AIAC
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CORSI TEORICO-PRATICI
Sleep Apnea 2020

Aritmie ventricolari e apnee notturne

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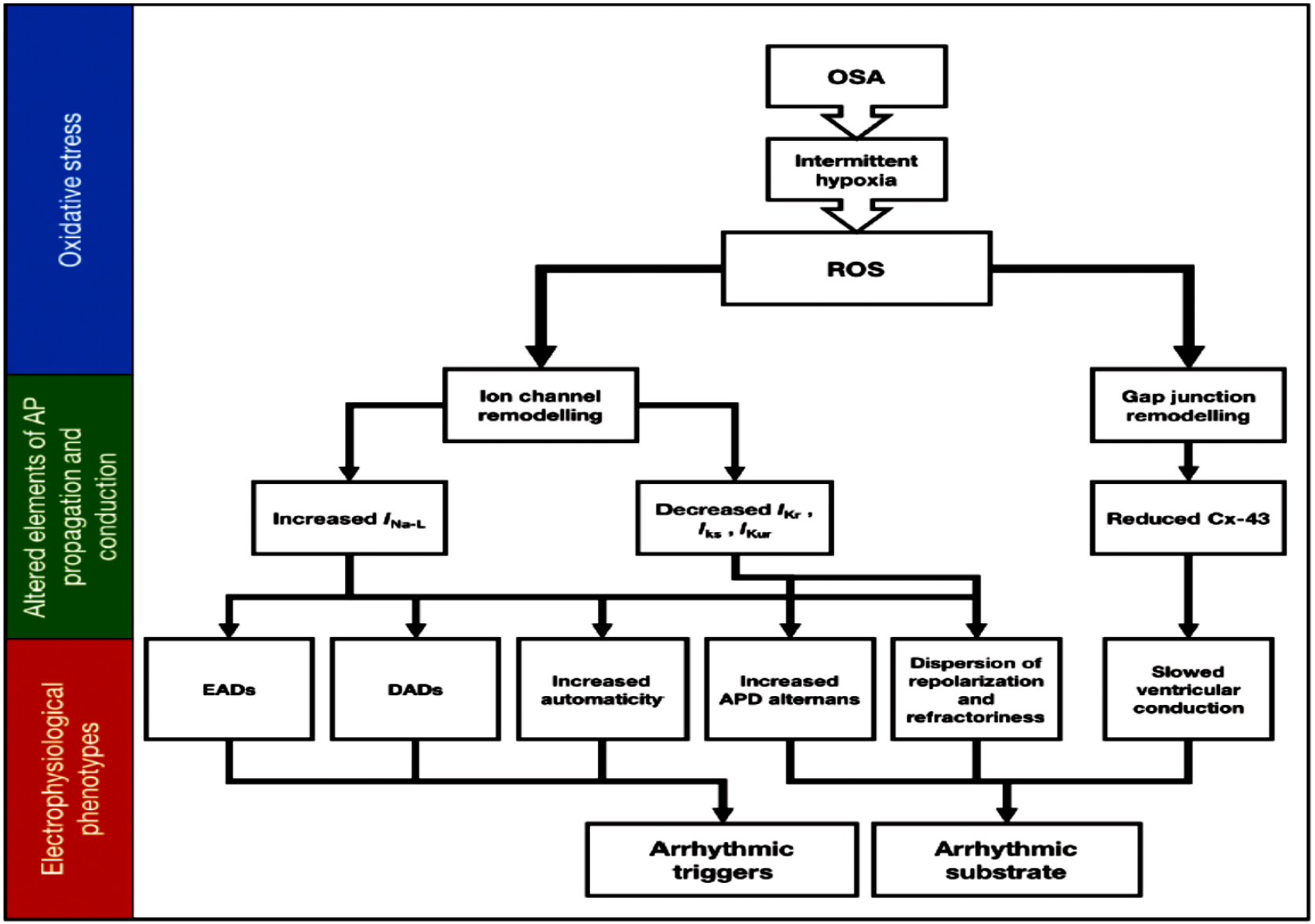
Development of arrhythmic triggers and arrhythmic substrate due to reactive oxygen species (ROS) generation because of oxidative stress



Chadda KR et al., SLEEPJ 2018, doi: 10.1093/sleep/zsy136

Obstructive Sleep Apnea and the Risk of Sudden Cardiac Death

A Longitudinal Study of 10,701 Adults

10.701 consecutive adults undergoing their first diagnostic polysomnogram between July 1987 and July 2003. During an average follow-up of 5.3 years, 142 pts had resuscitated or fatal SCD (annual rate 0.27%). In multivariate analysis, independent risk factors for SCD were age, hypertension, CAD, cardiomyopathy or heart failure, ventricular ectopy or NSVT, and lowest nocturnal O2sat (per 10% decrease, hazard ratio [HR]: 1.14; p=0.029)

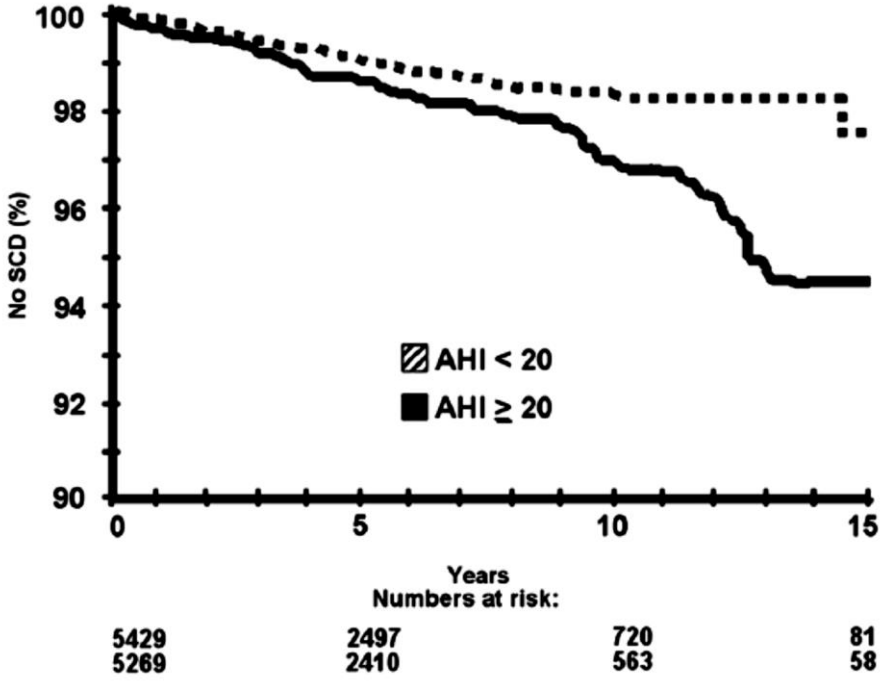


Figure 1 Survival Based on AHI

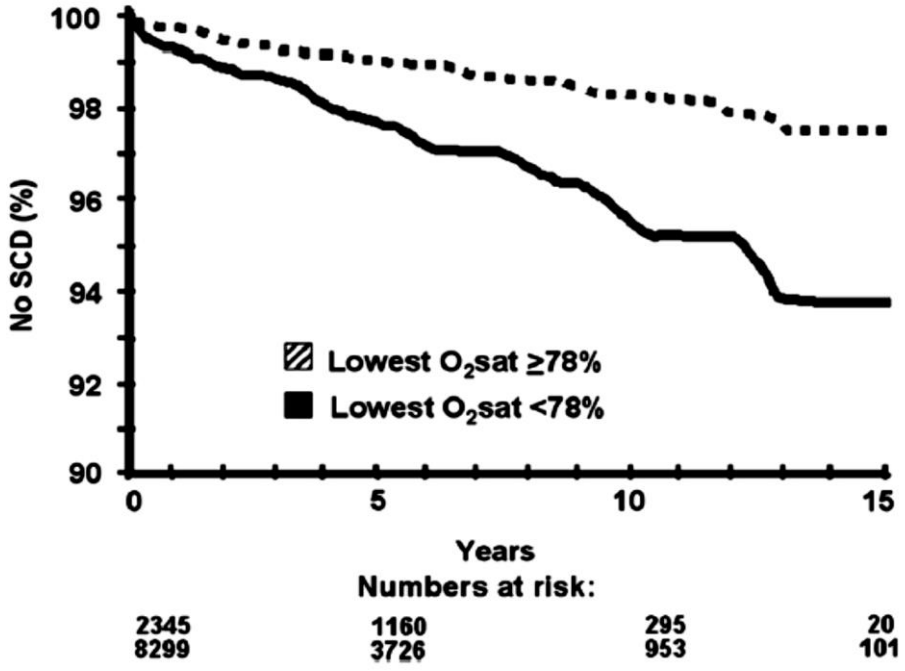


Figure 2 Survival Based on O_2sat

Gami AS et al., JACC 2013; 62: 610–6

Day–Night Pattern of Sudden Death in Obstructive Sleep Apnea

Polysomnograms and the death certificates of 112 Minnesota residents who had undergone polysomnography and died suddenly from cardiac causes between July 1987 and July 2003

