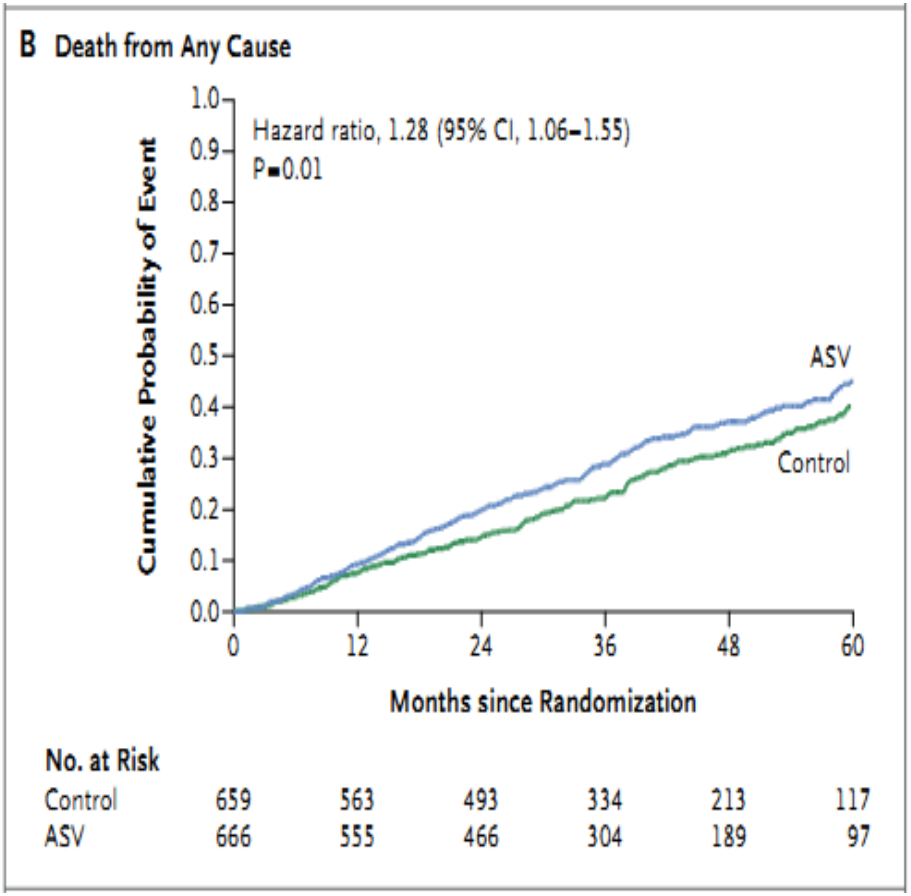
There was no difference in transplantation-free survival rates between the control group and the CPAP group (hazard ratio for transplantation-free survival, 1.16; P=0.54). However, there was an early divergence in the event rates that favored the control group (hazard ratio for transplantation-free survival, 1.5; P=0.02) that altered after 18 months to favor the CPAP group (hazard ratio for transplantation-free survival, 0.66; P=0.06).

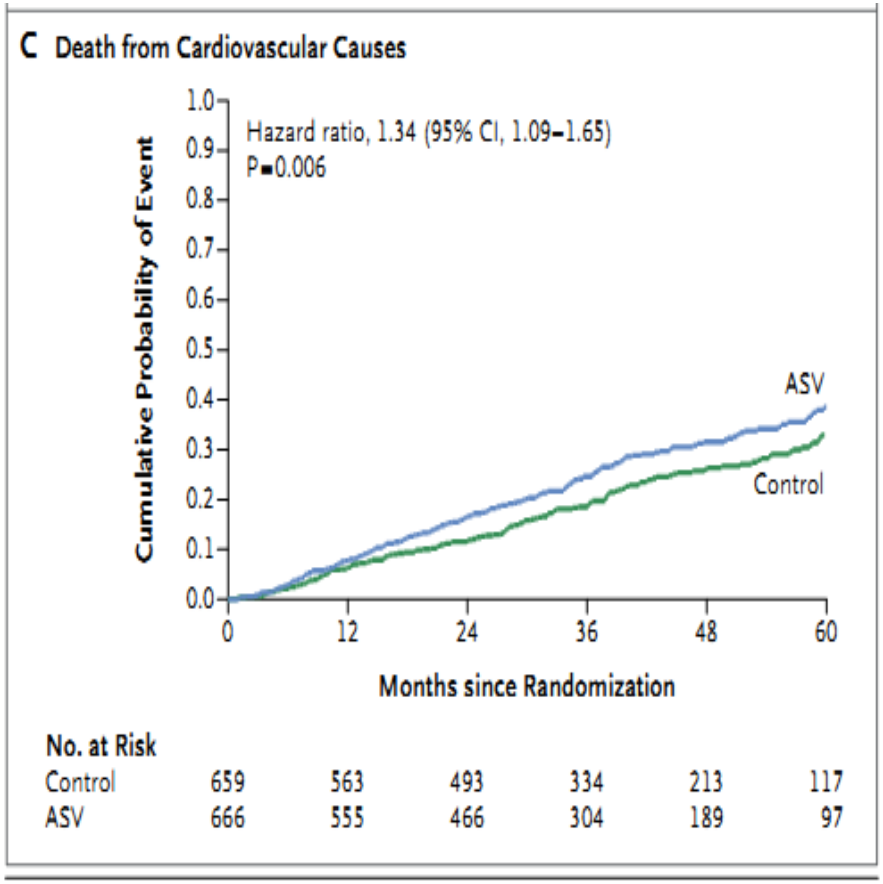
(CANPAP) trial N Engl J Med 2005;353:2025-33.

Transplant-free survival in HF patients according to effect of CPAP on CSA



The answer to the question of treating sleep-disordered breathing leading to improved heart failure outcomes is not clear



