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Sleep Apnea 2020

Sleep apnea e terapia con ICD nella pratica clinica

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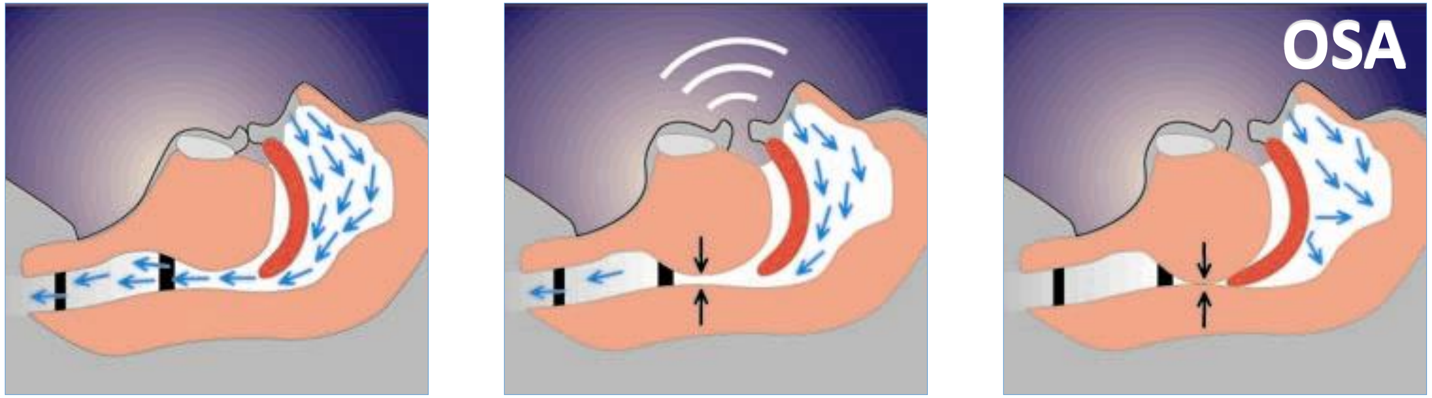
Sleep Apnea: Definitions

Obstructive Sleep Apnea (OSA):

Apnea with respiratory efforts due to collapse of superior airways



Central Sleep Apnea (CSA)

Apnea without respiratory efforts (no CNS control on respiration)

Cheyne-Stokes Respiration (CSR) is a subset of CSA

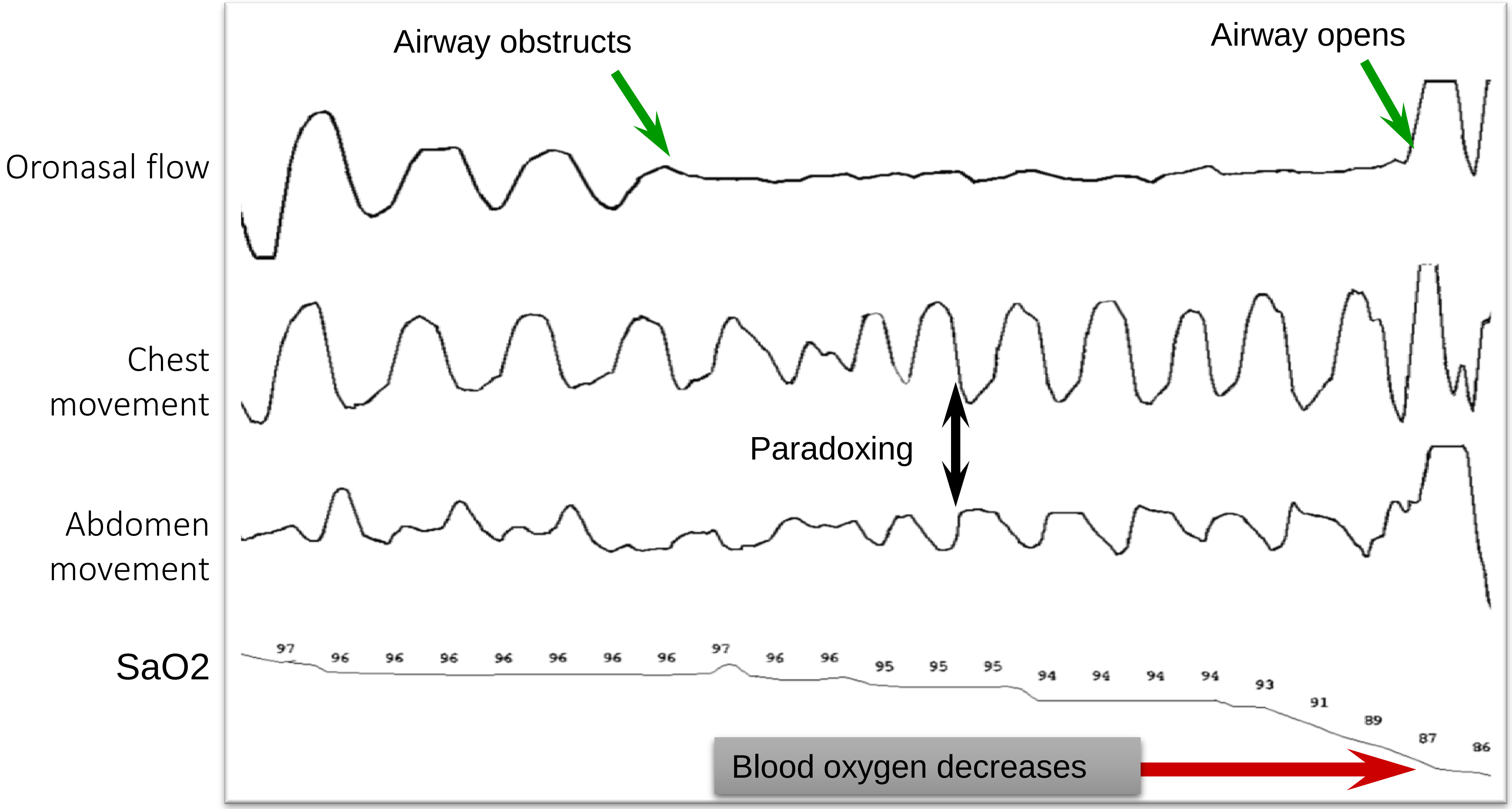
Mixed

Apnea of central origin evolving into an obstructive form. Often classified as obstructive

American Academy of Sleep Medicine Task Force, Sleep 1999; 22: 667-689

Sleep Apnea: Definitions

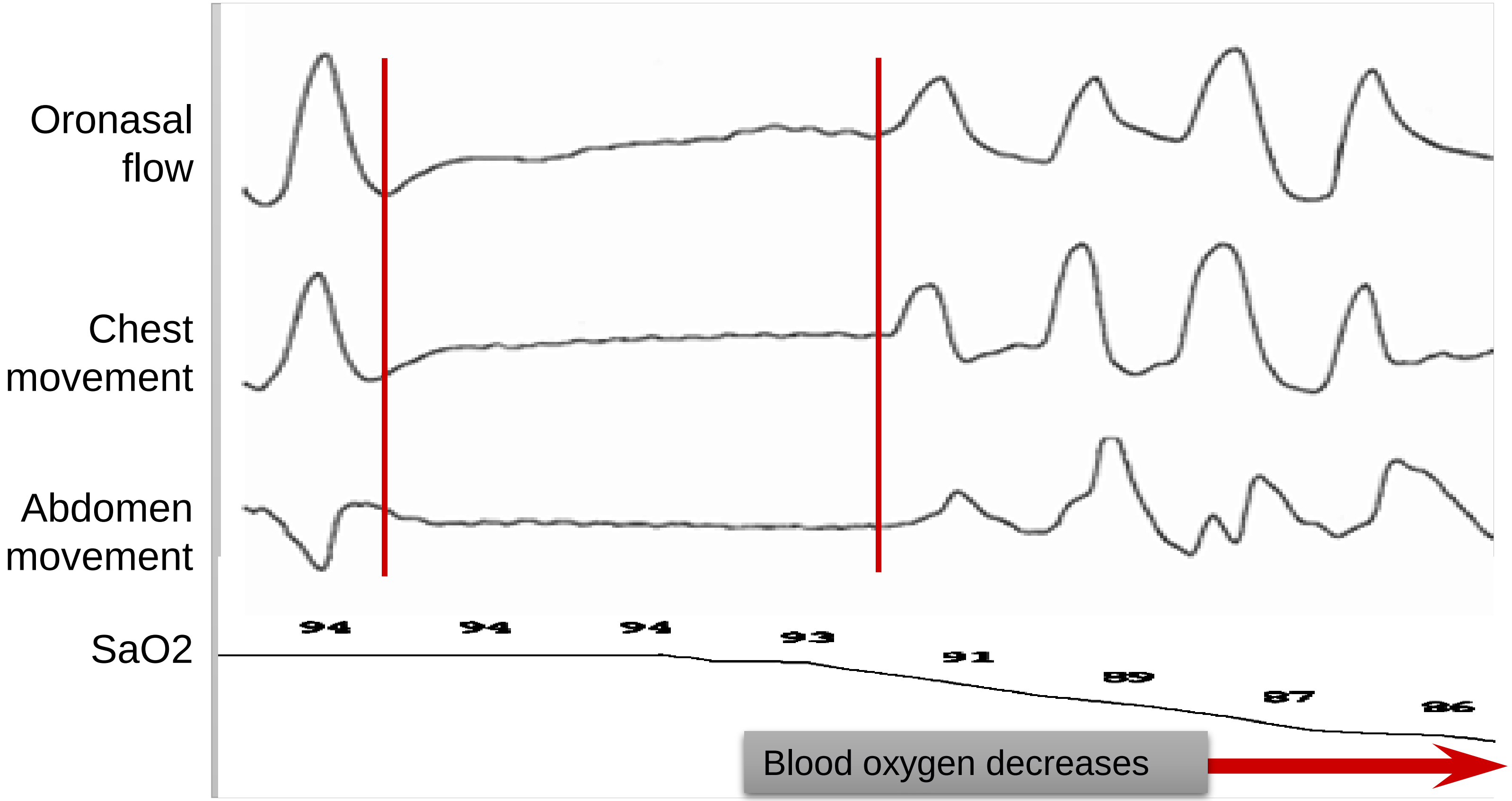
Obstructive Sleep Apnea (OSA):



American Academy of Sleep Medicine Task Force, Sleep 1999; 22: 667-689

Sleep Apnea: Definitions

Central Sleep Apnea (CSA):



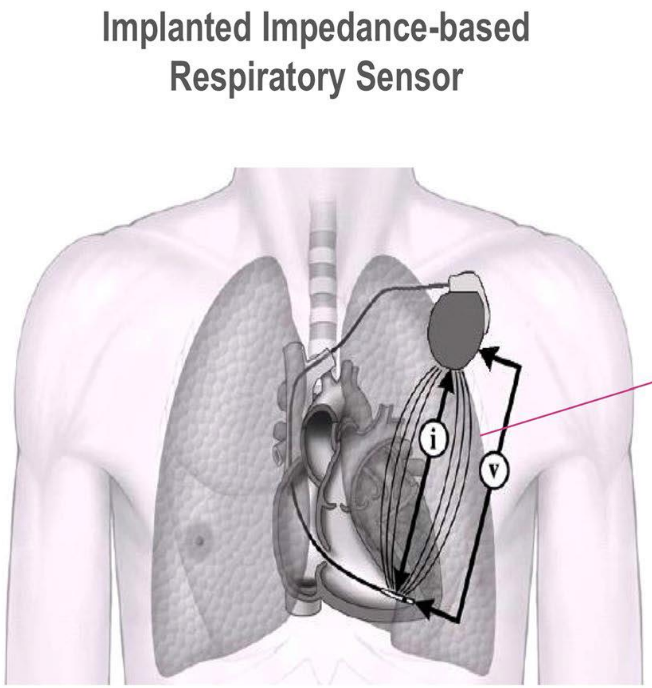
American Academy of Sleep Medicine Task Force, Sleep 1999; 22: 667-689

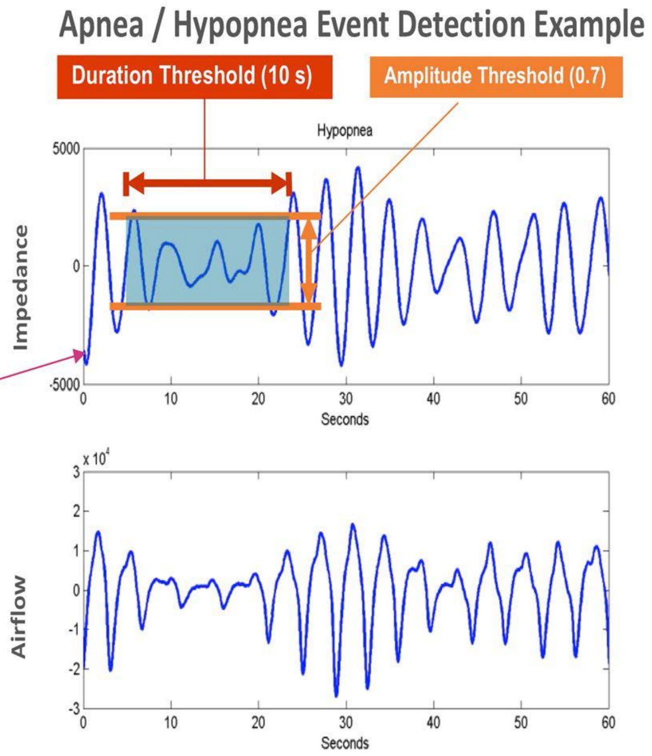
Pathogenesis of cardiovascular events in OSAS subjects

- The sleep fragmentation is the first consequence of OSAS and is considered to be responsible for hypertension development as it stimulates the renin angiotensin system and increases the cytokine production, leading to endothelial dysfunction.
- The intermittent hypoxia induces increased sympathetic activity, which exerts effects on blood pressure and heart rate, promotes free radical production and adhesion molecules expression and induces insulin resistance and leptin resistance.
- The cyclic airway occlusion also causes the intermittent generation of an elevated negative intrathoracic pressure and increases ventricular transmural pressure and ventricular after-load with a parallel raise in venous return; this latter mechanism leads to a reduction in left ventricular stroke volume.
- During the apneic event, hypoxia may cause an imbalance between the myocardial oxygen demand and supply, which may induce myocardial ischemia or arrhythmias.