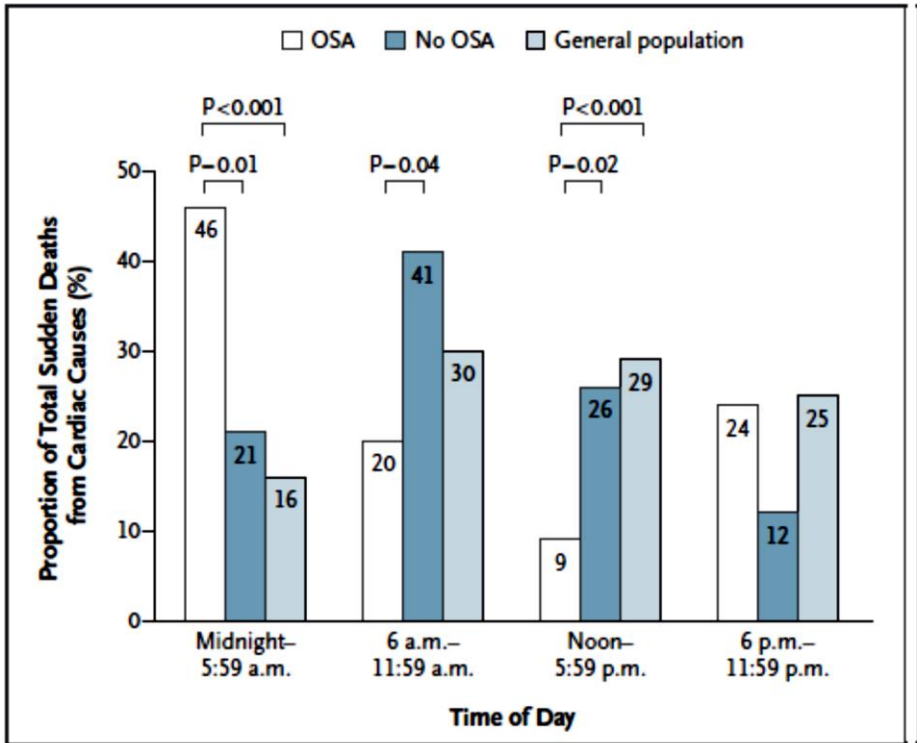
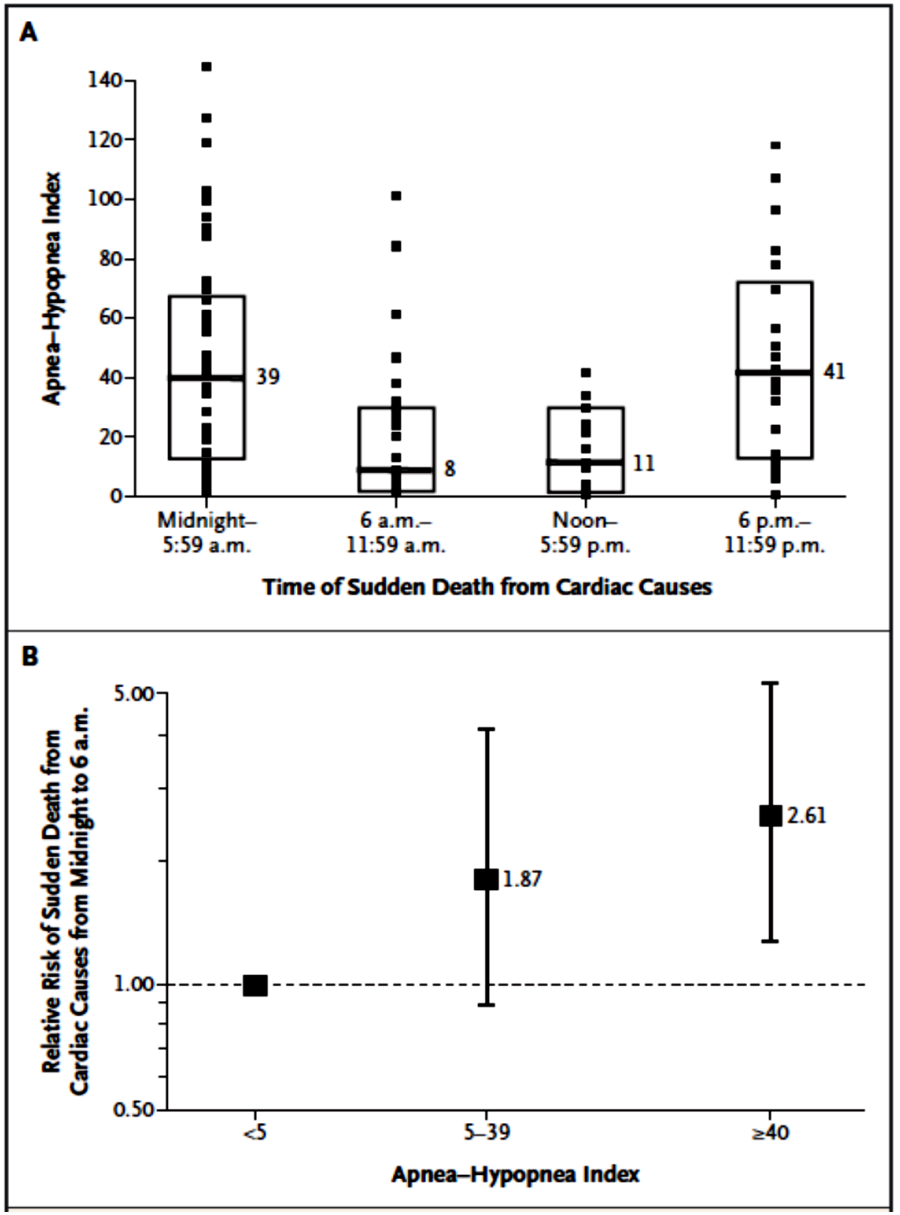


Figure 1. Day–Night Pattern of Sudden Death from Cardiac Causes in 78 Persons with and 34 Persons without Obstructive Sleep Apnea (OSA) and in the General Population.

Data for the general population were derived from Cohen et al.[1]



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

Is obstructive sleep apnea associated with VT?

A retrospective study from the National Inpatient Sample

Data from the national inpatient sample (NIS) 2012 to 2014, were reviewed. Discharges associated with OSA were identified as the target population using the relevant ICD-9-CM codes. Of 18 013 878 health encounters, 943 978 subjects (5.24%) had a diagnosis of OSA. VT and VF were more prevalent among patients with OSA compared to those without a diagnosis of OSA (2.24% vs 1.16%; P < 0.001 and 0.3% vs 0.2%; P < 0.001, respectively).