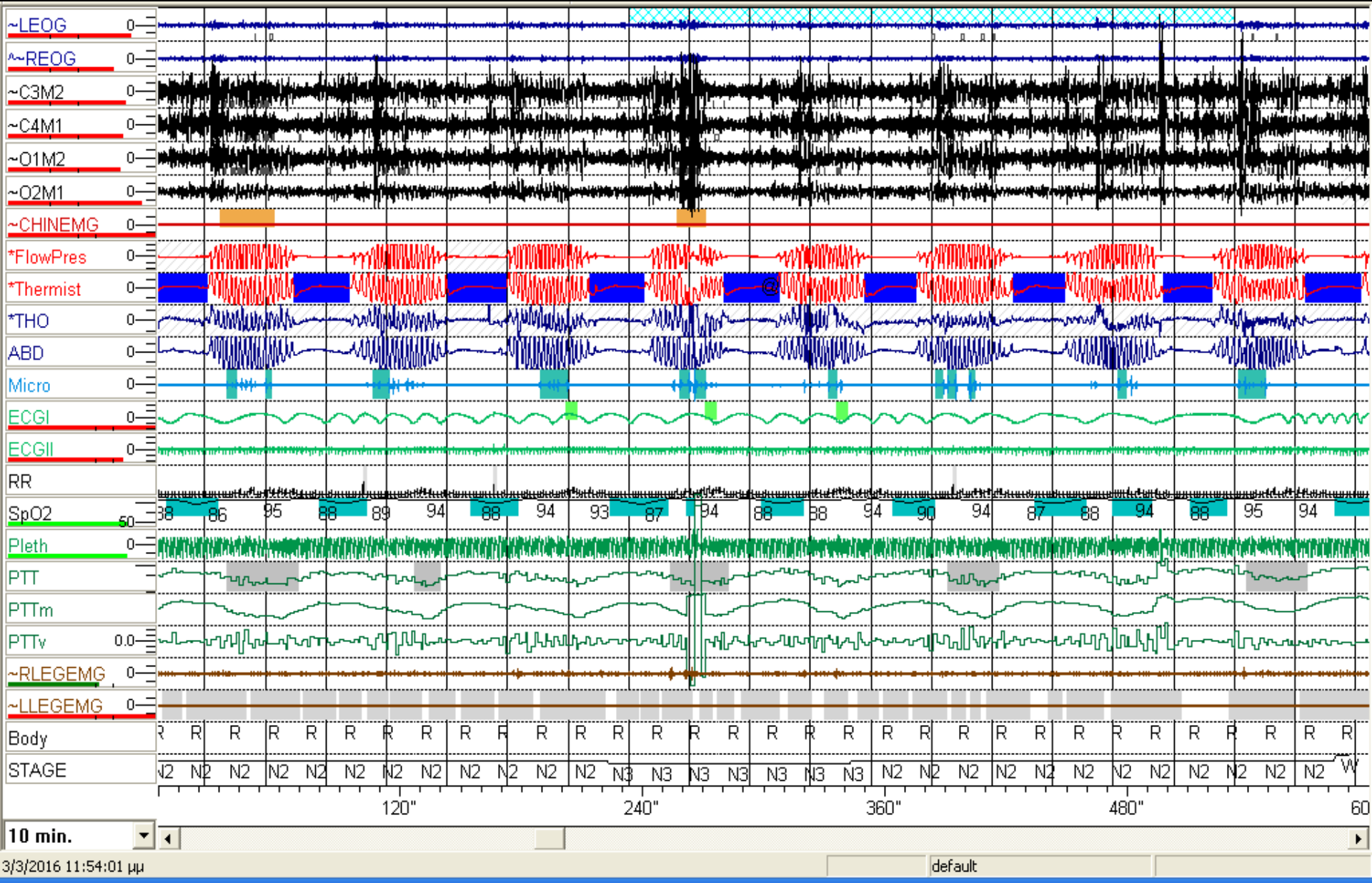


In conclusion, patients who had heart failure with a reduced ejection fraction and predominantly central sleep apnea, the addition of adaptive servo-ventilation to guideline-based medical treatment did not improve the outcome. The risk of **cardiovascular death was increased by 34%,** which was sustained through-out the trial, and there was no beneficial effect on quality of life or symptoms of heart failure.

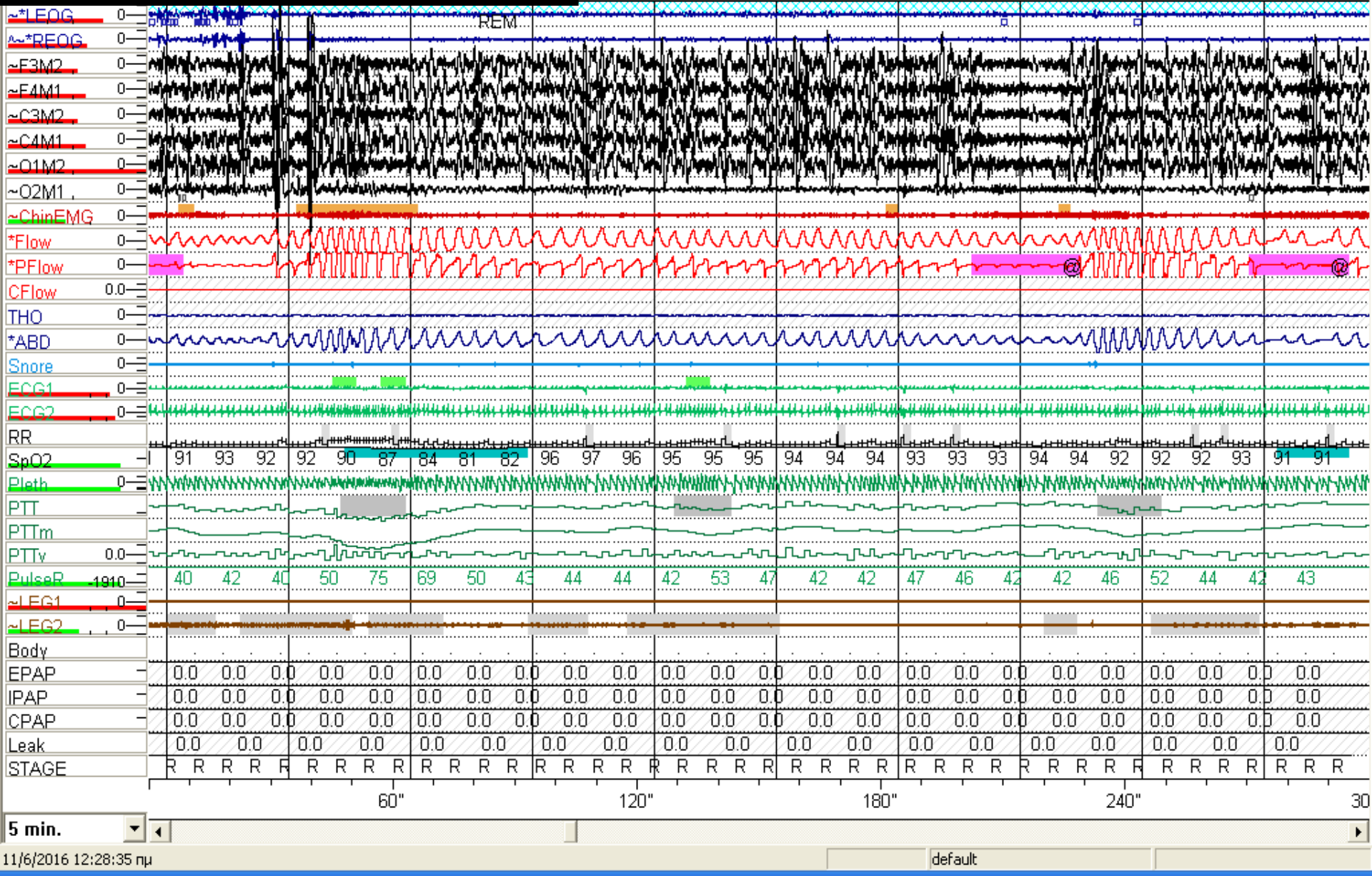
The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 SEPTEMBER 17, 2015 VOL. 373 NO. 12