Description

- ApneaScan uses the **Respiratory Sensor** to monitor breathing patterns
- ApneaScan identifies events when breathing amplitude is reduced by 26% or more for 10 seconds or more (includes full breathing pauses)



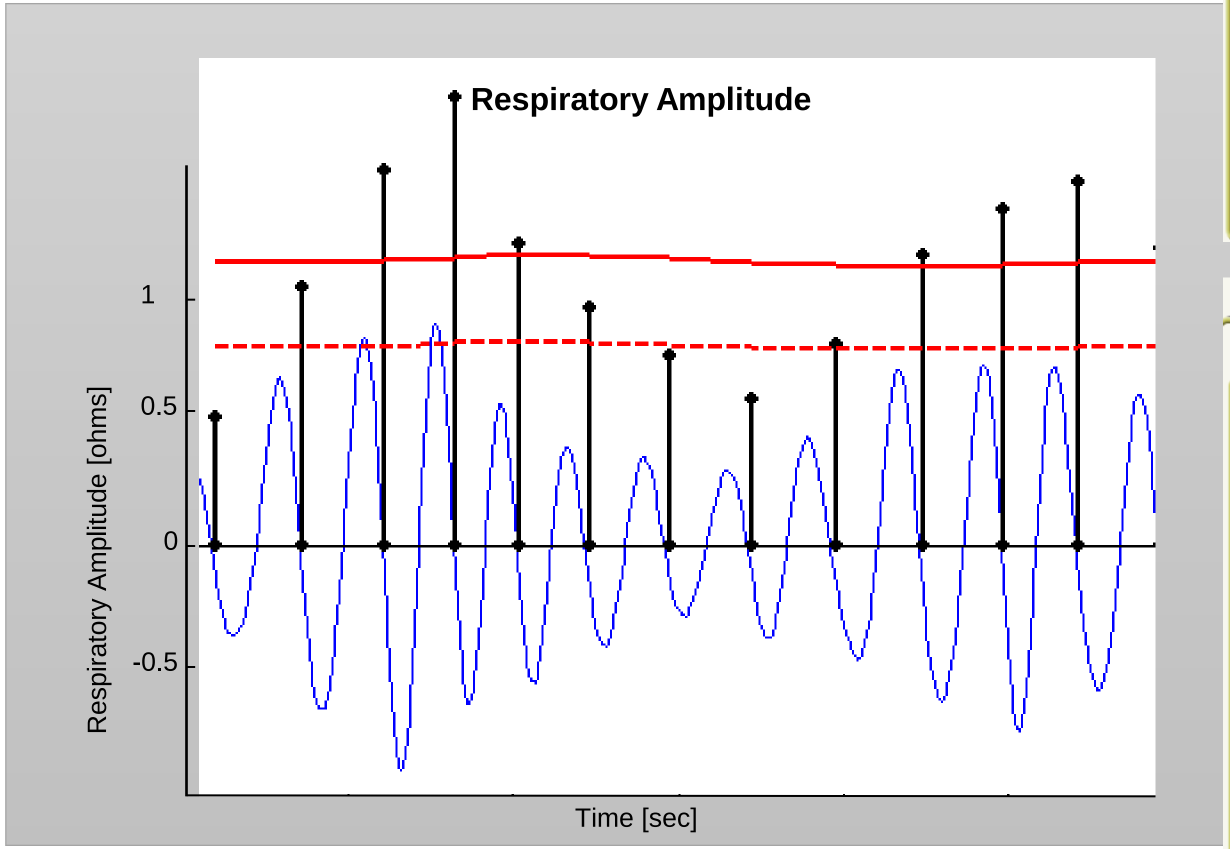


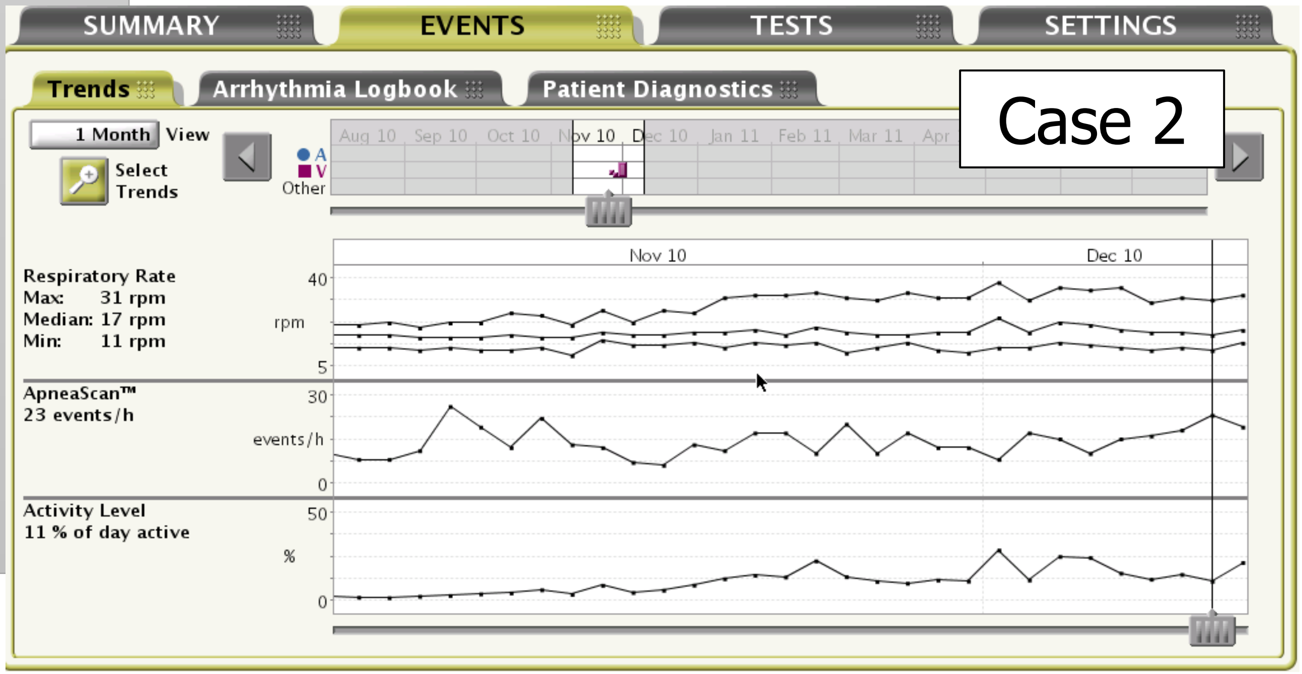
1. Program the Respiratory Sensor to On
2. Program the following Sleep Schedule parameters (available on the General tab of the Patient Information screen):
   - Sleep Start Time → time when you expect the patient to typically fall asleep each night
   - Sleep Duration → amount of time you expect the patient to typically sleep each night

- Every 50 ms (20 Hz), the device injects current between the RV Coil and Can.
- The device detects the resulting voltage modulations between the RV Tip and Can, and calculates transthoracic impedance
- During inspiration, the transthoracic impedance is high, and during expiration it is low

The Respiratory Disturbance Event data is presented as a trend, which physicians can use as a screening tool for severe sleep apnea

(Respiratory Disturbance Index RDI ≥ 32)

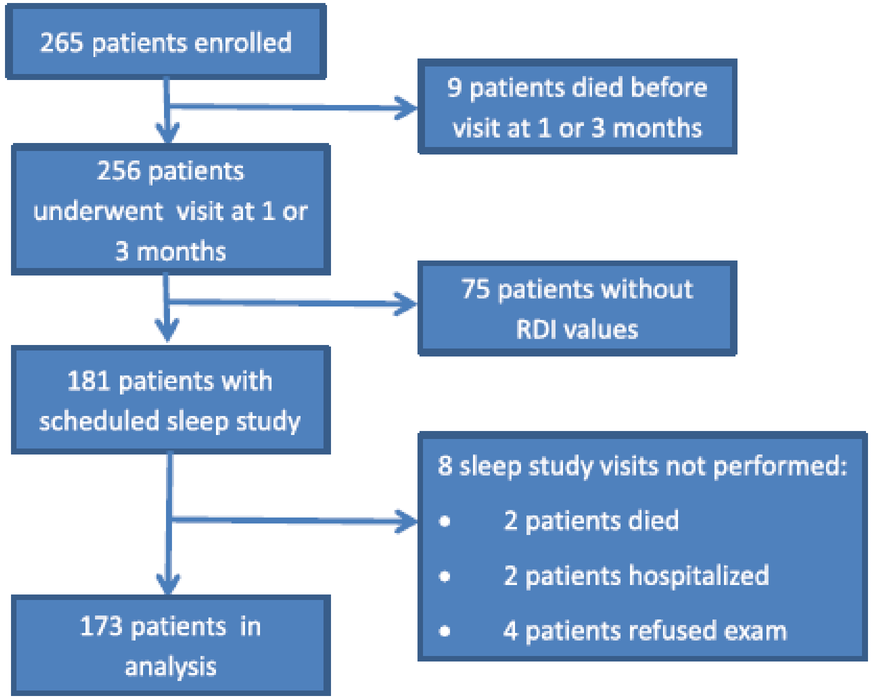


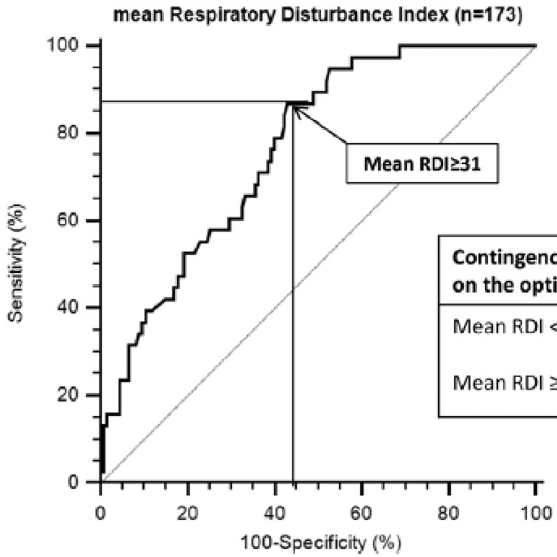


The DASAP-HF Study

The purpose of this study was to evaluate in pts with ICDs the performance of the respiratory disturbance index (RDI) computed by the ApneaScan algorithm.