TABLE 2 Independent predictors of ventricular tachycardia in subjects with obstructive sleep apnea

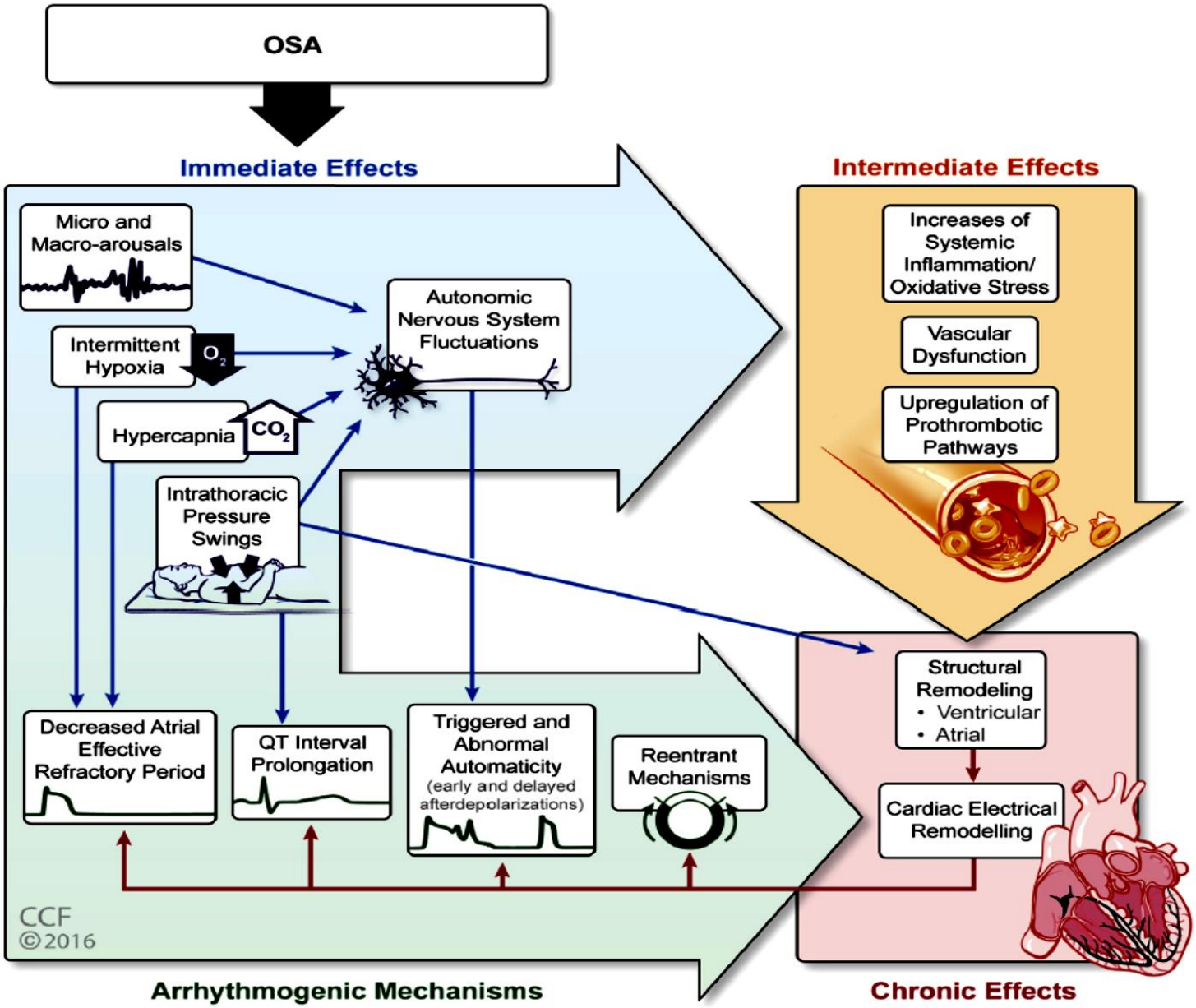
Variables	Odds ratio	95% confidence interval	*P*-value
Age	1.012	1.011–1.012	< 0.001
Male gender	1.98	1.96–1.99	< 0.001
Obstructive sleep apnea	1.22	1.20–1.24	< 0.001
Diabetes mellitus	0.80	0.80–0.81	< 0.001
Hypertension	1.04	1.03–1.05	< 0.001
Acute kidney injury	1.42	1.41–1.46	< 0.001
Obesity	1.10	1.08–1.11	< 0.001
Acute coronary syndrome	3.12	3.08–3.16	< 0.001
Coronary artery disease	1.71	1.70–1.73	< 0.001
Heart failure	2.71	2.68–2.75	< 0.001
Diastolic heart failure	2.10	2.07–2.14	< 0.001
Systolic heart failure	6.30	6.22–6.38	< 0.001
Hyperlipidemia	1.14	1.13–1.16	< 0.001
Tobacco smoking	1.07	1.06–1.08	< 0.001
Charlson-Deyo index	1.019	1.017–1.022	< 0.001

TABLE 3 Independent predictors of ventricular fibrillation in subjects with obstructive sleep apnea

Variables	Odds ratio	95% confidence interval	*P*-value
Age	0.996	0.996–0.997	< 0.001
Male gender	2.02	1.99–2.08	< 0.001
Obstructive sleep apnea	1.02	0.98–1.07	0.27
Diabetes mellitus	0.79	0.77–0.81	< 0.001
Hypertension	0.91	0.89–0.93	< 0.001
Acute kidney injury	2.16	2.11–2.22	< 0.001
Obesity	1.12	1.08–1.16	< 0.001
Acute coronary syndrome	12.35	12.05–12.65	< 0.001
Coronary artery disease	1.86	1.81–1.91	< 0.001
Heart failure	2.47	2.39–2.55	< 0.001
Diastolic heart failure	0.99	0.94–1.05	0.78
Systolic heart failure	3.27	3.17–3.37	< 0.001
Hyperlipidemia	0.97	0.95–1.00	0.03
Tobacco smoking	0.99	0.97–1.01	0.24
Charlson-Deyo index	0.98	0.97–0.98	< 0.001

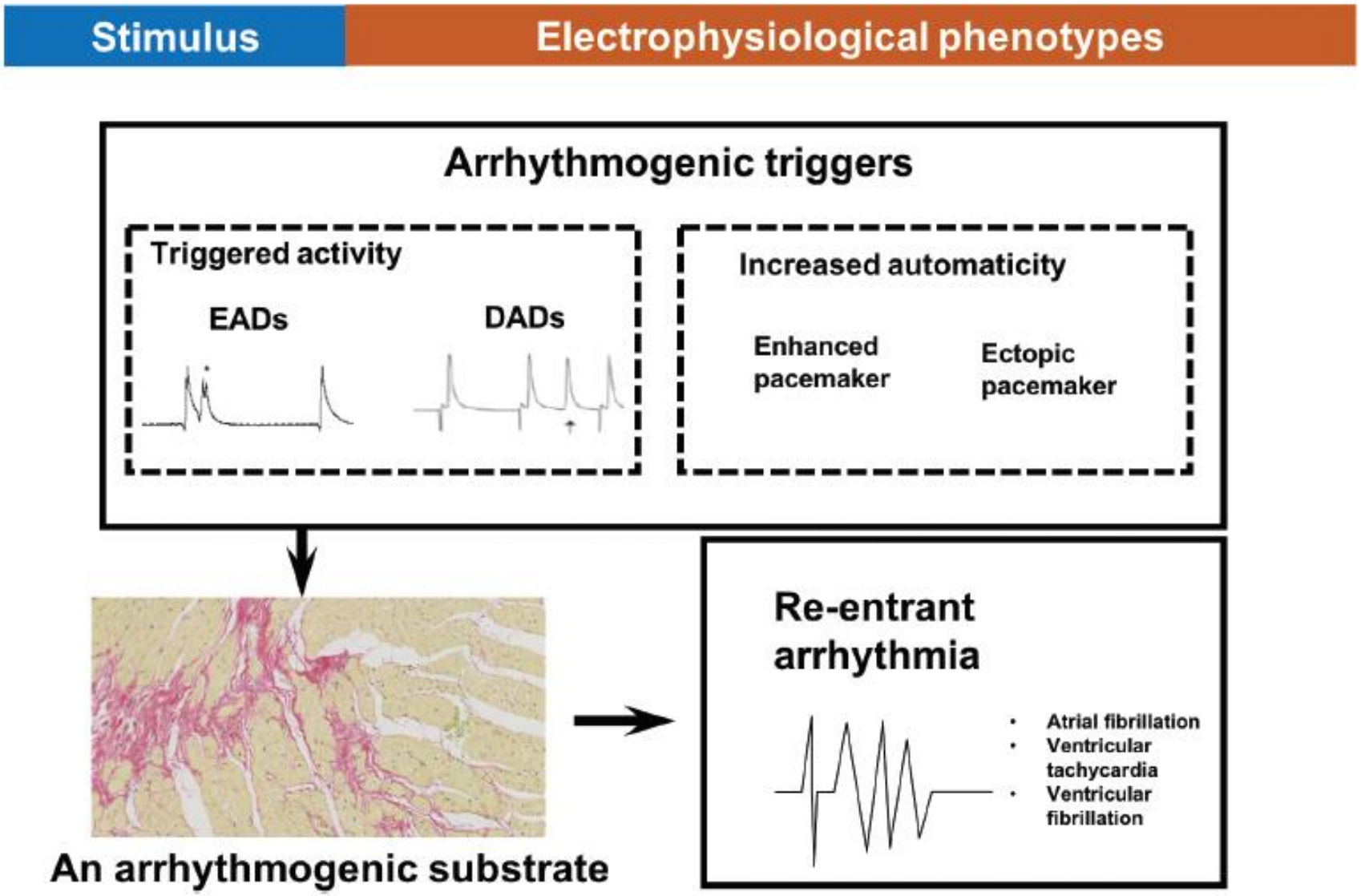
Salama A et al., Clinical Cardiology 2018;41:1543–1547