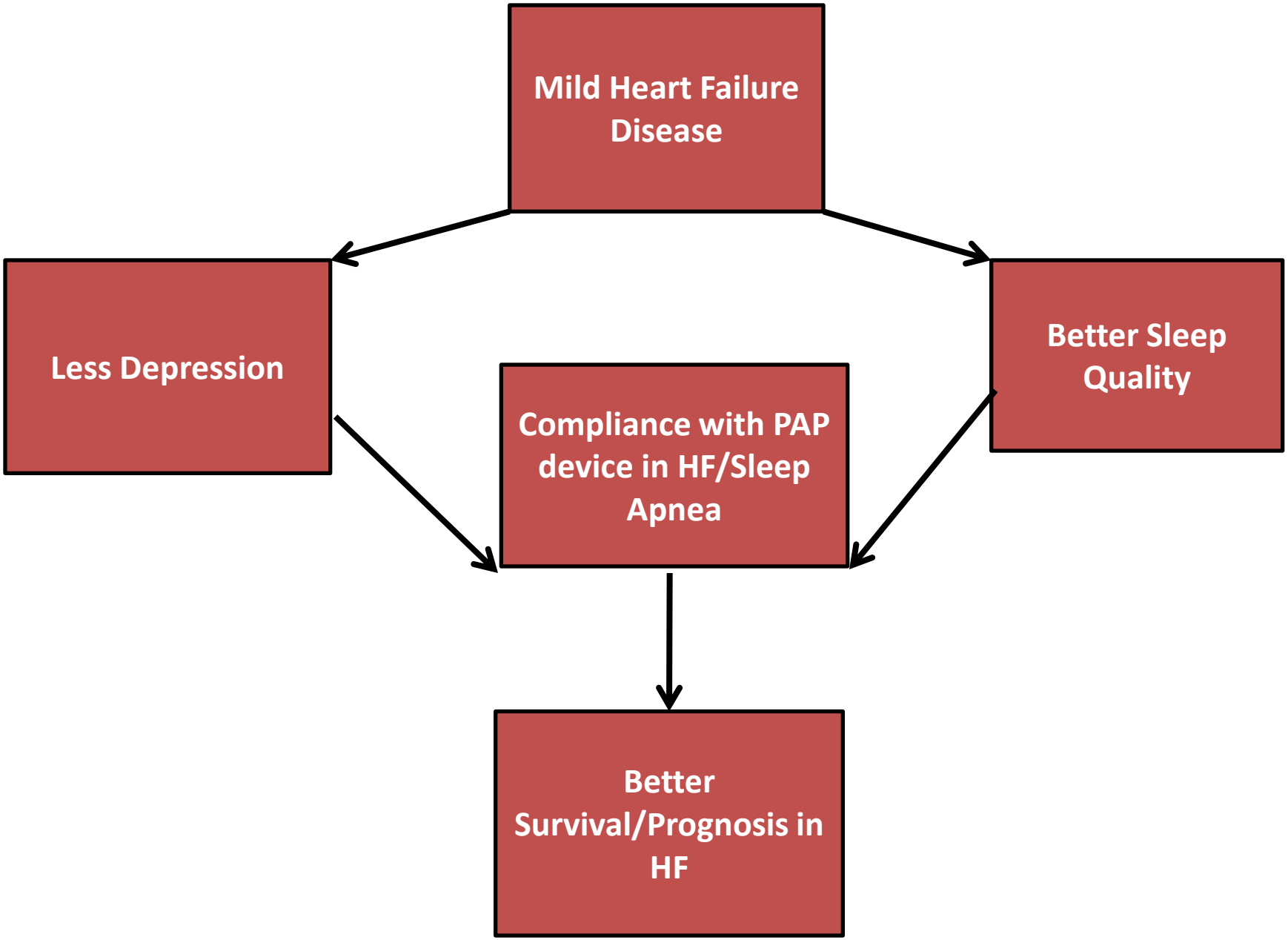
Adaptive Servo-Ventilation for Central Sleep Apnea in Systolic Heart Failure

Cheyne Stokes Respiration in Heart Failure



3 Months After Treatment of Heart Failure
Appearance Obstructive Hypopneas




Mild Heart Failure Disease
Less Depression
Better Sleep Quality
Compliance with PAP device in HF/Sleep Apnea
Better Survival/Prognosis in HF

HF-SLEEP DISORDERS

Review

European Journal of Preventive Cardiology

ESC European Society of Cardiology

European Journal of Preventive Cardiology
0(00) 1–15

DOI: 10.1177/2047487319879526
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SAGE

Sleep – the yet underappreciated player in cardiovascular diseases: A clinical review from the German Cardiac Society Working Group on Sleep Disordered Breathing