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





Contingency table based on the optimal cut-off	AHI <30 episodes/h	AHI ≥30 episodes/h
Mean RDI < 31 episodes/h	78 (45%)	5 (3%)
Mean RDI ≥ 31 episodes/h	58 (33%)	33 (19%)

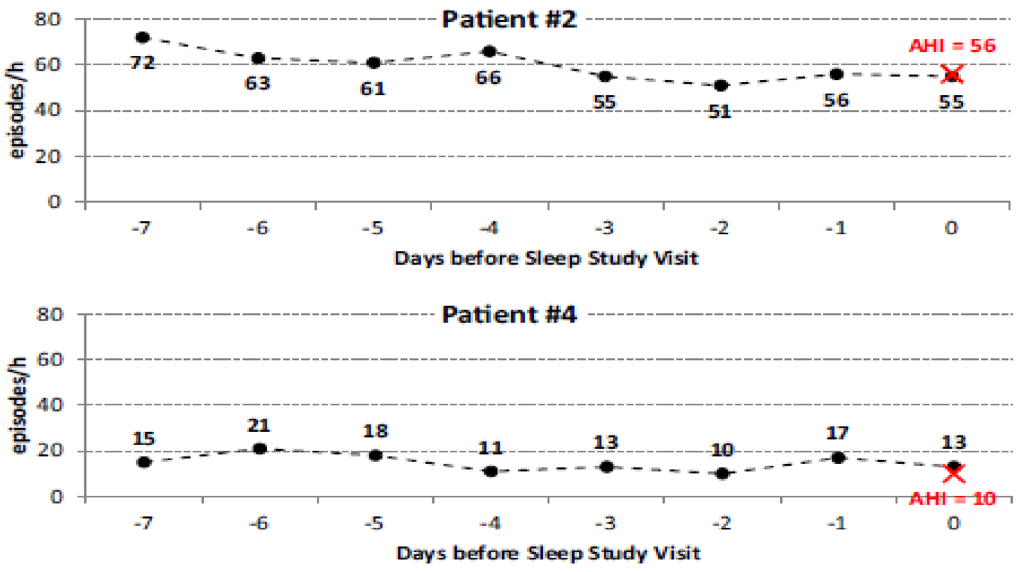
Figure 2 Receiver operating characteristic curve analysis of the RDI. Sensitivity and specificity were 87% (95% confidence interval 72%–96%) and 56% (95% confidence interval 48%–66%), respectively, at 31 episodes/h. AHI = apnea-hypopnea index; RDI = respiratory disturbance index.

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

D'Onofrio A et al. Heart Rhythm 2018; 15: 211-217

The DASAP-HF Study

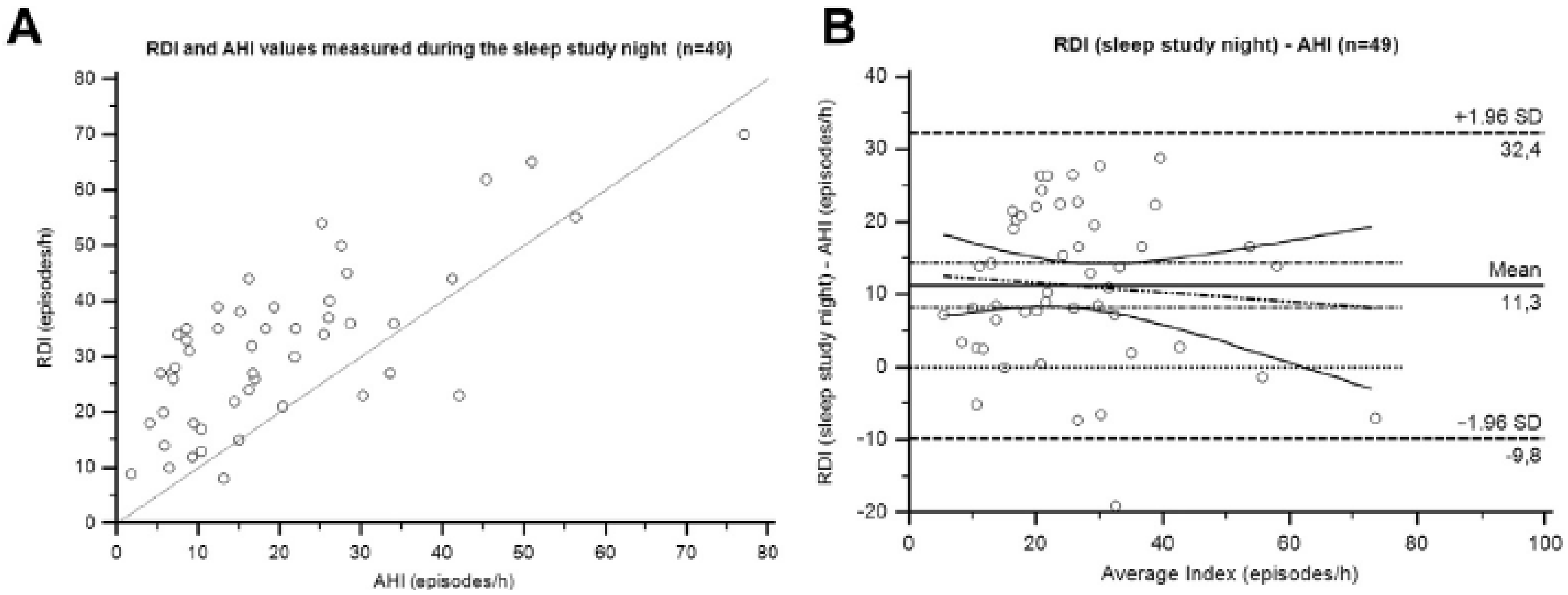
D'Onofrio A et al. Heart Rhythm 2018; 15: 211-217



RDI closely correlated with AHI recorded during the same night (r 5 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.

Table 1 Demographic characteristics and baseline clinical parameters (N = 173)

Parameter	Value
Age (y)	68 ± 10
Sex: male	139 (80)
Body mass index (kg/m^2)	27 ± 8
Primary prevention	152 (88)
NYHA class III–IV	91 (53)
QRS duration (ms)	126 ± 38
Sinus rhythm	133 (77)
Ischemic heart disease	91 (53)
Hypertension	38 (22)
History of atrial fibrillation	31 (18)
Pulmonary diseases	60 (35)
COPD	22 (13)
Chronic kidney disease	17 (10)
Diabetes	47 (27)
LV ejection fraction (%)	29 ± 5
LVESV (mL)	84 ± 74
LVEDV (mL)	122 ± 99
Creatinine level (mg/dL)	1.08 ± 0.62
ACE-inhibitor use	151 (87)
Aldosterone antagonist use	100 (58)
β-Blocker use	165 (96)
Diuretic use	162 (94)
Antiarrhythmic drug use	44 (25)
CRT-D device	87 (50)

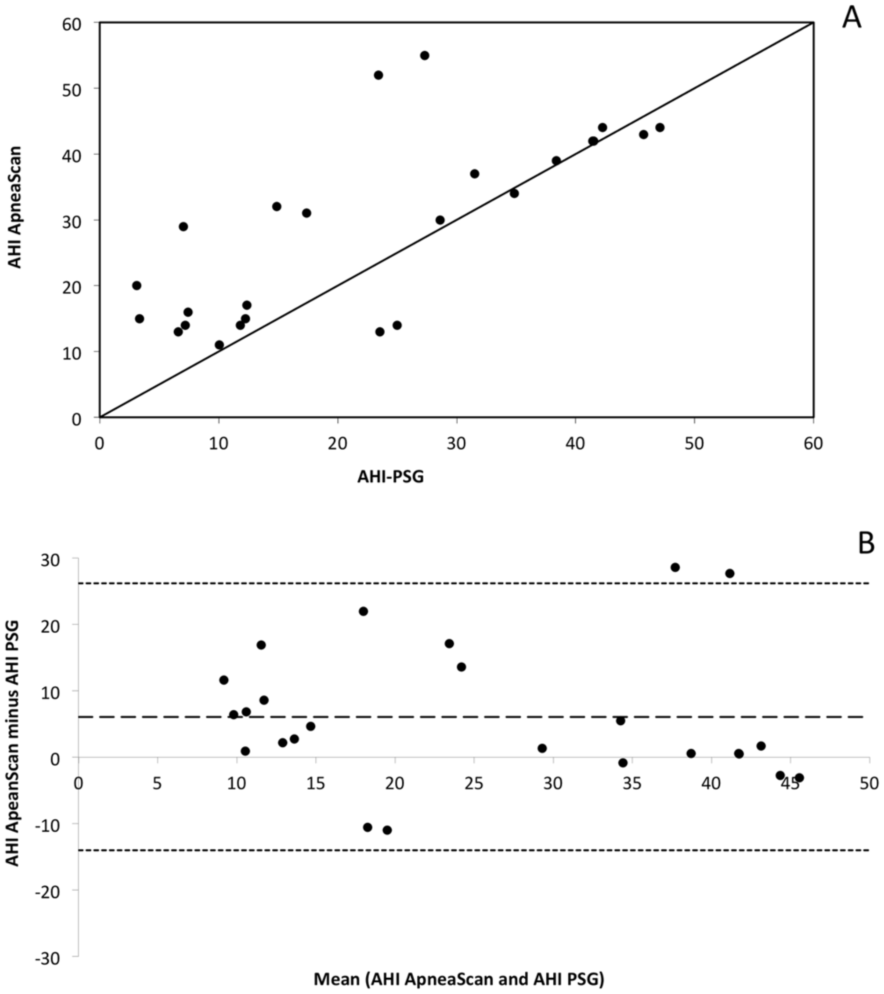


Conclusion

The ICD-computed RDI accurately identified severe SA and demonstrated good agreement with AHI values measured during the same night by ambulatory polygraphy. The RDI may serve as an efficient tool for screening patients at risk of severe SA. The ability of ICDs to continuously and remotely monitor respiratory disturbances could allow both the evolution of SA and the possible impact of therapeutic interventions to be assessed.

AIRLESS Study

Validation of an apnea and hypopnea detection algorithm implemented in implantable cardioverter defibrillators.



Parameter	Mean (SD)
Male gender, n(%)	24 (96)
Age (years)	59.9 (14.4)
BMI (kg/m²)	25.9 (4.2)
Apnea hypopnea index (events/hr)	21.9 (19.1)
LVEF (%)	30.3 (6.4)
Coronary artery disease n(%)	25(48)
Atrial fibrillation n(%)	12 (48)
NYHA class III-IV n(%)	6 (24)

The AIRLESS study shows that a transthoracic impedance sensor implemented in the ICDs for SA detection is a reliable tool to identify patients suffering of severe sleep disorders.

The availability of this new technology might improve the clinical management of this patient population.

Larger and long-term prospective studies are needed to collect data on the clinical impact.

Defaye P, Sci Rep 2019; 9(1): 9597

Sleep Apnea and cardiac rhythm abnormalities

The prevalence of arrhythmias was compared in 2 samples of participants from the Sleep Heart Health Study frequency-matched on age, sex, race/ethnicity, and body mass index:

(1) 228 subjects with sleep-disordered breathing (respiratory disturbance index>or=30) and
(2) 338 subjects without sleep-disordered breathing (respiratory disturbance index<5).

- Severe Sleep Apnea is associated with an increased prevalence of arrhythmias

Sleep Disordered Breathing patients

Non Sleep Disordered Breathing patients

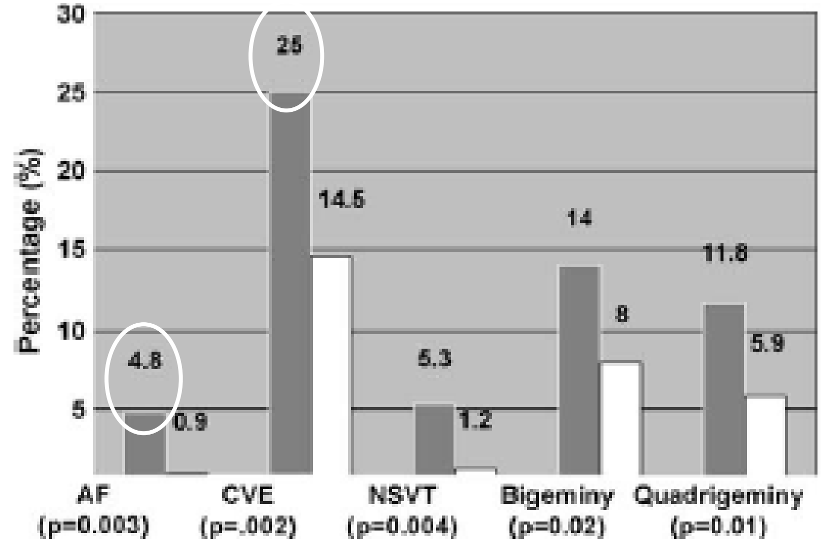


Figure 1. Arrhythmia prevalence (%) according to sleep-disordered breathing (SDB) status. *Shaded bars*, SDB; *open bars*, non-SDB. AF, atrial fibrillation; CVE, complex ventricular ectopy; NSVT, nonsustained ventricular tachycardia. n = 228 with SDB and n = 338 without SDB.

Mehra R et al. Am J Respir Crit Care Med 2006 Apr 15;173(8):910-6.