Arrhythmogenic mechanisms of OSA in HF patients



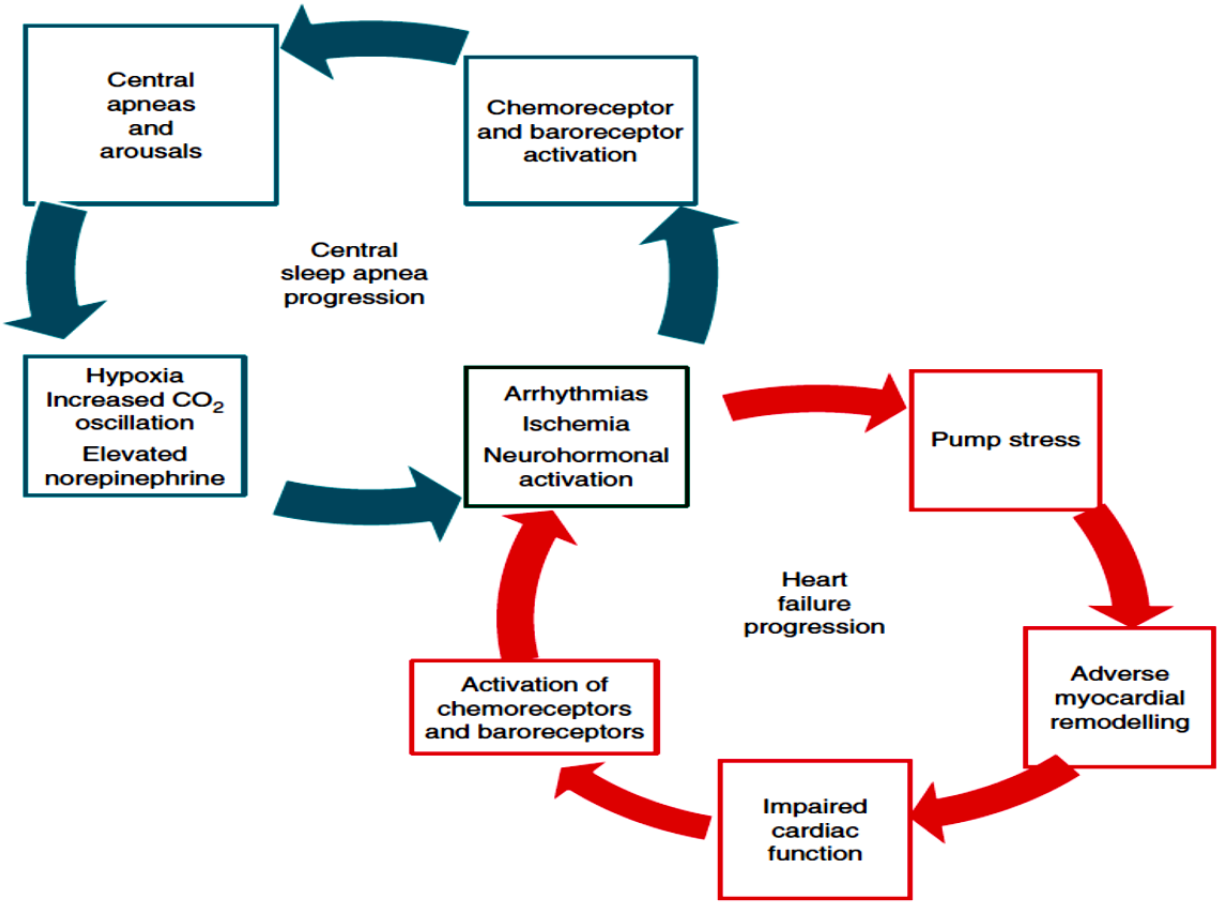
May AM et al., Chest 2017; 151: 225-241

Arrhythmogenic mechanisms of OSA in HF patients



Chadda KR et al., SLEEPJ 2018, doi: 10.1093/sleep/zsy136

Pathophysiology and relationship between HF, CSA and ventricular arrhythmias

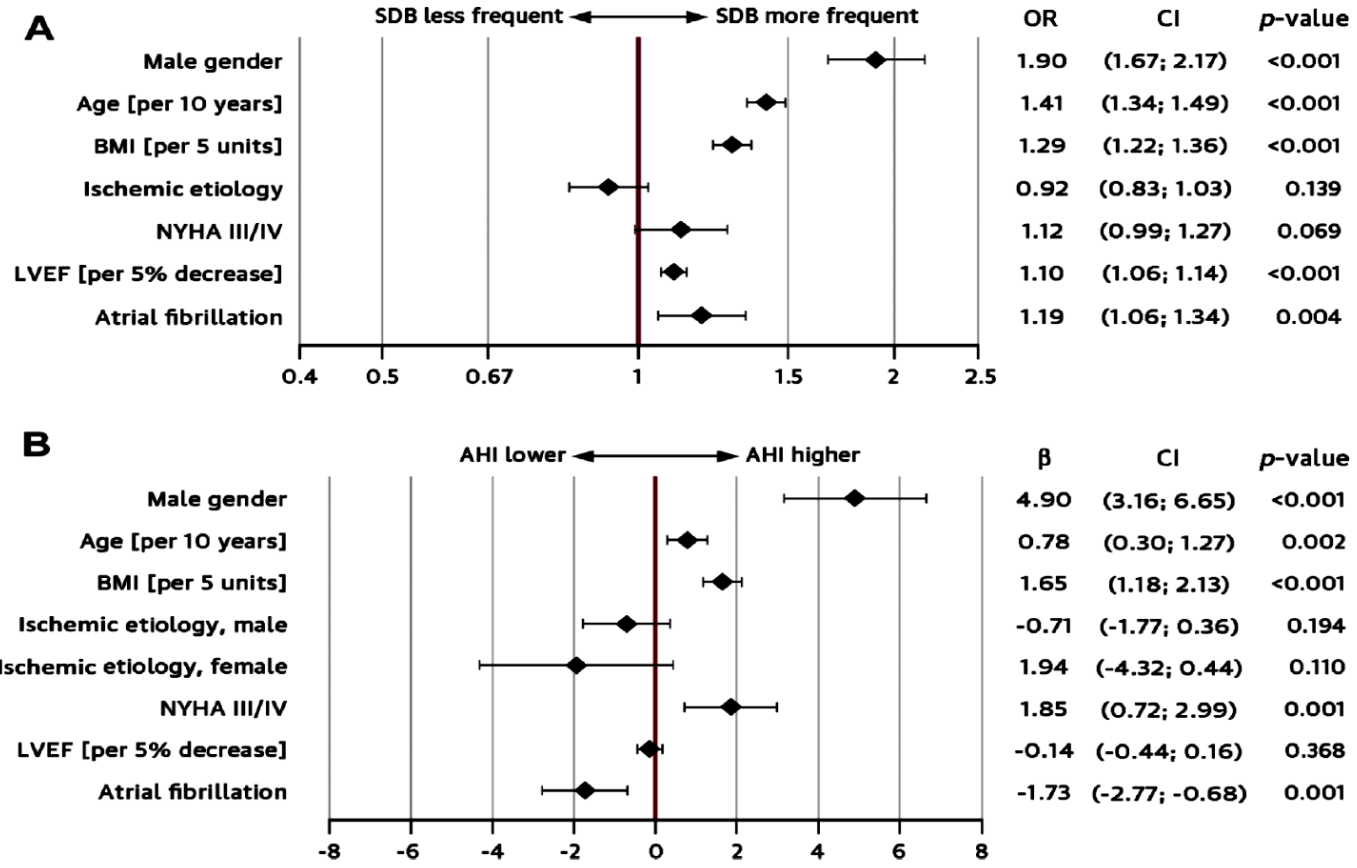


Each episode of central apnoea and arousal results in hypoxia, norepinephrine, and wide oscillations in carbon dioxide. Hypoxia results in cardiac ischaemia, plaque rupture, and dementia. Elevated norepinephrine causes atrial and ventricular arrhythmias and activates the renin–angiotensin system resulting in sodium retention and neurohormonal activation. Neurohormonal activation and ischaemia further activate central and peripheral chemoreceptors and baroreceptors further destabilizing breathing and triggering CSA. In addition to CSA, feeding back to continue the CSA cycle, ischaemia, and neurohormonal activation causes additional pump stress leading to adverse myocardial remodelling.With adverse remodelling, cardiac function is further impaired and worsens the downward progression of HF.