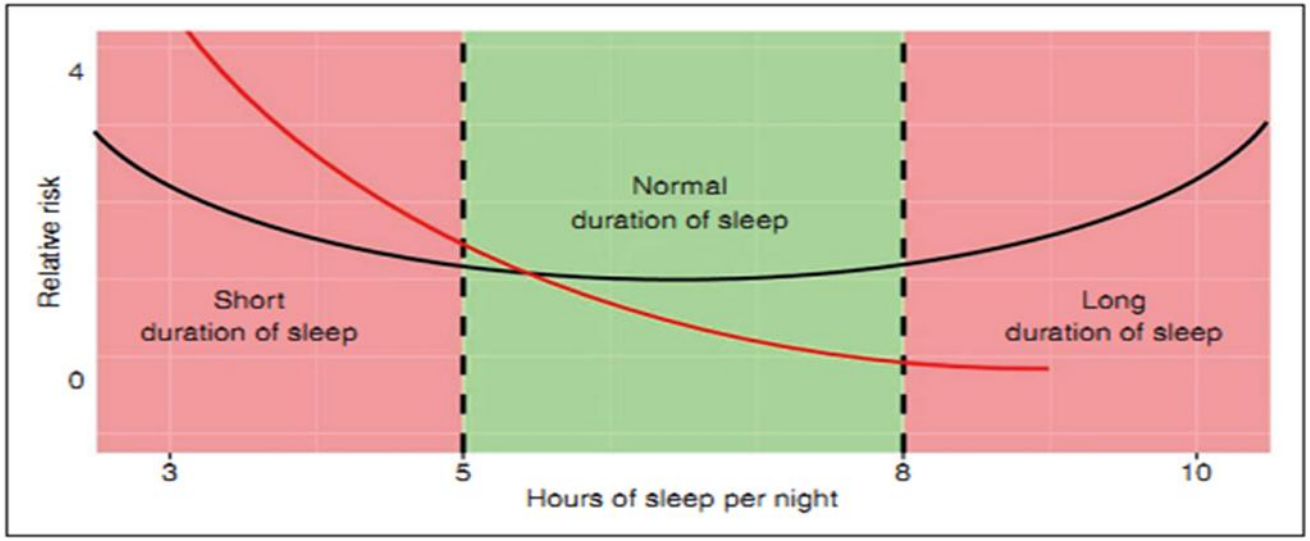


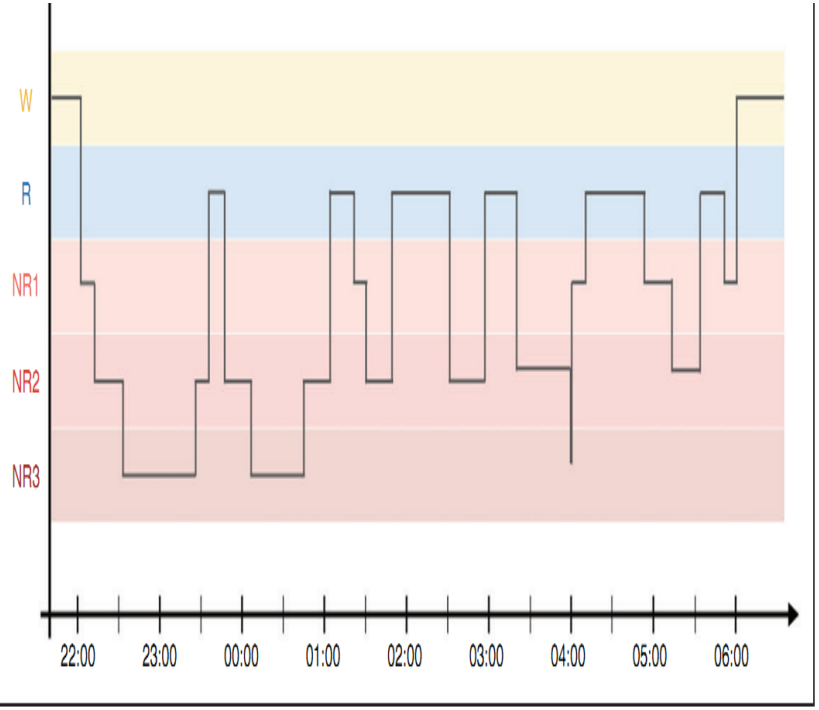
Figure 2. Schematic illustration of the association between sleep duration and the risk of developing or dying of total cardiovascular disease. While for self-reported sleep duration both long and short sleep duration are associated with an increased risk (black line), only short objective sleep duration is associated with an increased risk (red line). In fact, when sleep is measured objectively, short sleep and poor sleep quality, but not long sleep, is a risk factor for mortality.[14]

- **Insomnia symptoms, including having difficulty initiating sleep, maintaining sleep, or having poor sleep quality, are highly prevalent among heart failure (HF) patients. Recent studies indicate that the prevalence of these symptoms among HF patients ranges from 23 to 73%**

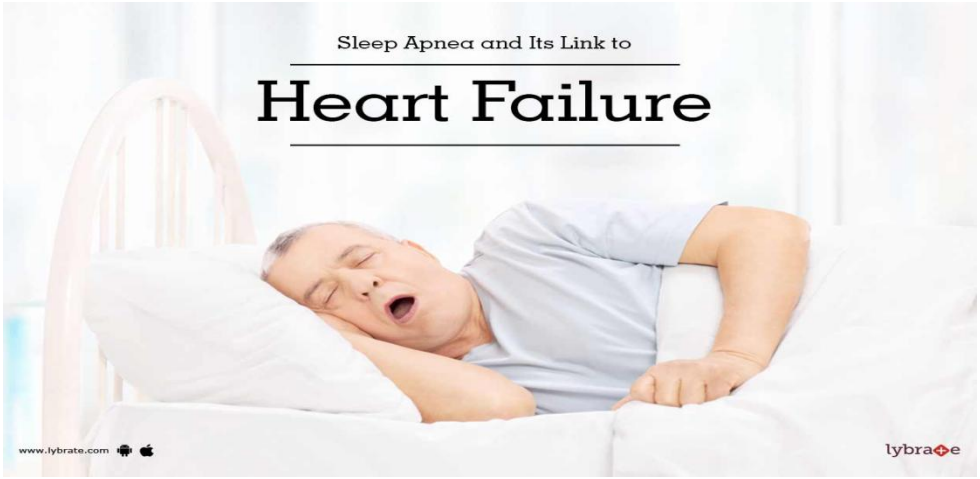
Little is known about sleep quality in patients with HF

The distribution of overnight sleep stages has a significant influence on autonomic function and is therefore directly relevant to cardiovascular medicine

Slow-wave (N3) sleep is associated with an increase in vagal tone, whereas REM sleep is associated with an increase in sympathetic neural traffic



igure 1. Representative polysomnogram showing healthy sleep architecture with characteristic and repetitive passage through eep cycles. N3 represents slow-wave sleep, which occurs more during the first half of the night, whereas REM sleep is more common uring the second half of the night. Pathological sleep is characterised by a reduction in slow-wave sleep and/or REM sleep and/or sleep