Obstructive Sleep Apnea and the Risk of Sudden Cardiac Death: A Longitudinal Study of 10,701 Adults

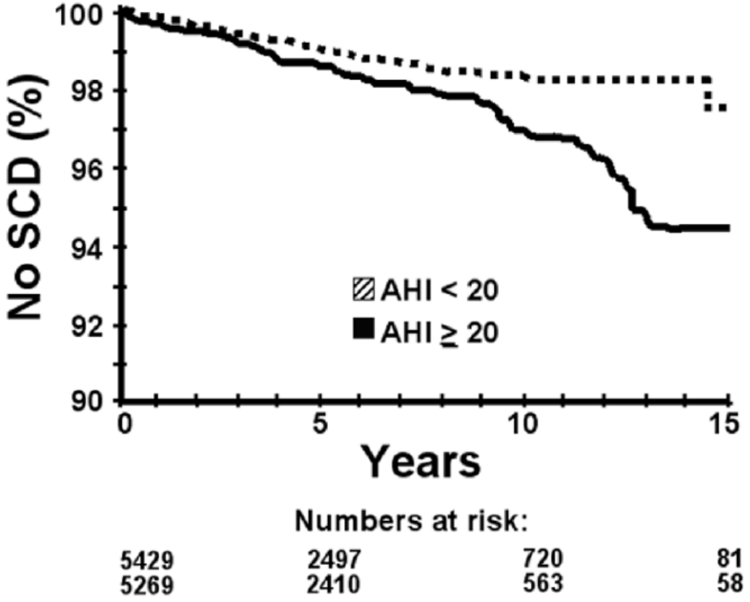


Figure 1. Survival based on apnea hypopnea index
Survival free of fatal or resuscitated sudden cardiac death (SCD) in the total study population, based on the apnea hypopnea index (AHI) threshold determined by classification and regression tree analysis (AHI < 20 vs. AHI ≥ 20). Hazard ratio = 1.60, 95% CI 1.14 – 2.24, P = 0.007.

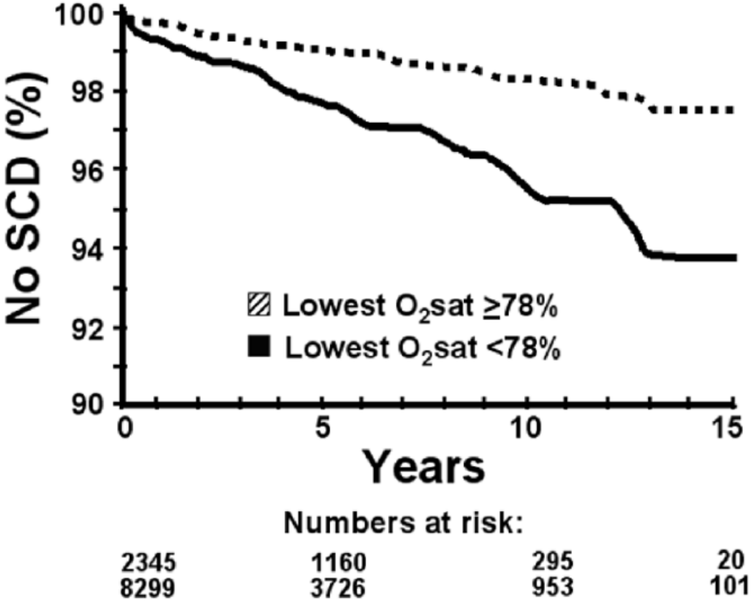


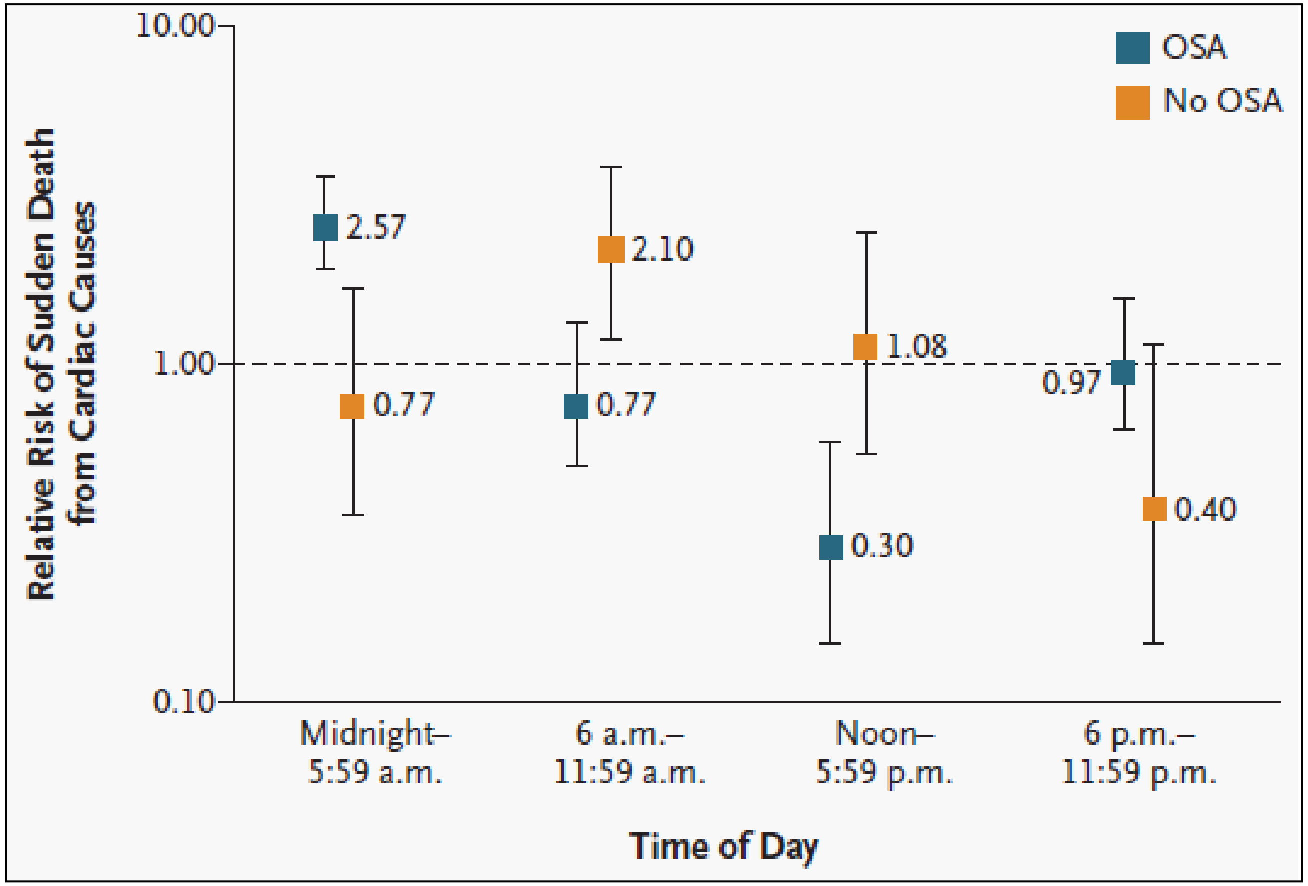
Figure 2. Survival based on oxygen saturation
Survival free of fatal or resuscitated sudden cardiac death (SCD) in the total study population, based on the lowest nocturnal oxygen saturation (O_2sat) threshold determined by classification and regression tree analysis (≥ 78% vs. < 78%). In multivariate analysis, hazard ratio = 1.81, 95% CI 1.28 – 2.56, p=0.0008.

Independent predictors of SCD in OSAS (results of multivariate regression)

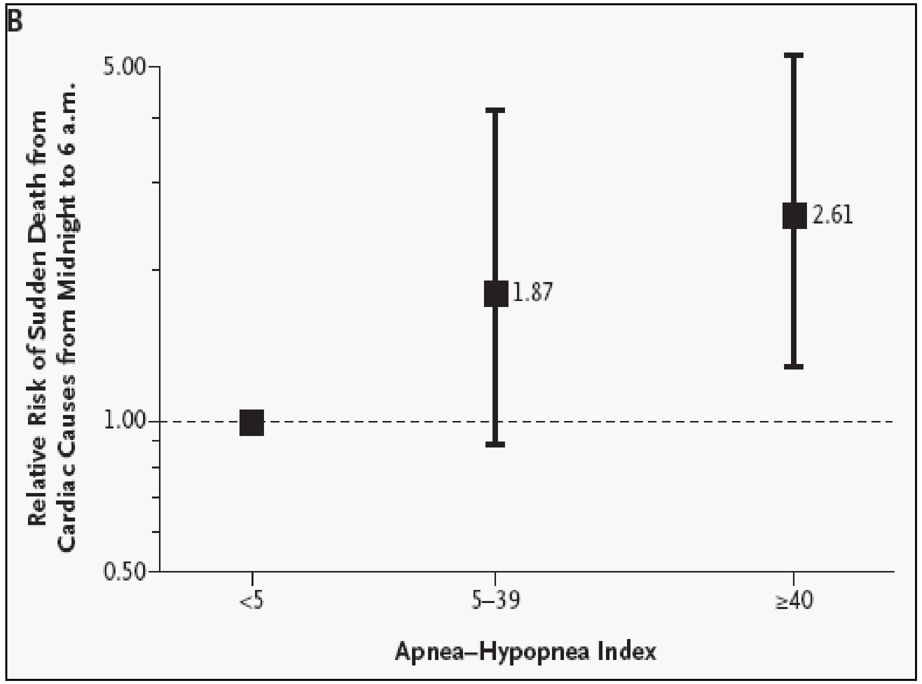
	HR	95% CI	P value
Age, yrs	1.02	(1.002,1.04)	0.03
Hypertension	1.57	(1.01,2.44)	0.04
Coronary artery disease	5.88	(3.64,9.48)	<0.001
Cardiomyopathy or heart failure	7.20	(4.71,11.0)	<0.001
Ventricular ectopy or NSVT	4.08	(1.64,10.14)	0.002
Sleep parameters			
Apnea-hypopnea index (per 10)	1.06	(1.0,1.13)	0.05
Lowest nocturnal O_2 saturation (per 10%)	1.13	(1.0,1.29)	0.05

Gami AS et al. JACC 2013 ; 62(7)

Obstructive Sleep Apnea associated with increased risk of nocturnal sudden death



Characteristic	OSA Status		
	OSA (N=78)	No OSA (N=34)	P Value
Age — yr	70±10	67±13	0.18
Male sex — no. (%)	64 (82)	21 (62)	0.02
Body-mass index‡	34±7	33±9	0.71
Hypertension — no. (%)	51 (65)	22 (65)	0.94
Diabetes mellitus — no. (%)	32 (41)	12 (35)	0.57
Coronary artery disease — no. (%)	54 (69)	19 (56)	0.29
Congestive heart failure — no. (%)	43 (55)	18 (53)	0.83
Cerebrovascular disease — no. (%)	17 (22)	7 (21)	0.89
Dysrhythmia — no. (%)§	14 (18)	3 (9)	0.22



Death certificates of 112 Minnesota residents who had undergone polysomnography and had died suddenly

Gami AS et al. N Engl J Med 2005 ; 352 : 1206-14

Ventricular arrhythmia, Cheyne-Stokes respiration, and death: observations from patients with defibrillators

Table 1 Baseline characteristics of implantable cardioverter defibrillator (ICD) recipients with and without Cheyne-Stokes respiration (CSR)

	No CSR (n = 59)	CSR (n = 42)	p Value
Age(years)	65.6 (1.4)	68.1 (1.3)	0.21
BMI (kg/m^2)	26.3 (0.6)	28.2 (0.8)	0.06
NYHA class	2.1 (0.1)	2.5 (0.1)	0.02
Number of diseased arteries on coronary angiography	1.7 (0.1)	2.0 (0.2)	0.11
Ejection fraction (%)	36.6 (2)	28.7 (1.9)	0.005
Coronary artery disease	45/59 (76%)	36/42 (86%)	0.24
Atrial fibrillation	5/59 (8%)	8/42 (19%)	0.21
Bundle branch block	27/59 (46%)	17/42 (40%)	0.21
VT/VF inducible at PES	17/59 (29%)	7/42 (17%)	0.18
NYHA class			0.08
I	17/56 (30%)	4/42 (10%)	
II	20/56 (36%)	17/42 (40%)	
III	17/56 (30%)	18/42 (43%)	
IV	2/56 (4%)	3/42 (7%)	
Index arrhythmia			0.83
VT	36/59 (61%)	23/42 (55%)	
VF	9/59 (15%)	7/42 (17%)	
PP	14/59 (24%)	12/42 (29%)	
Medications			
Diuretic	38/59 (64%)	38/42 (90%)	0.004
ACE inhibitor	49/59 (83%)	41/42 (98%)	0.02
Spironolactone	16/59 (27%)	16/42 (38%)	0.28
Amiodarone	13/59 (22%)	10/42 (24%)	1
β Blocker	33/59 (56%)	27/42 (64%)	0.42
Mean SaO_2 (%)	93.3 (0.5)	91.8 (0.7)	0.005
Minimum SaO_2 (%)	86.5 (0.6)	80.2 (1.3)	<0.001
Desaturation index (dips/hour)	7.1 (0.5)	26.9 (1.8)	<0.001
Recording time with SaO_2 <90% (%)	4.3 (1.7)	12.8 (2.4)	<0.001

All values are mean (SEM) or number (%).
ACE, angiotensin converting enzyme; BMI, body mass index; NYHA, New York Heart Association; PES, programmed electrical stimulation; PP, primary prevention; SaO_2, overnight transcutaneous oxygen saturation; VF, ventricular fibrillation; VT, ventricular tachycardia.