Prevalence and Predictors of Sleep-Disordered Breathing in Pts With Stable Chronic HF

The SchlaHF Registry

Data from 6,876 pts. The prevalence of moderate-to-severe SDB was 46%, with a sex difference: 36% in women (n=1,448) versus 49% in men (n=5,428). Prevalence of SDB rose with increasing age.



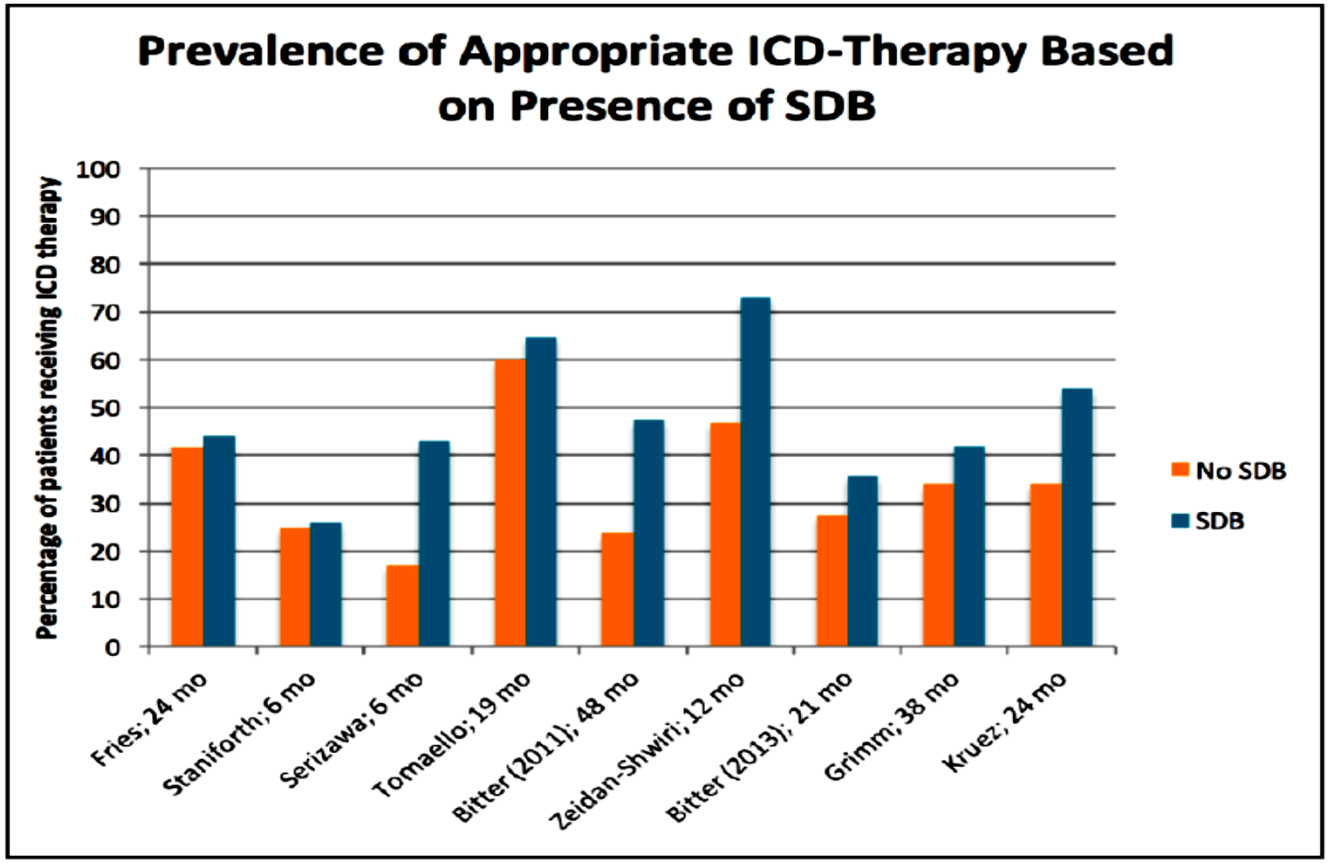
Predictors of Sleep-Disordered Breathing and Apnea-Hypopnea Index (AHI ≥15/h)

Artz M et al., J Am Coll Cardiol HF 2016;4:116–25

Effect of Sleep-Disordered Breathing on Appropriate ICD Therapy in Pts With HF

A Systematic Review and Meta-Analysis

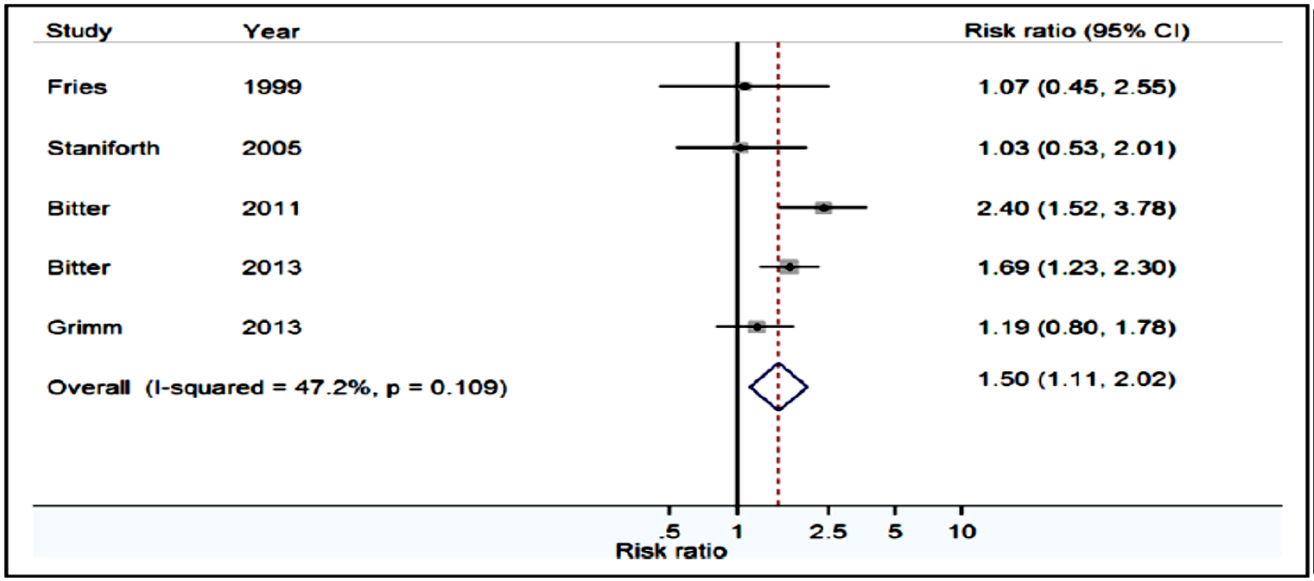
Nine prospective cohort studies (n=1274) were included in this analysis. SDB was present in 52% of the participants. SDB was associated with a 55% higher risk of appropriate ICD therapies (45% versus 28%; risk ratio, 1.55; 95% confidence interval, 1.32–1.83).