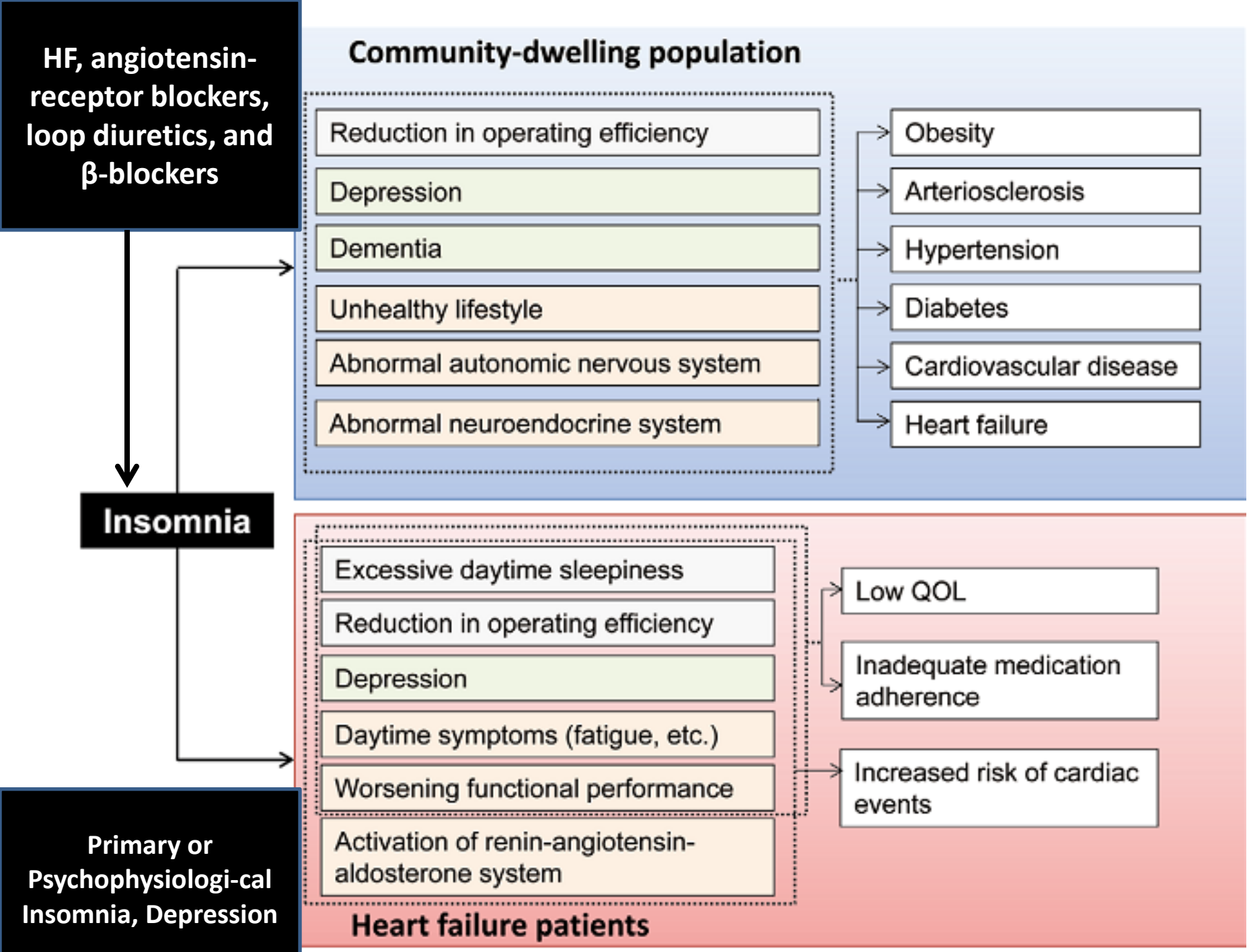
Short sleep time and Low Sleep Quality

1. Sleep fragmentation
2. Nonrestorative sleep
3. Difficulties in initiating sleep
4. Waking up too early in the morning
5. Chronic Insomnia:

-Primary or psychophysiologi-cal insomnia (mood disorders and psychological stress)

-Secondary insomnia caused by the HF itself or by adverse effects of commonly prescribed HF medications, such as angiotensin- receptor blockers, loop diuretics, and B--blockers

6. Nocturia


HF, angiotensin-receptor blockers, loop diuretics, and β-blockers
Community-dwelling population
Reduction in operating efficiency
Depression
Dementia
Unhealthy lifestyle
Abnormal autonomic nervous system
Abnormal neuroendocrine system
Obesity
Arteriosclerosis
Hypertension
Diabetes
Cardiovascular disease
Heart failure
Insomnia
Excessive daytime sleepiness
Reduction in operating efficiency
Depression
Daytime symptoms (fatigue, etc.)
Worsening functional performance
Activation of renin-angiotensin-aldosterone system
Low QOL
Inadequate medication adherence
Increased risk of cardiac events
Heart failure patients
Primary or Psychophysiologi-cal Insomnia, Depression

Review

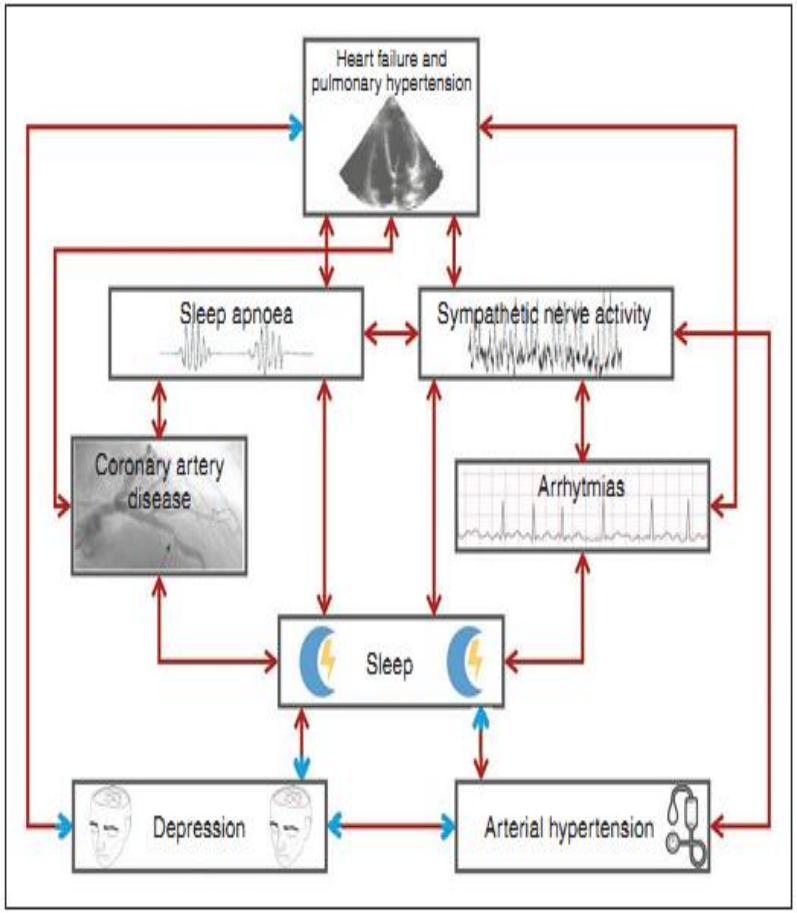
European Journal of Preventive Cardiology

ESC European Society of Cardiology

Sleep – the yet underappreciated player in cardiovascular diseases: A clinical review from the German Cardiac Society Working Group on Sleep Disordered Breathing