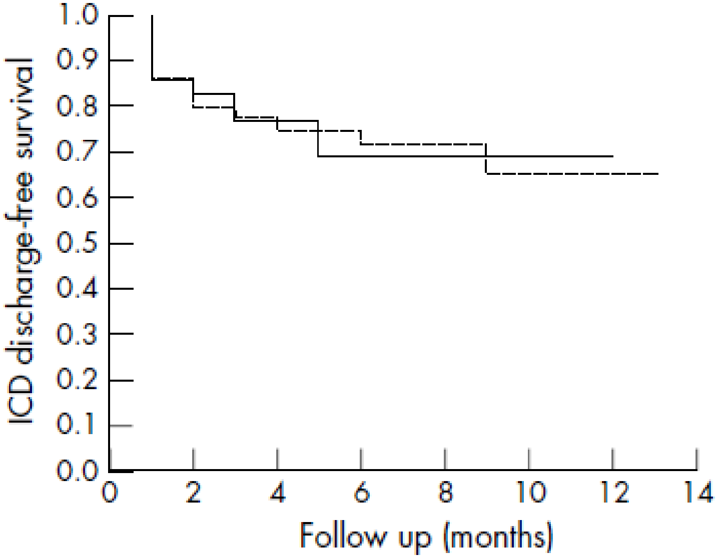


Figure 2 Survival to first appropriate implantable cardioverter-defibrillator (ICD) discharge for serious ventricular arrhythmia in patie with and without CSR. Cox proportional hazard analysis showed tha patient with CSR had a relative risk for discharge of 1.0 (95% confiden interval 0.5 to 2.2, p = 1).

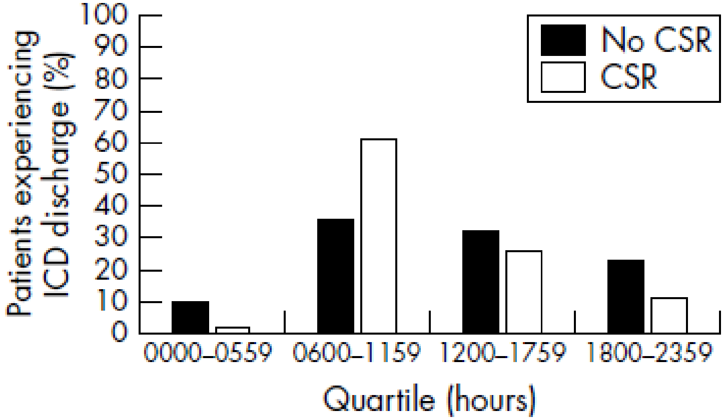


Figure 3 Diurnal variation of ICD discharges in patients with and without CSR.

Staniforth AD et al. Heart 2005 ; 91: 1418-1422

Sleep Disordered Breathing is Associated with Appropriate Implantable Cardioverter Defibrillator Therapy in Congestive Heart Failure Patients

N=22
17 ICD pts showed SDB

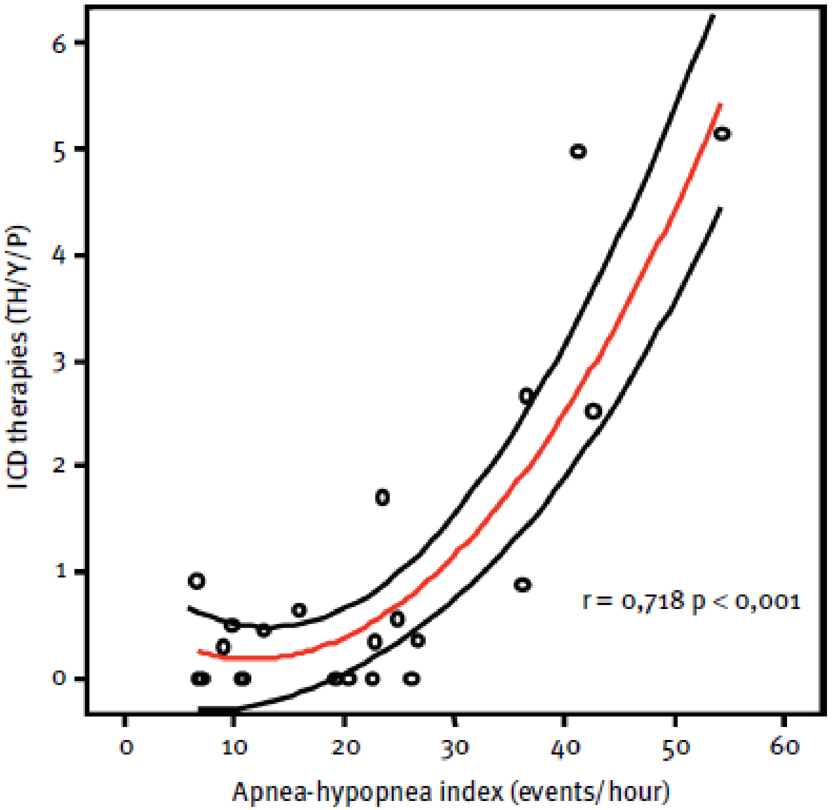


Figure 1. Correlation between apnea-hypopnea index (ev/h) and number of ICD therapies (therapies for year of implant for patient [ThYP]) in patients with CHF.

Table 1. Baseline Characteristics of Patients Included in the Study

Characteristic	Patients Affected by SDB (n = 17)	Patients Unaffected by SDB (n = 5)
Age (yr)	65 ± 8	60 ± 12
Body mass index (kg/m²)	28 ± 3	27 ± 2
Ischemic etiology (%)	60%	80%
NYHA class	2 ± 0.7	2.2 ± 0.8
Ejection fraction (%)	29 ± 5	26 ± 6
Duration of follow-up (mo)	19 ± 14	26 ± 15

Abbreviations: SDB, sleep disordered breathing.

Sleep disordered breathing is frequent in ICD recipients due to left systolic ventricular dysfunction and may increase the risk of ventricular arrhythmia and appropriate ICD discharges.

Tomaello L et al. Clin Cardiol 2010 ; 33: E27-E30

Sleep Apnea associated with increased life threatening arrhythmias in HF

- In patients with HF, CSA and OSA are independently associated with an increased risk for ventricular arrhythmias and appropriate cardioverter-defibrillator therapies

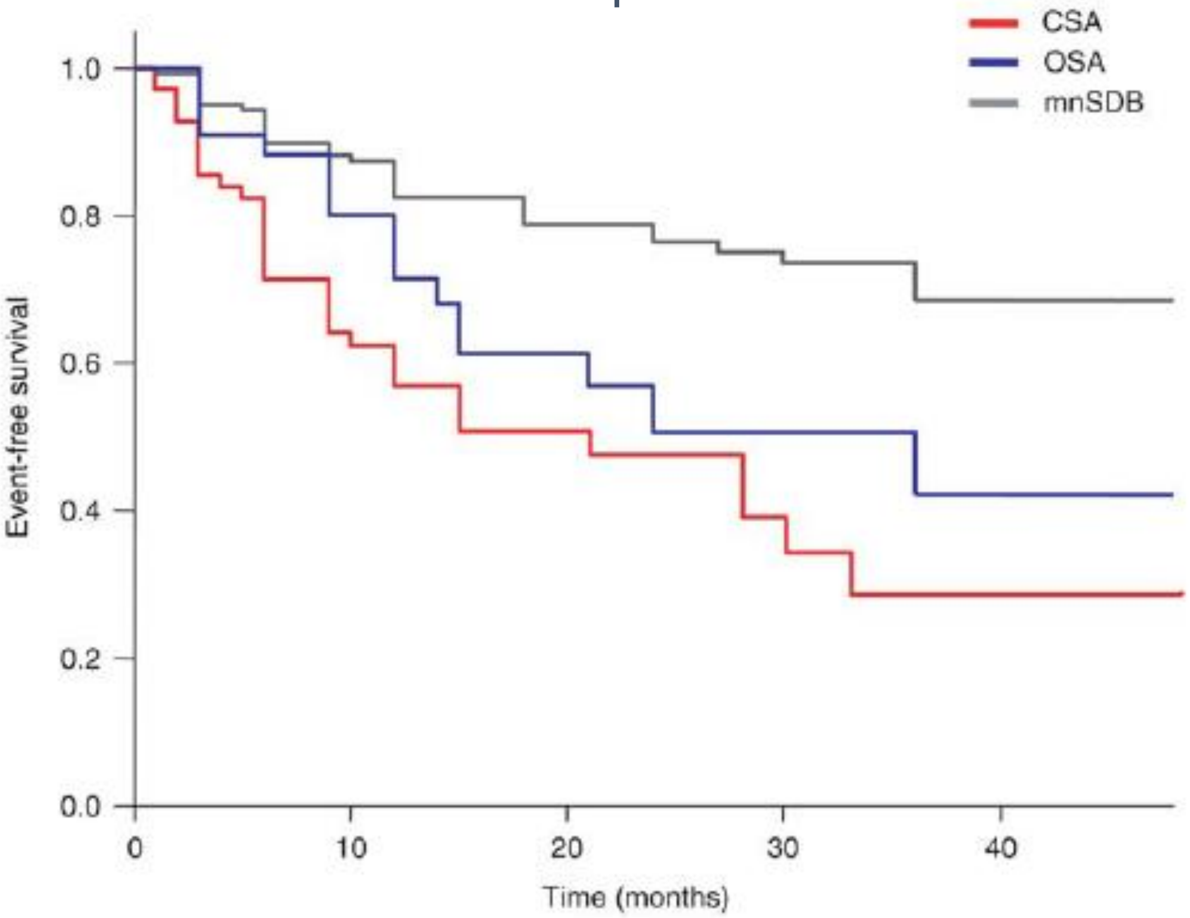
- Increased appropriate therapies (AHI ≥15):
  - CSA: by 3.4-fold
  - OSA: by 2.1-fold

POPULATION: 255 CRTD pts

FU: 4 years

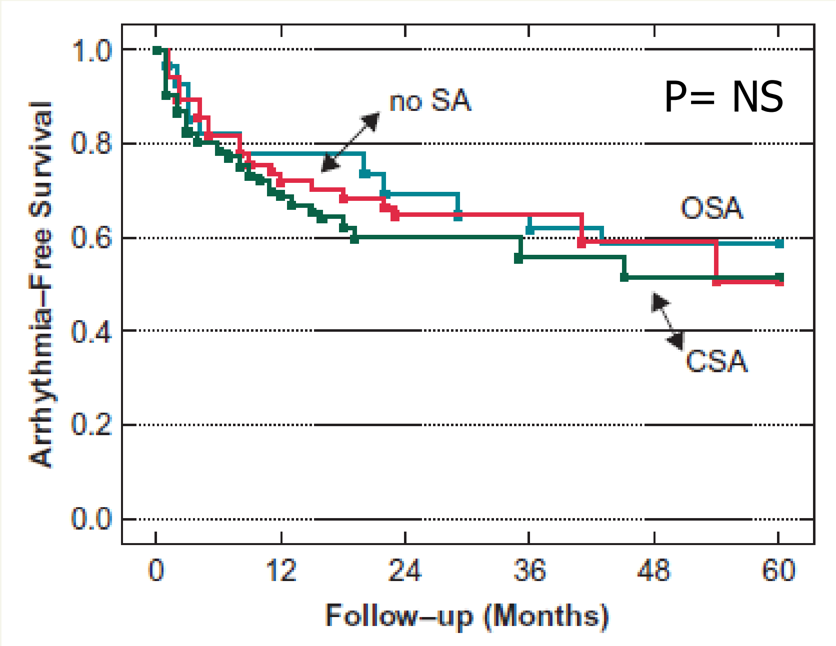
Primary Endpoint: event-free survival time period to first appropriate cardioverter-defibrillator therapy