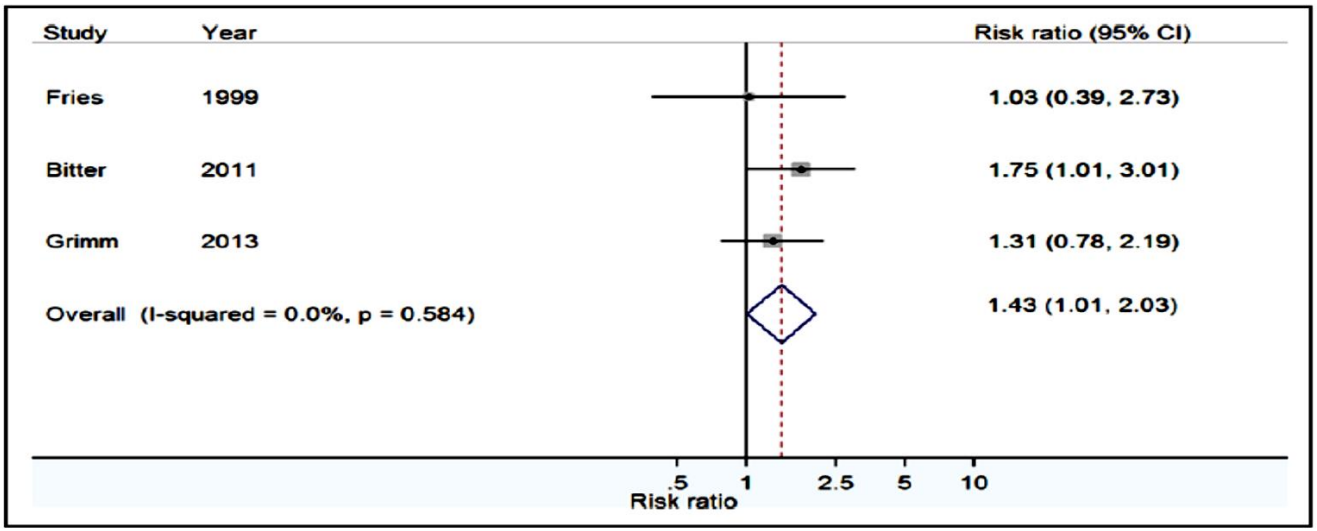
Kwon Y et al., Circ Arrhythm Electrophysiol. 2017. DOI:10.1161/CIRCEP.116.004609

Effect of Sleep-Disordered Breathing on Appropriate ICD Therapy in Pts With HF

A Systematic Review and Meta-Analysis



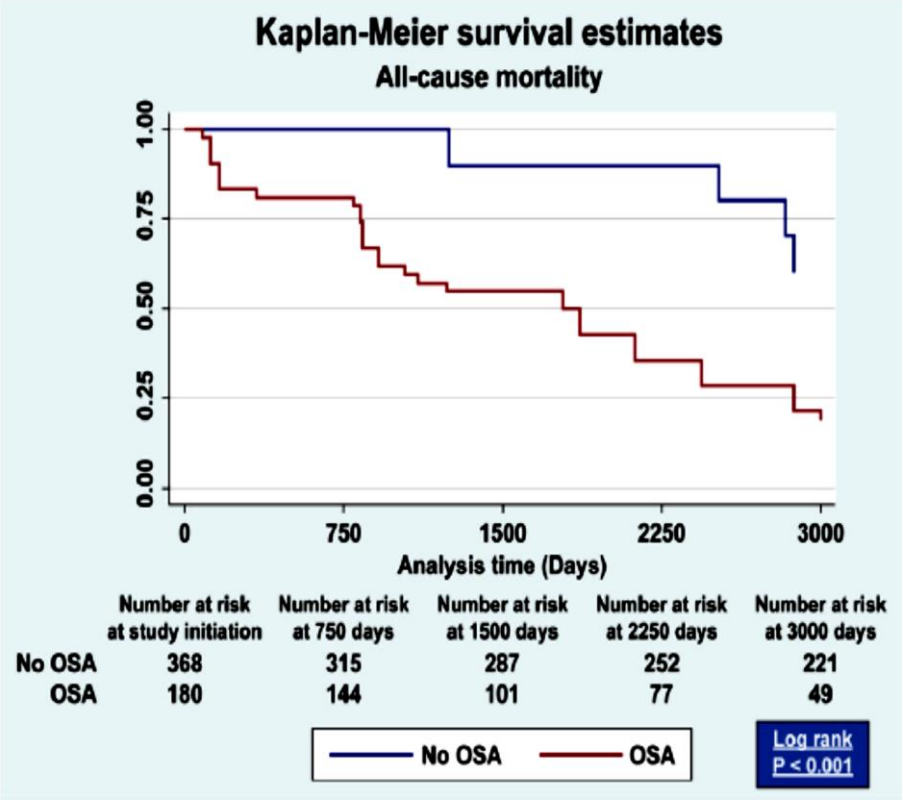
Risk of ICD therapy in pts with central sleep apnea (CSA) vs those without CSA

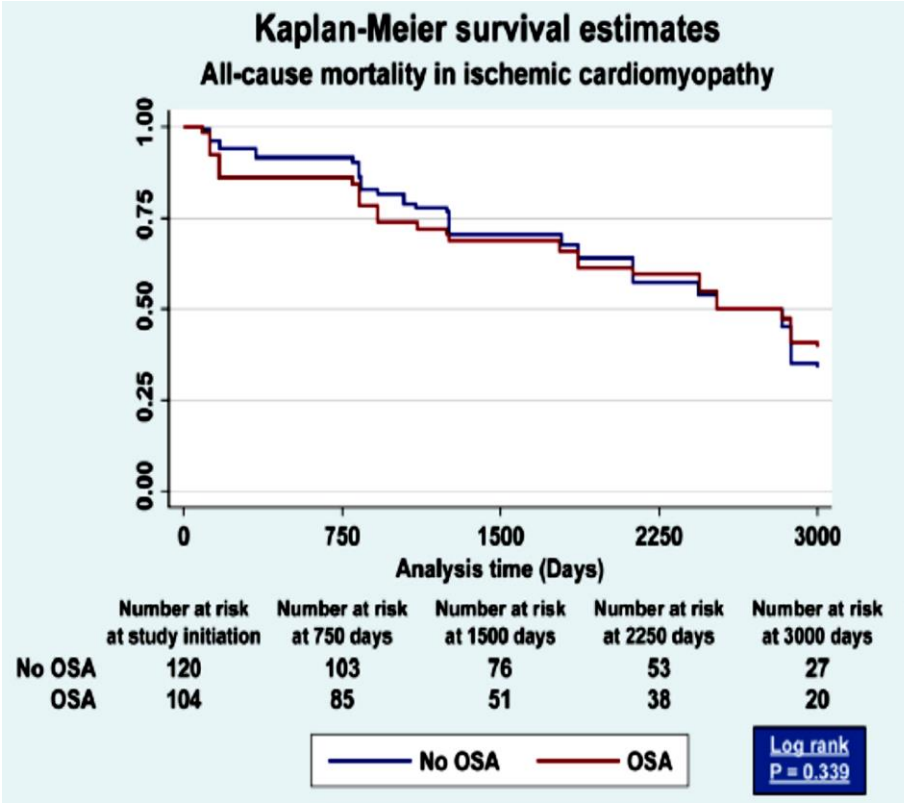


Risk of ICD therapy in pts with obstructive sleep apnea (OSA) vs those without OSA

Role of obstructive sleep apnea on the response to CRT and all-cause mortality

Out of 548 consecutive patients who received a CRT-D (mean age 65 6 13 years; 216 (39%) women; mean follow-up period 76.6±17 months), a total of 180 patients (33%) had OSA. Study participants were categorized to have mild, moderate, and severe OSA if they had an AHI between 5 and 15, between 15 and 30, and >30 events/h of sleep.