European Journal of Preventive Cardiology
0(00) 1–15

DOI: 10.1177/2047487319879526
journals.sagepub.com/home/cpr
SAGE



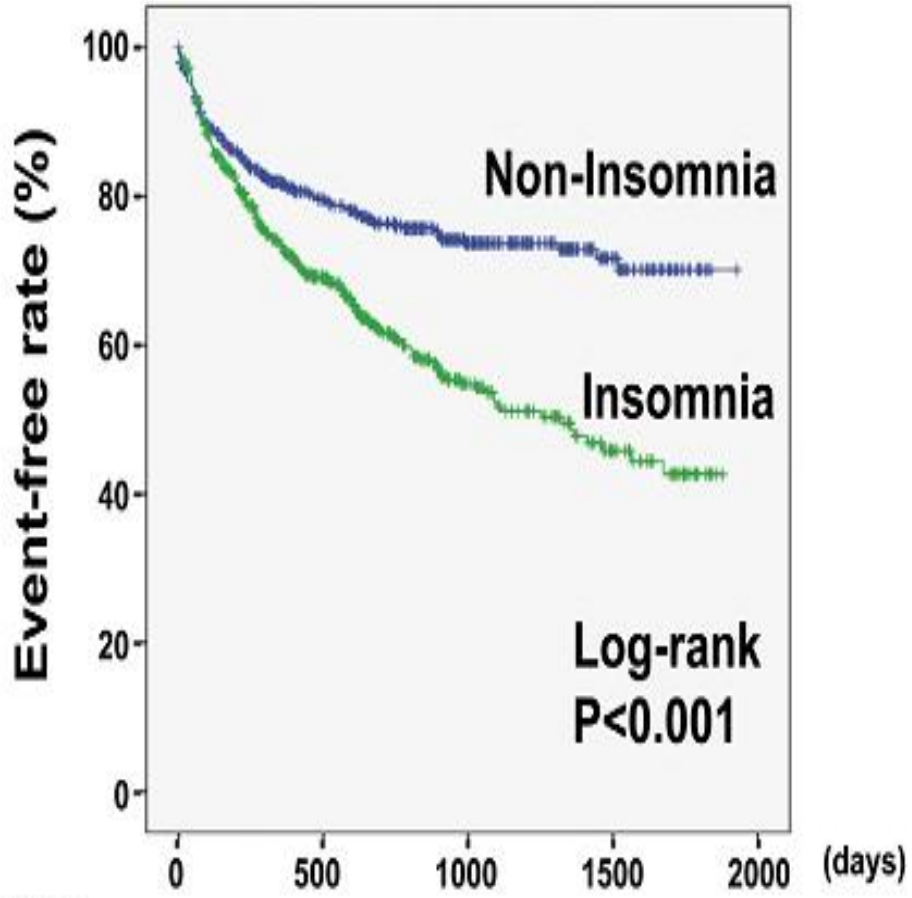
esumed complex pathophysiological interplay of sleep with various cardiovascular comorbidities. Arrows high
t insufficient objective and/or high-quality data exist to support the notion of an association, while red arrow
exist, making the association highly likely.

Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

ORIGINAL ARTICLE
Heart Failure

Prognostic Significance of Insomnia in Heart Failure

Yuki Kanno, MD; Akiomi Yoshihisa, MD, PhD; Shunsuke Watanabe, MD; Mai Takiguchi, MD; Tetsuro Yokokawa, MD; Akihiko Sato, MD; Shunsuke Miura, MD; Takeshi Shimizu, MD, PhD; Yuichi Nakamura, MD, PhD; Satoshi Abe, MD, PhD; Takamasa Sato, MD, PhD; Satoshi Suzuki, MD, PhD; Masayoshi Oikawa, MD, PhD; Shu-ichi Saitoh, MD, PhD; Yasuchika Takeishi, MD, PhD



No. at risk

Non-Insomnia	492	286	159	49	0
Insomnia	519	258	100	38	0

Interestingly, it has that voluntary daytime naps of <2 hours have recently been shown to decrease sympatho-vagal balance in a similar way to that seen during slow-wave sleep

Whitehurst LN et al. Comparing the cardiac autonomic activity profile of daytime naps and nighttime sleep. Neurobiol Sleep Circadian Rhythm 2018

Cellini N et al.Heart rate variability during daytime naps in healthy adults: autonomic profile and short-term reliability. Psychophysiology 2016

On the contrary, spontaneous daytime naps that are highly prevalent in patients with cardiovascular diseases especially at durations longer than 30 minutes may have a compenasatory role but they have beeen associated with unfavourable changes in the regulation of metabolic and endocrine hormones

The potential of melatonin administration for promoting sleep quality in HF patients has not been proved until now

In the future the demonstration of conservative measures such as teaching sleep hygiene or using behavioural therapy could improve sleep quality in patients with cardiovascular disorders

Prognostic Impact of Restless Legs Syndrome on Patients with Heart Failure

8.6% in HF patients had RLS

HF patients with RLS had a higher prevalence of anemia, higher levels of BNP, impaired cardiac function of the right and left ventricles

RLS could promote sympathetic arousal and sympathetic overactivity, activate the hypothalamic-pituitary-adrenal axis and increase the levels of pro-inflammatory cytokines and circulating catecholamine and all conditions leads to adverse prognosis of HF

CVD could produce RLS through vascular changes in the central nervous system or in the periphery or through the influence of medications (e.g., inotropic agents) for CVD. Thus, presence of RLS may present severity of CVD or HF

Int Heart J. 2019

Relation of Periodic Leg Movements During Sleep and Mortality in Patients With Systolic Heart Failure

Dai Yumino, MD, PhD[a,d], Hanqiao Wang, MD[a,d], John S. Floras, MD, DPhil[b,c], Gary E. Newton, MD[b], Susanna Mak, MD, PhD[b], Pimon Ruttanaumpawan, MD[a,d], John D. Parker, MD[b,c], and T. Douglas Bradley, MD[a,c,d,*]