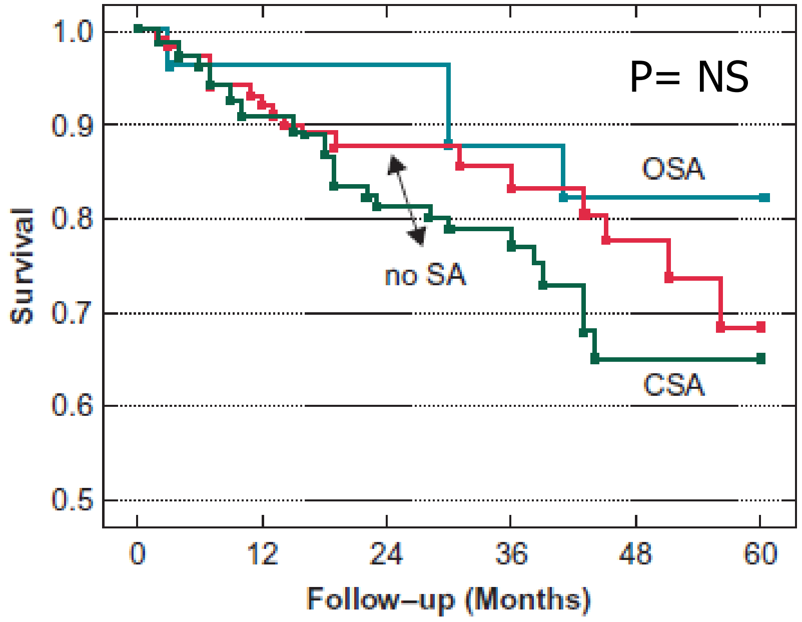
PROTOCOL excluded patient undergoing CPAP

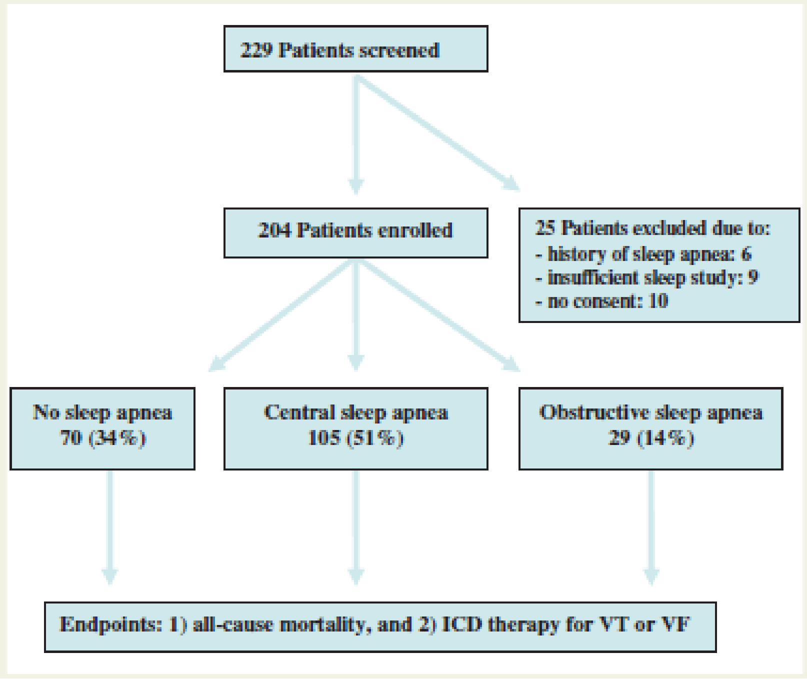


Bitter T et al. Eur Heart J. 2011 ; 32 : 61-74

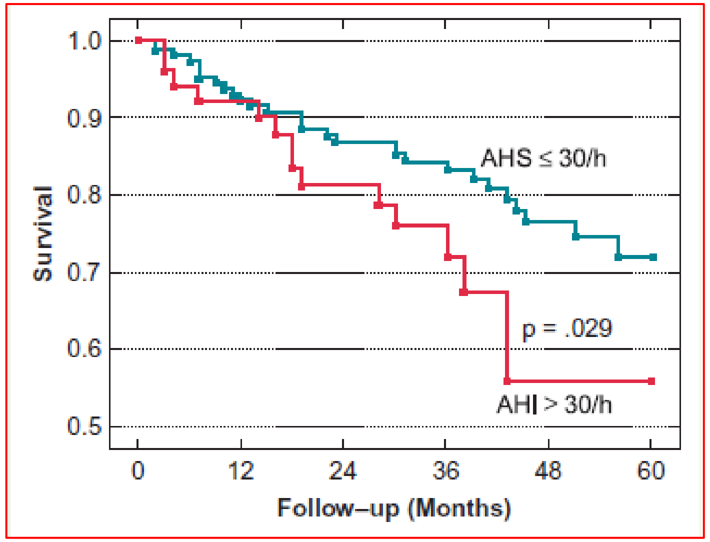
Sleep-disordered breathing in patients with implantable cardioverter-defibrillator







The hypothesis that CSA apnoea is merely a marker but not an independent risk factor for an adverse prognosis in patients with heart failure.

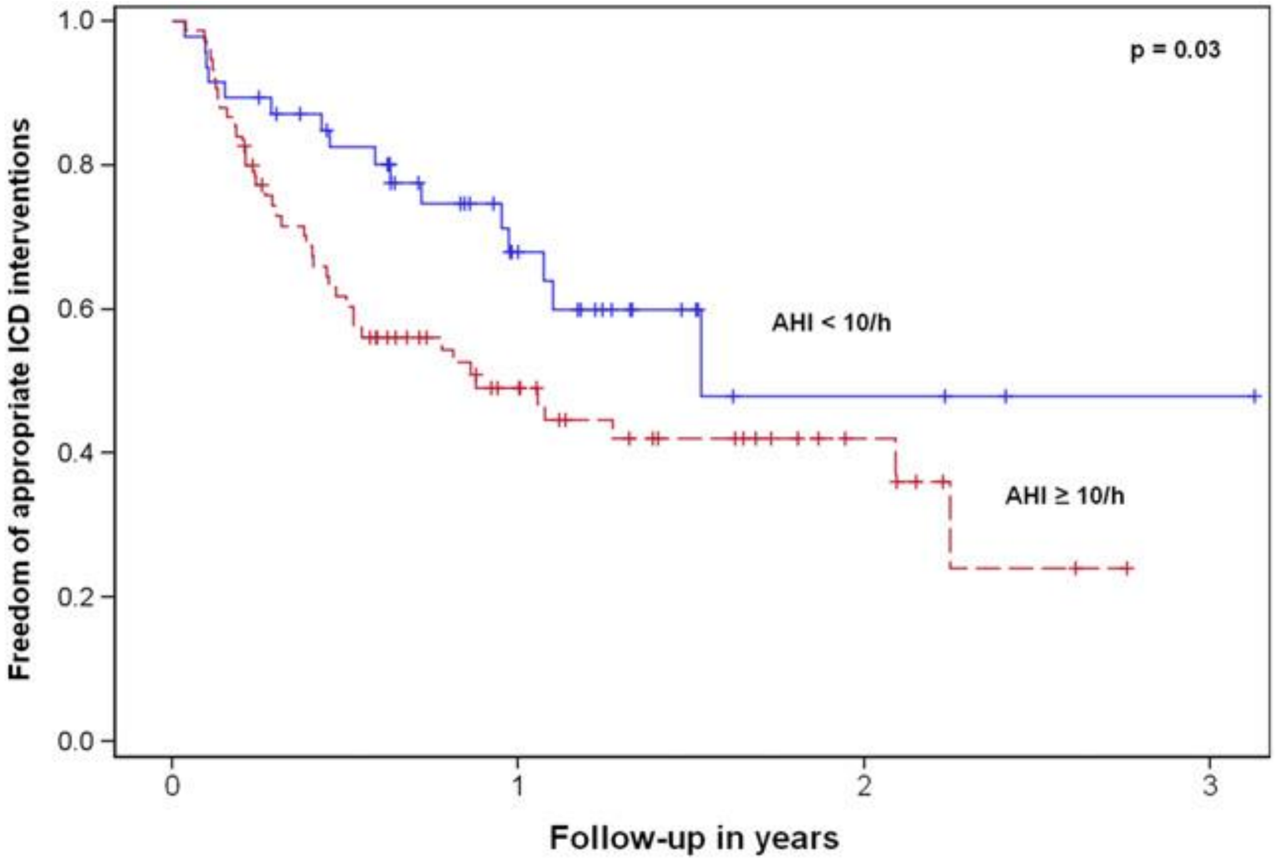


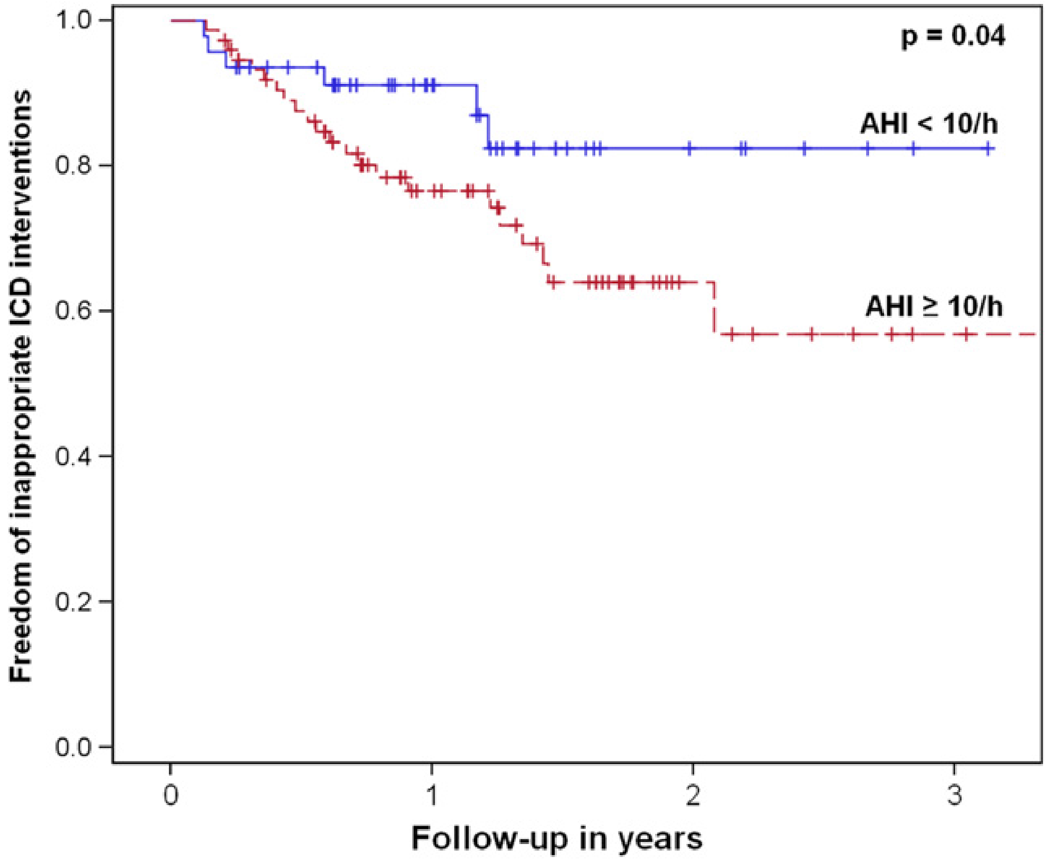
Grimm W et al. Europace 2013 ; 15: 515-522

Usefulness of Sleep-Disordered Breathing to Predict Occurrence of Appropriate and Inappropriate ICD Therapy in Pts With ICD for Primary Prevention of SCD

N=133 (primary prevention)

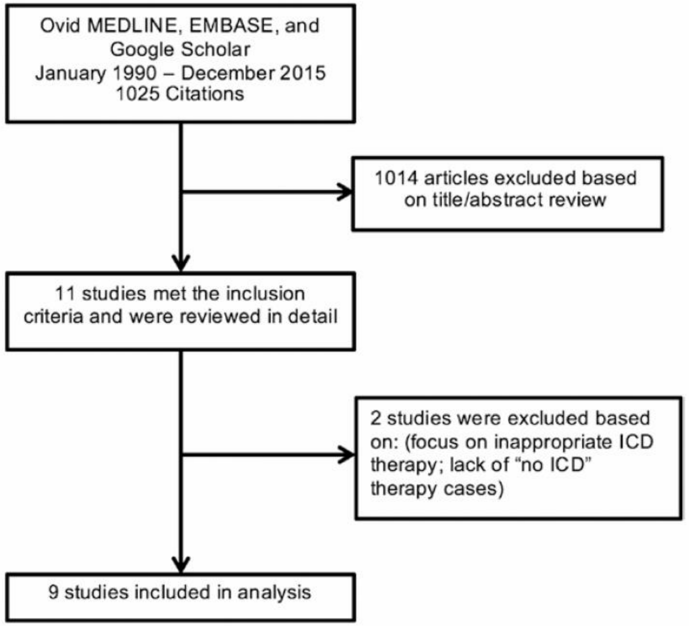
These results indicate that a preimplantation sleep study will identify patients with HF prone to receive appropriate and inappropriate ICD therapy