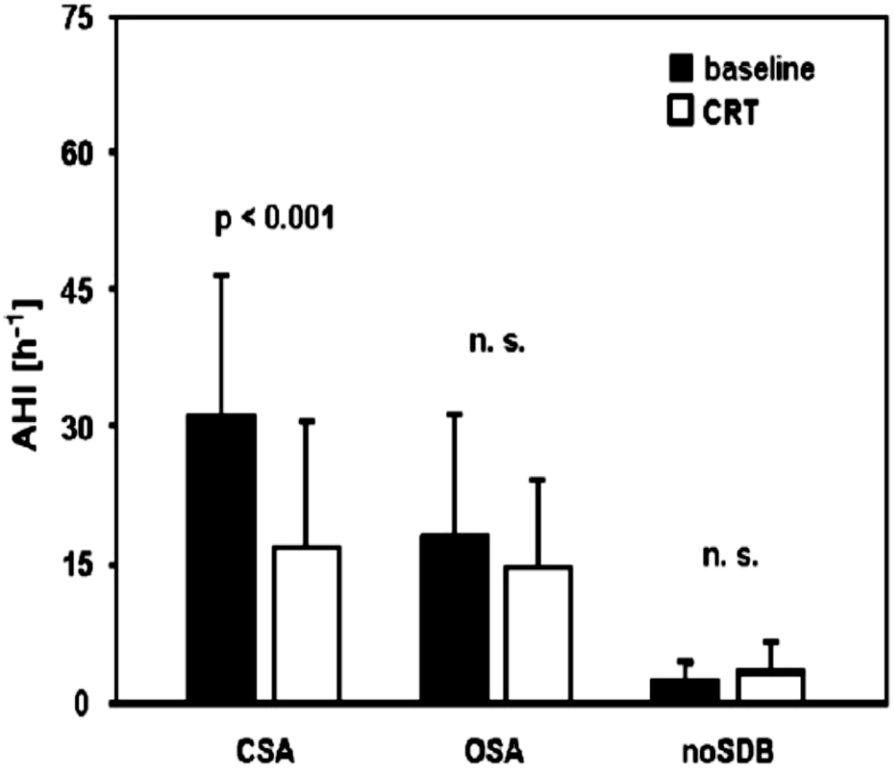


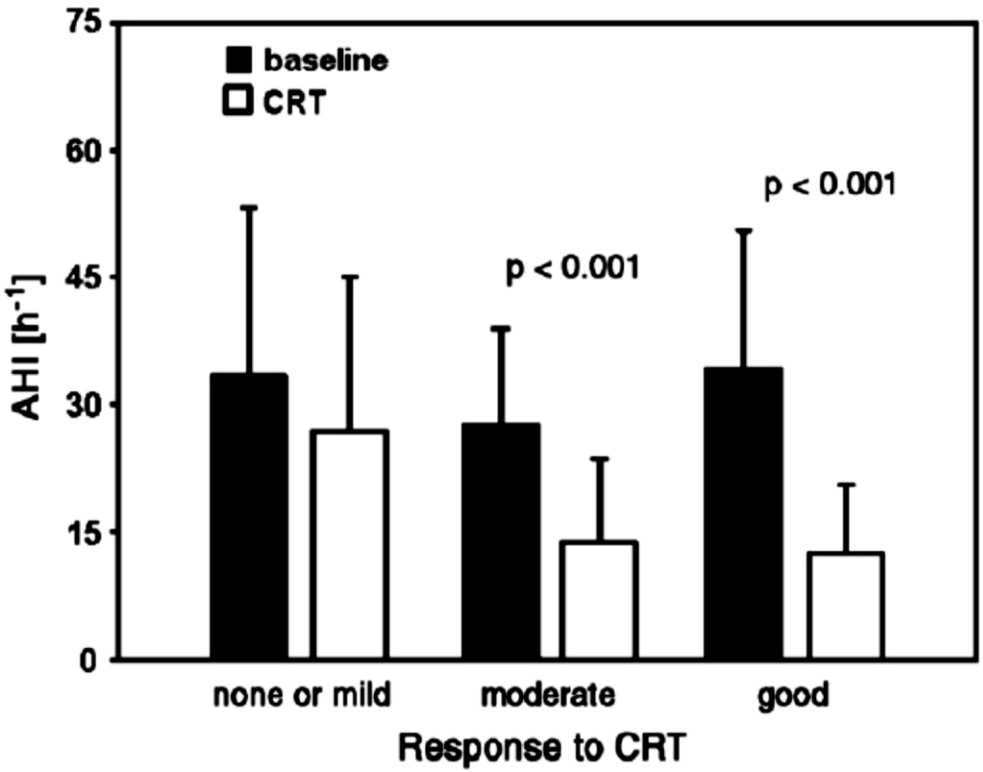


Shantha G et al., Heart Rhythm 2018; 15: 1283–1288

Influence of CRT on different types of sleep disordered breathing

Seventy-seven patients with HF (19 females; 62.6±10 years); central sleep apnoea (CSA) was documented in 36 (47%), obstructive sleep apnoea (OSA) in 26 (34%), and no SDB in 15 (19%) patients. CRT improved clinical and haemodynamic parameters. SDB parameters improved in CSA patients only

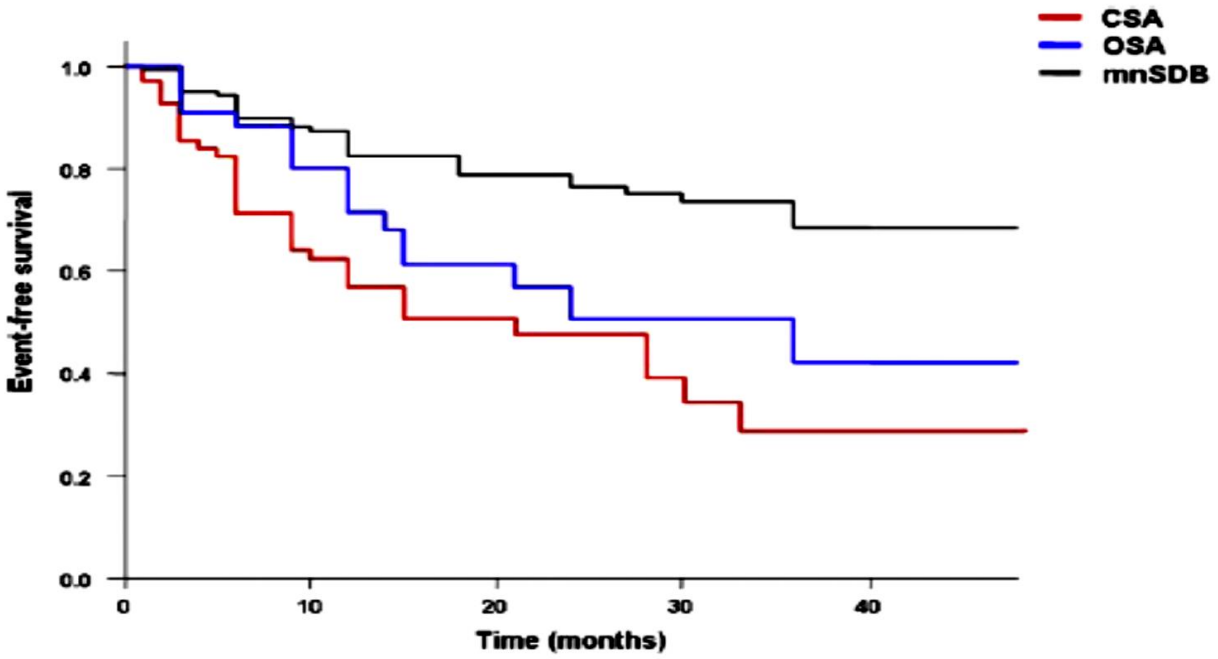




Oldenburg O et al., Eur J Heart Fail 2007; 9: 820–826

Cheyne–Stokes respiration and obstructive sleep apnoea are independent risk factors for malignant VAs requiring appropriate ICD therapies in HF pts

283 pts [170 with mild or no sleep disordered breathing (mnSDB) and 113 pts declined ventilation therapy] were included into this study. During follow-up (48 months), data on appropriately monitored VAs as well as appropriate ICD therapies were obtained from 255 of these pts (90.1%).