Am J Cardiol 2011

37% of unselected patients with HF had PLMs at a rate of 5 per hour of sleep

compared with a prevalence of 4% to 8% in subjects without HF

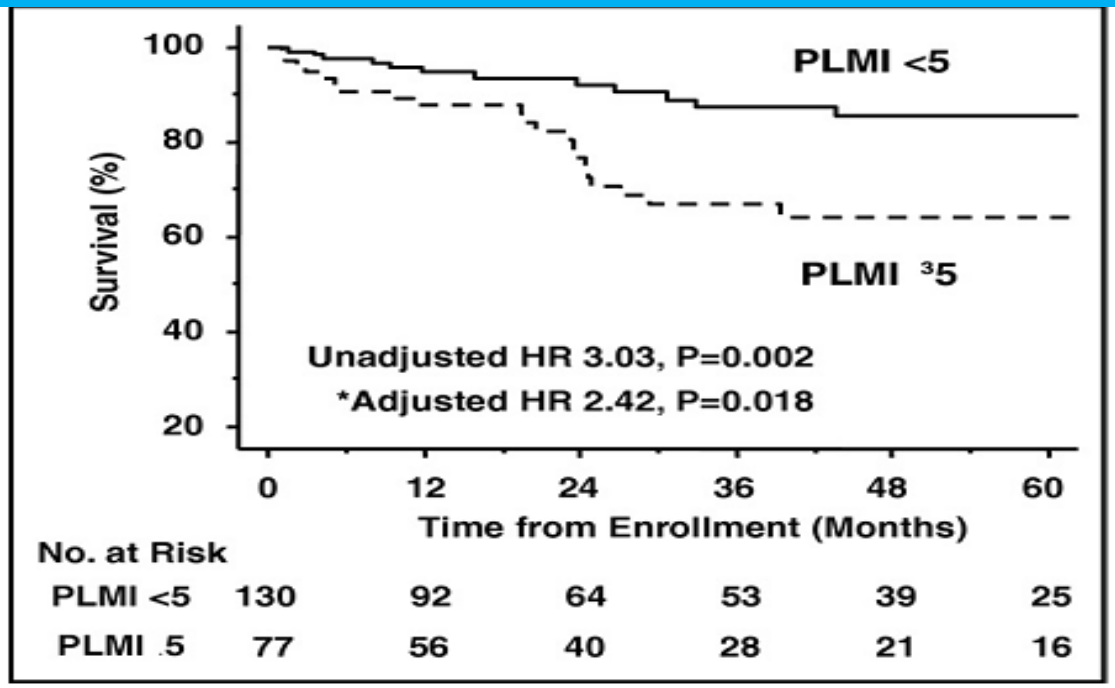


Figure 2. Kaplan-Meier plots comparing survival between patients with HF with PLMIs ≥5 and those with PLMIs <5. *Adjusted HR for significant confounding factors included age, NYHA class, LVEF, ischemic cause of HF, and central sleep apnea.

International Journal of Cardiology 212 (2016) 11–13

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journal homepage: www.elsevier.com/locate/ijcard

Correspondence

Prognostic significance of periodic leg movements during sleep in heart failure patients

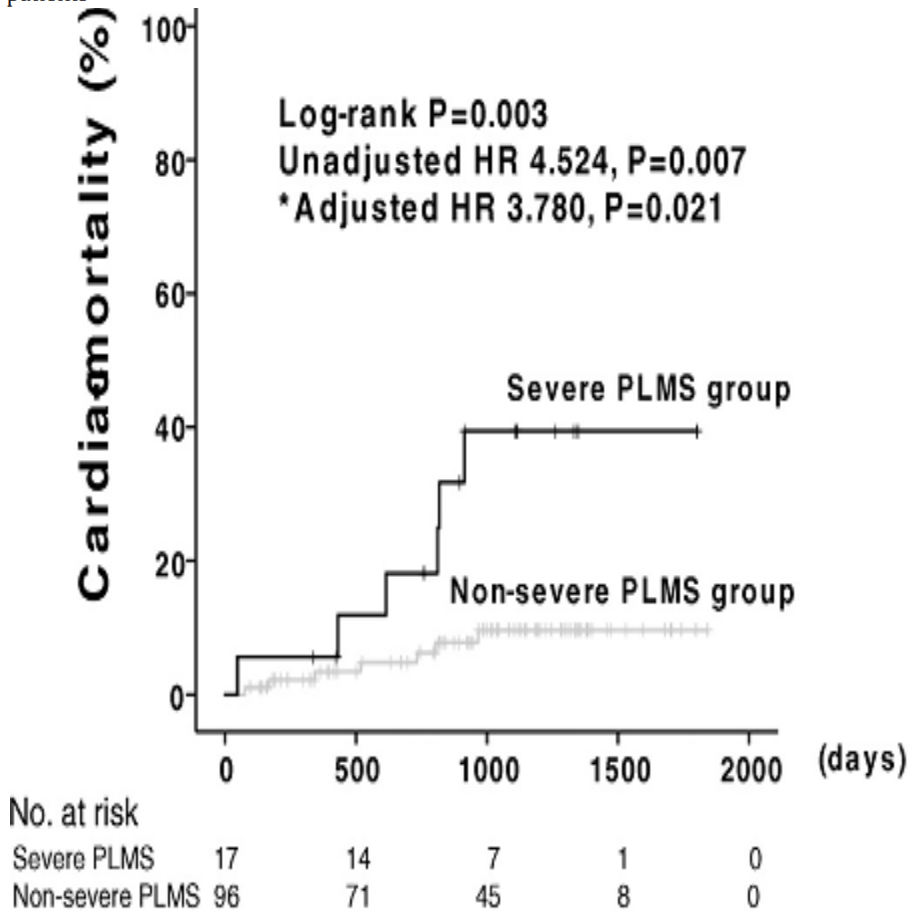


Fig. 1. Comparison of cardiac mortality between the severe PLMS group and the non-severe PLMS group. Kaplan–Meier analysis for cardiac mortality (severe PLMS vs. non-

Circ J 2017; **81**: 495–500
doi:10.1253/circj.CJ-16-0934

ORIGINAL ARTICLE
Heart Failure

Impact on Clinical Outcomes of Periodic Leg Movements During Sleep in Hospitalized Patients Following Acute Decompensated Heart Failure

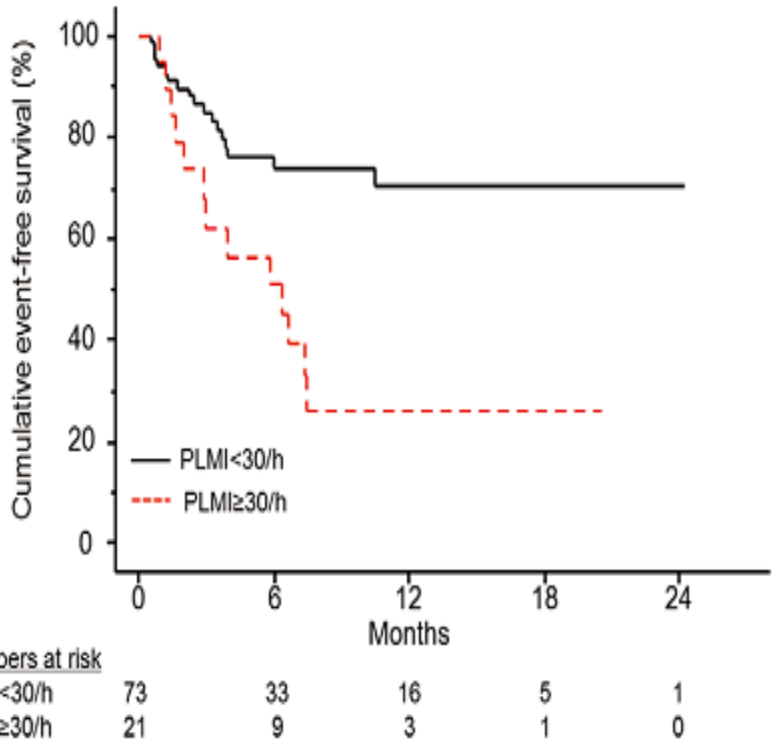


Figure. Cumulative event-free survival curves in patients with acute decompensated heart failure and PLMI <30 or ≥30/h. Cumulative event-free survival from all-cause death and rehospitalizations was significantly better in patients without severe PLM (i.e., PLMI <30/h) compared with those with severe PLM (i.e., PLMI ≥30/h) (log-rank test: P=0.002). PLM,