Kreuz J et al. Am J Cardiol 2013 ; 111: 1319-1322

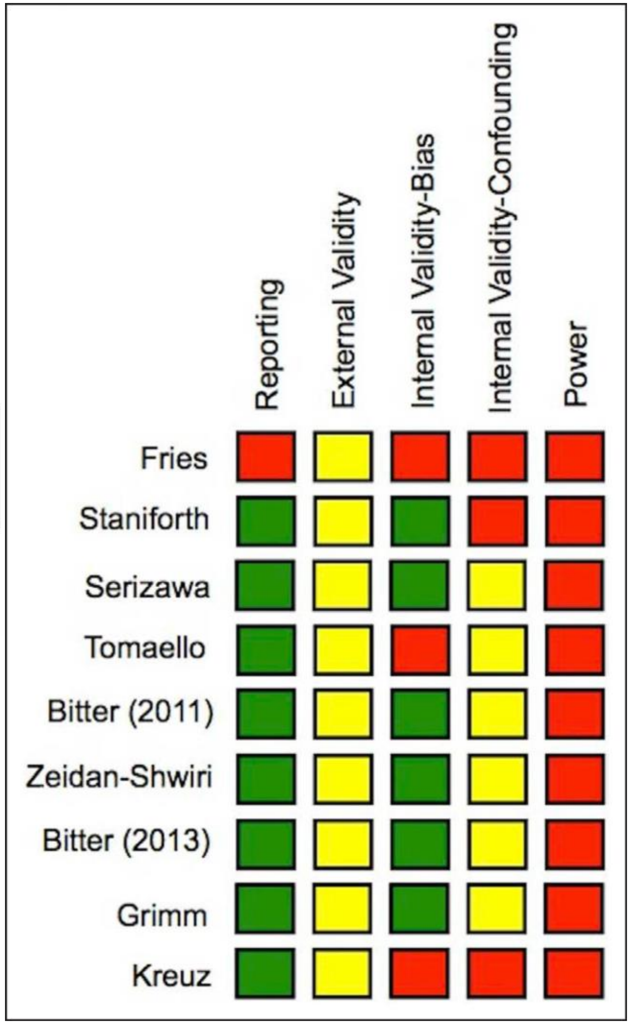
Effect of Sleep-Disordered Breathing on Appropriate ICD Therapy: Meta-Analysis

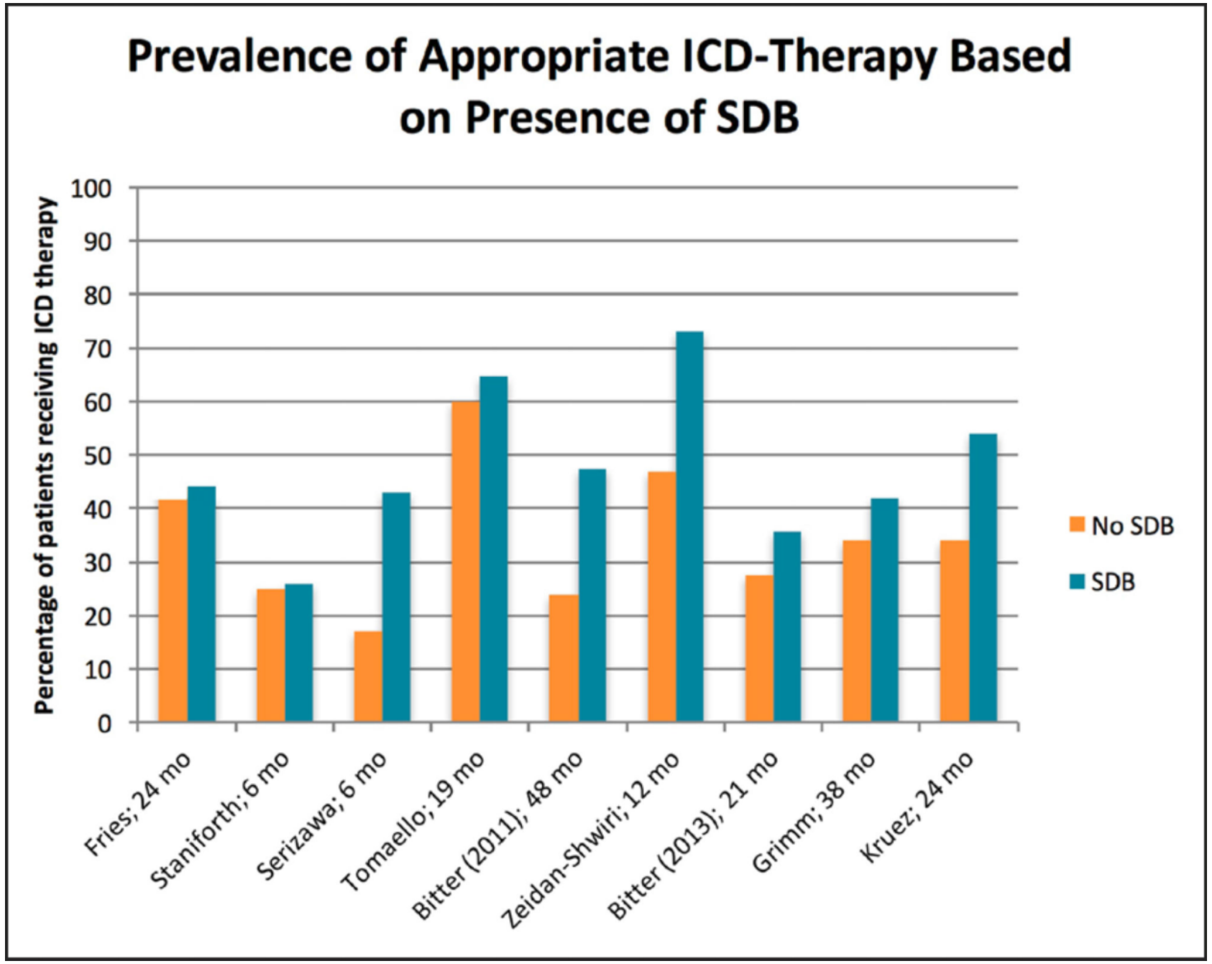


High risk of bias

Medium risk of bias

Low risk of bias

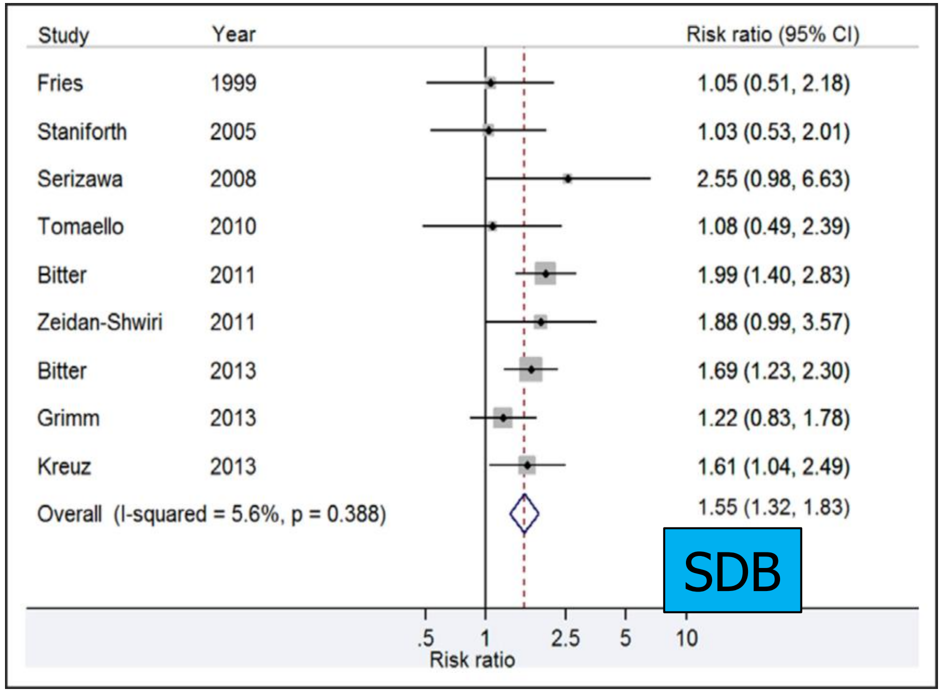




Kwon Y et al. Circ Arrhythm Electrophysiol. 2017 February ; 10(2): e004609

Appropriate ICD Therapy Meta-Analysis

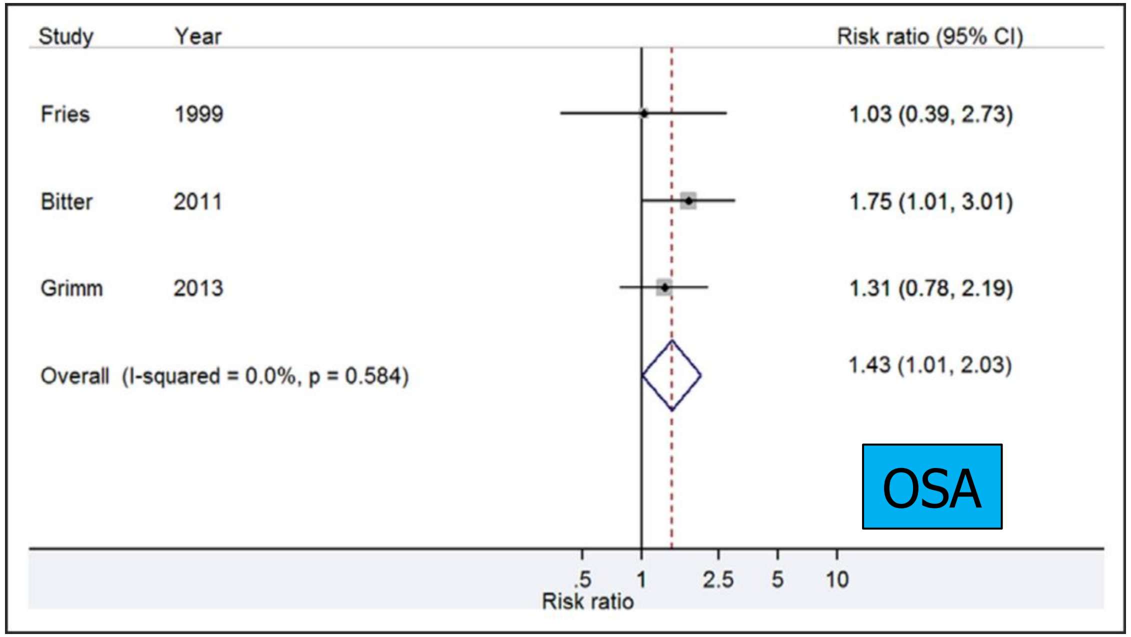
N= 1274

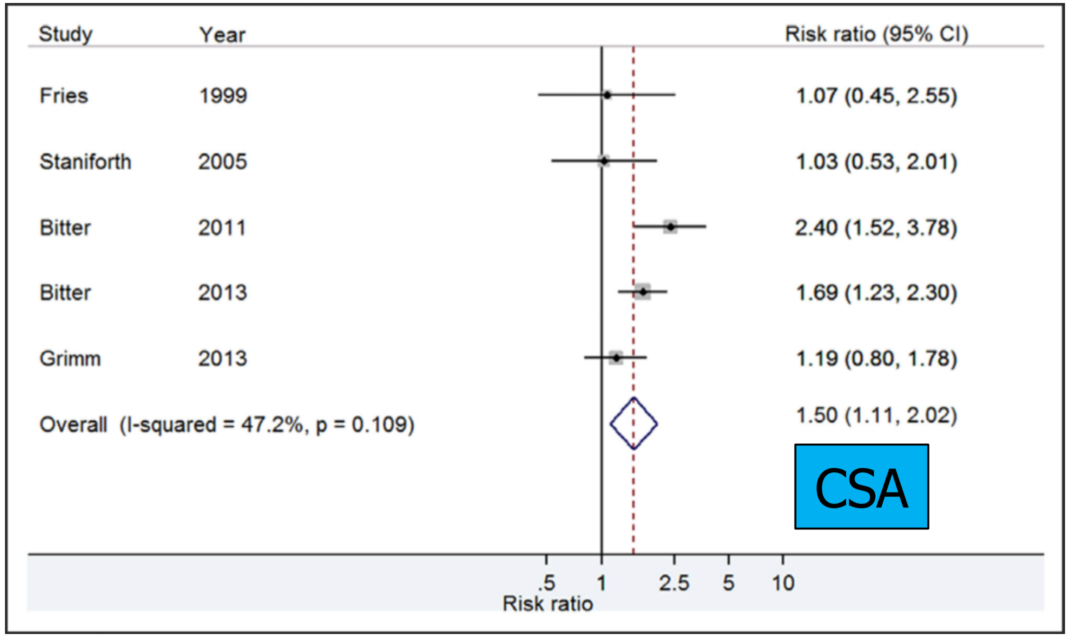


SDB was present in 52% of the participants

SDB was associated with a 55% higher risk of appropriate ICD therapies

The risk was higher in both and obstructive sleep apnea.