TREAT or not to TREAT RLS/PLMs

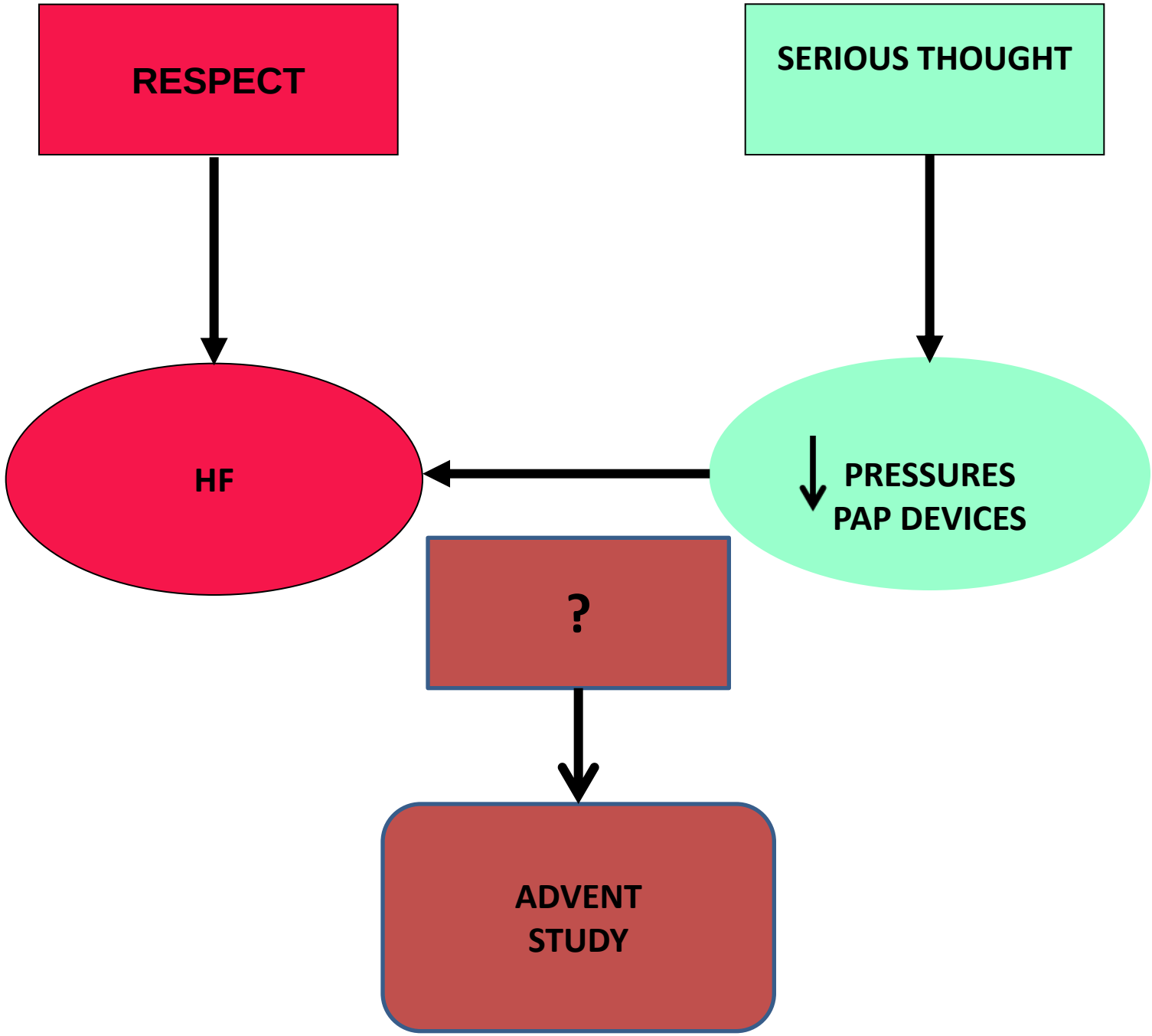
ΣΥΜΠΕΡΑΣΜΑ

- **Οι ασθενείς με HF εμφανίζουν πολύ συχνά διαταραχές ύπνου γι' αυτό θα πρέπει να αξιολογούνται στο Εργαστήριο Μελέτης Ύπνου για τον καθορισμό της διαταραχής ύπνου που τυχόν εμφανίζουν με εξέταση εκλογής την Πολυπνογραφία**

- **Ειδικά η αναγνώριση και αντιμετώπιση των διαταραχών της αναπνοής στον ύπνο σε ασυμπτωματικούς ασθενείς με καρδιακή ανεπάρκεια αποτρέπει την εξέλιξη της καρδιακής νόσου σε βαρύτερες μορφές**

- **Οι εξετάσεις με τις φορητές συσκευές θα μπορούσαν να χρησημοποιηθούν στη διάγνωση των αναπνευστικών διαταραχών κατά περίπτωση (δεν υπάρχουν μέχρι τώρα επαρκή δεδομένα για τους ασθενείς με HF)**

- **Η συνεργασία του Καρδιολόγου με τον Ειδικό Ιατρό στην Ιατρική του Ύπνου αποτελεί απαραίτητη προυπόθεση για τη λήψη της τελικής θεραπευτικής απόφασης της αντιμετώπισης της διαταραχής ύπνου**


RESPECT
SERIOUS THOUGHT
HF
PRESSURES
PAP DEVICES
?
ADVENT
STUDY

28ο ΠΑΝΕΛΛΗΝΙΟ
Πνευμονολογικό ΣΥΝΕΔΡΙΟ
12-15 ΔΕΚΕΜΒΡΙΟΥ 2019 | ATHENS HILTON

16:00-17:30 **Στρογγυλή Τράπεζα**
Ο ρόλος του εργαστηρίου ύπνου: πέρα από τους ασθενείς με σύνδρομο απνοιών-υποπνοιών

Ευχαριστώ

Ο ρόλος του εργαστηρίου ύπνου σε ασθενείς με καρδιακή ανεπάρκεια

Βλάμη Αικατερίνη

Εργαστήριο Μελέτης Ύπνου
Πανεπιστημιακό Γενικό Νοσοκομείο ΑΤΤΙΚΟΝ