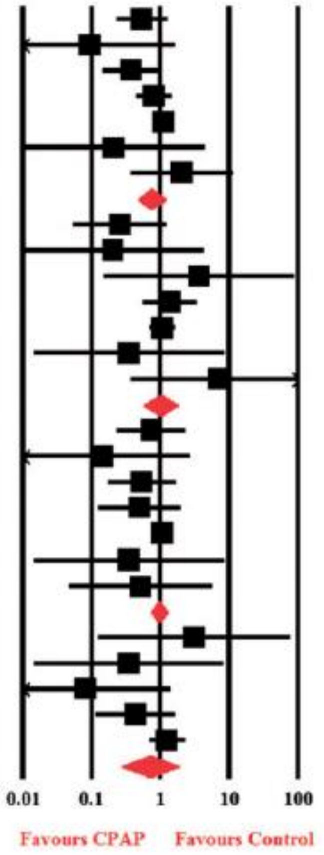


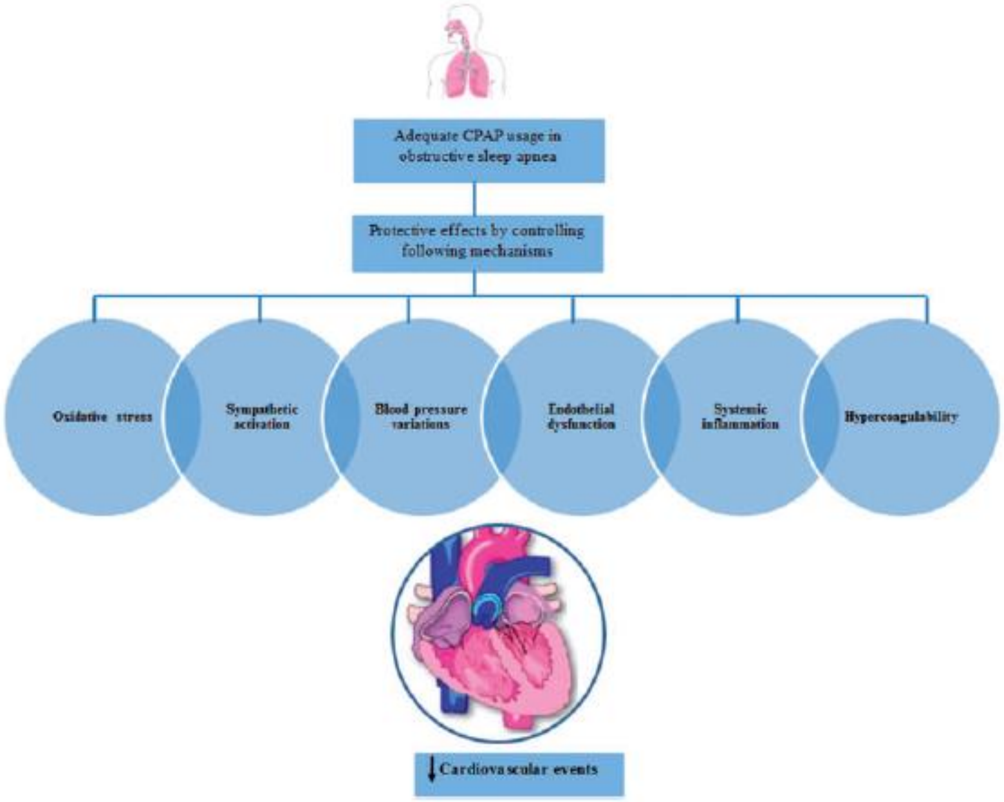
Kwon Y et al. Circ Arrhythm Electrophysiol. 2017 February ; 10(2): e004609

A meta-analysis of continuous positive airway pressure therapy in prevention of cardiovascular events in patients with obstructive sleep apnoea

Adverse Events	Study	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	Relative weight
MACE	Barbe F et al	0.55	0.23	1.27	-1.40	0.16	16.50
	Huang et al	0.09	0.01	1.63	-1.63	0.10	2.39
	Parra et al	0.38	0.15	0.97	-2.02	0.04	14.55
	RICCADSA	0.81	0.45	1.46	-0.70	0.48	23.30
	SAVE	1.10	0.88	1.37	0.84	0.40	34.89
	HeartBeat	0.21	0.01	4.29	-1.02	0.31	2.16
	PREDICT	2.05	0.38	10.99	0.84	0.40	6.21
		0.74	0.47	1.17	-1.30	0.19	
MI	Barbe F et al	0.26	0.05	1.20	-1.73	0.08	10.85
	Huang et al	0.21	0.01	4.14	-1.03	0.30	3.21
	Parra et al	3.62	0.15	87.21	0.79	0.43	2.87
	RICCADSA	1.38	0.57	3.30	0.71	0.48	25.77
	SAVE	1.07	0.70	1.65	0.32	0.75	51.12
	HeartBeat	0.35	0.01	8.43	-0.65	0.52	2.86
	PREDICT	7.18	0.38	137.51	1.31	0.19	3.32
		0.99	0.57	1.72	-0.03	0.98	
Stroke	Barbe F et al	0.73	0.23	2.29	-0.54	0.59	5.70
	Huang et al	0.15	0.01	2.74	-1.28	0.20	0.86
	Parra et al	0.54	0.17	1.66	-1.08	0.28	5.84
	RICCADSA	0.50	0.13	1.95	-1.00	0.32	3.97
	SAVE	1.07	0.79	1.45	0.46	0.64	81.61
	HeartBeat	0.35	0.01	8.43	-0.65	0.52	0.73
	PREDICT	0.51	0.05	5.58	-0.55	0.58	1.30
		0.95	0.72	1.24	-0.40	0.69	
Cardiovascular mortality	Barbe F et al	3.08	0.13	75.24	0.69	0.49	7.61
	Huang et al	0.34	0.01	8.14	-0.66	0.51	7.73
	Parra et al	0.08	0.00	1.38	-1.74	0.08	9.32
	RICCADSA	0.43	0.11	1.62	-1.25	0.21	27.22
	SAVE	1.25	0.70	2.23	0.74	0.46	48.12
		0.70	0.27	1.80	-0.74	0.46	

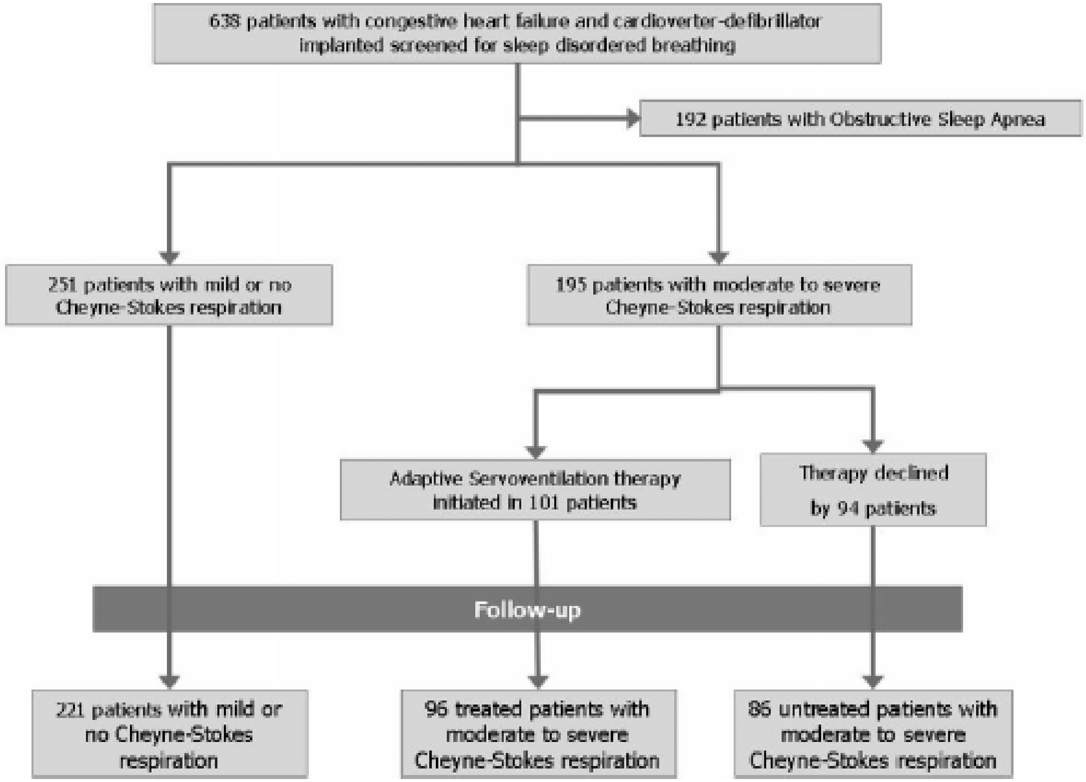
Risk ratio and 95% CI

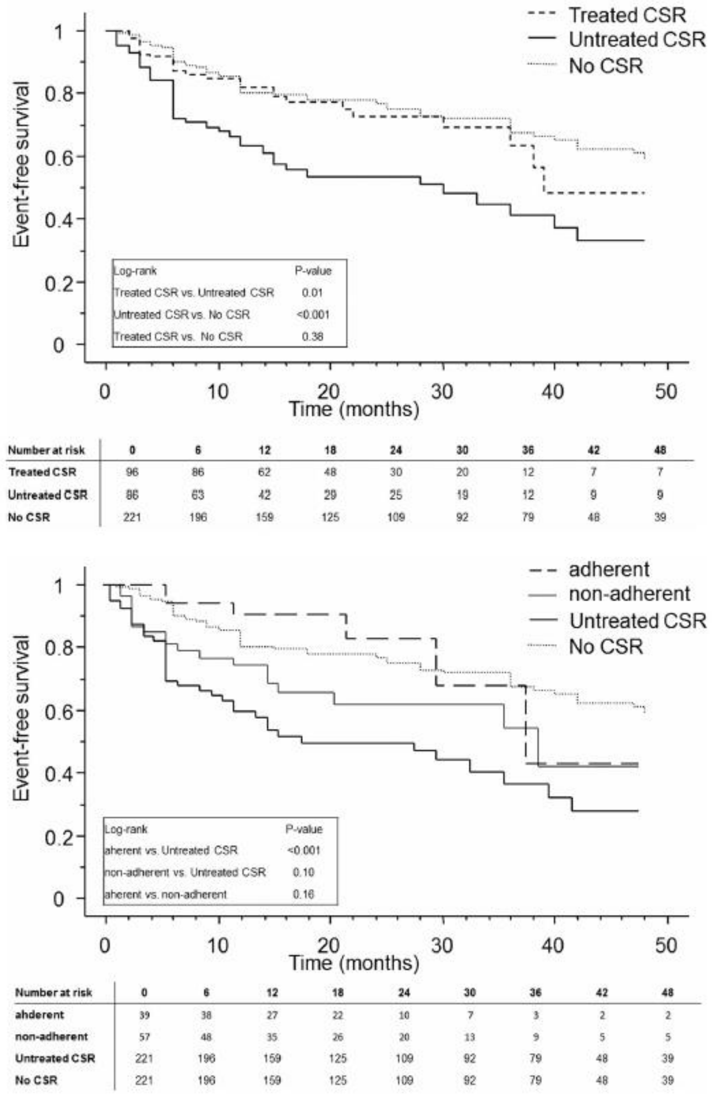




Khan SU et al. Eur Heart J 2018; 39: 2291-2297

Treatment of Cheyne-Stokes Respiration Reduces Arrhythmic Events in Chronic Heart Failure





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Conclusions

SDB are marker for an adverse prognosis in patients with heart failure.

SDB seem to be associated with an increased risk of appropriate ICD therapy in patients with heart failure and reduced ejection fraction.

Treatment of SDB could reduces arrhythmic events and consequently ICD therapies