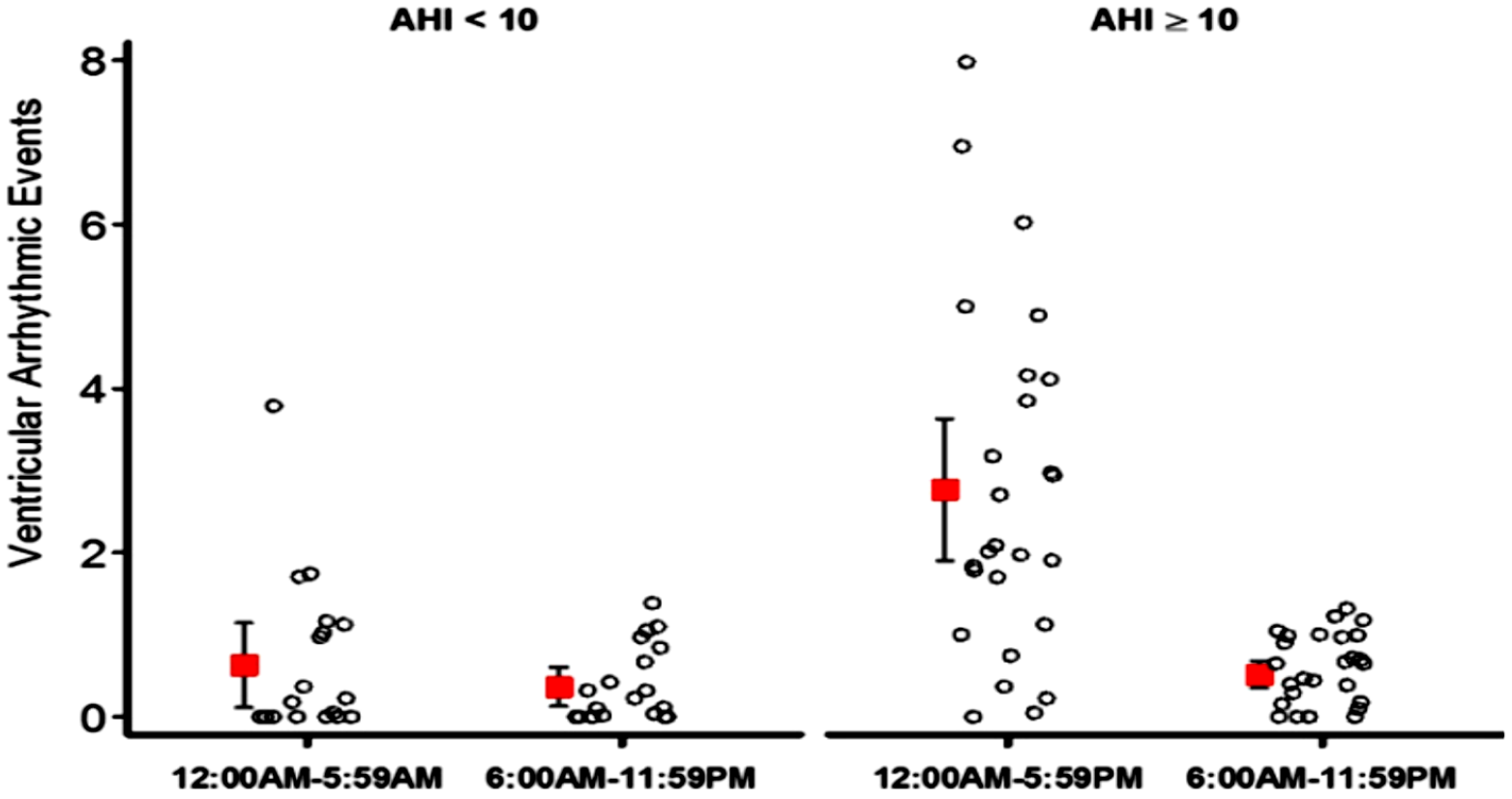


No. at risk	0	6	12	18	24	30	36	42	48
CSA	68	45	28	20	9	7	6	4	4
OSA	44	30	21	13	10	7	5	4	4
mnSDB	143	113	83	70	47	41	30	28	27

Bitter T et al., European Heart Journal 2011; 32: 61–74

Circadian pattern of life-threatening VA in pts with sleep-disordered breathing and ICDs

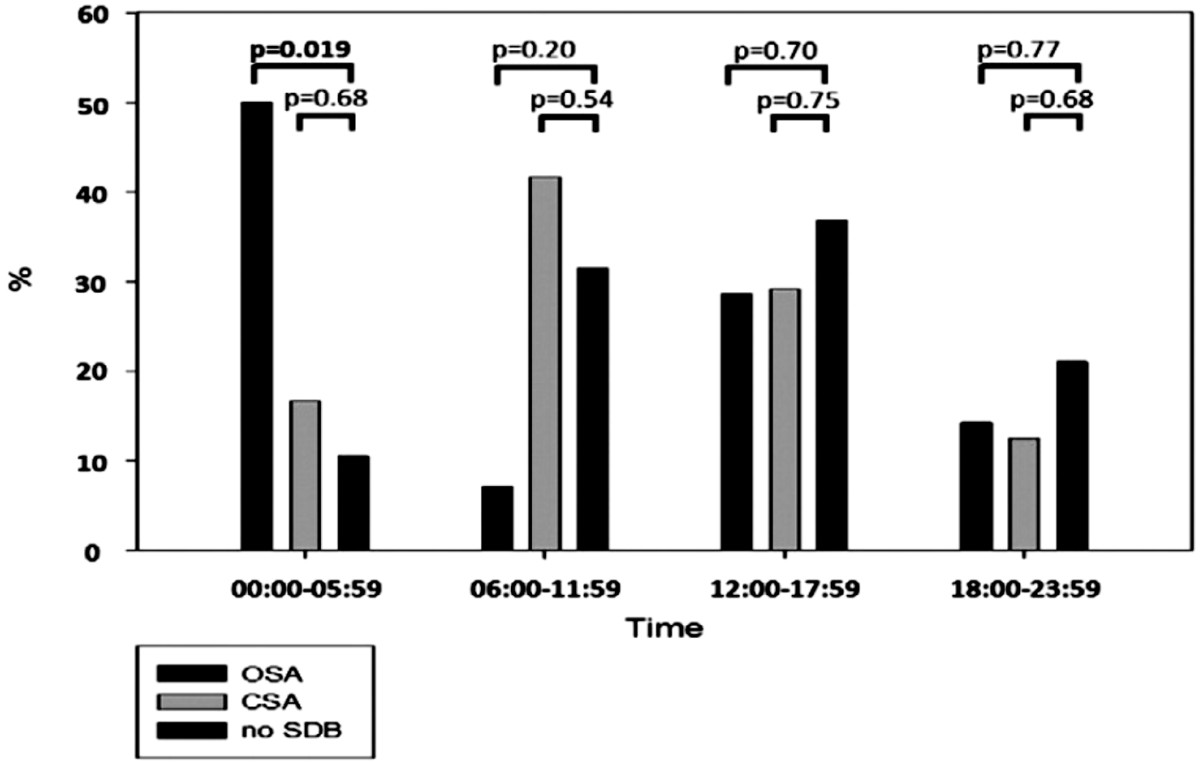
45 pts with an ICD. SDB was defined as an apnea-hypopnea index (AHI) >10 events/hour based on an overnight sleep study. SDB was present in 26 (57.8%) pts. Appropriate ICD therapies were higher among patients with SDB (73% vs 47%, p = .02). Logistic regression identified SDB as a predictor of appropriate ICD therapy (OR 4.4, 95% CI 1.4 –15.3, p = .01).



Zeidan-Shwiri T et al., Heart Rhythm 2011;8:657– 662

Circadian variation of ICD shocks in pts with chronic HF: the impact of Cheyne- Stokes respiration and obstructive sleep apnea

A total number of 216 patients with reduced LVEF and chronically implanted CRT-D



Frequency distribution of appropriate ICD shocks for the four six-hour intervals for pts with OSA (apnea–hypopnea index (AHI) ≥ 10/h, N 50% obstructive events), CSA with Cheyne–Stokes respiration (AHI ≥ 10/h, N 50% central events), and no SDB

Bitter T et al., Int J Cardiol 2014; 176: 1033-5.

Central sleep apnoea and inflammation are independently associated with arrhythmia in HF pts

178 pts (age 70±1 years) admitted to the hospital for worsening HF. Obstructive sleep apnoea was excluded and pts were dichotomized based on the median value of the central apnoea index (CAI) of 7.5/h. The CAI and C-reactive protein were independently associated with NSVT during both daytime (1.22, 95%CI 1.00–6.92; and 5.82, 2.58–56.1, respectively) and night-time periods (3.57, 95% CI 1.06–13.1; and 10.7, 3.30–44.4, respectively).

Table 3 Multivariate logistic regression analysis

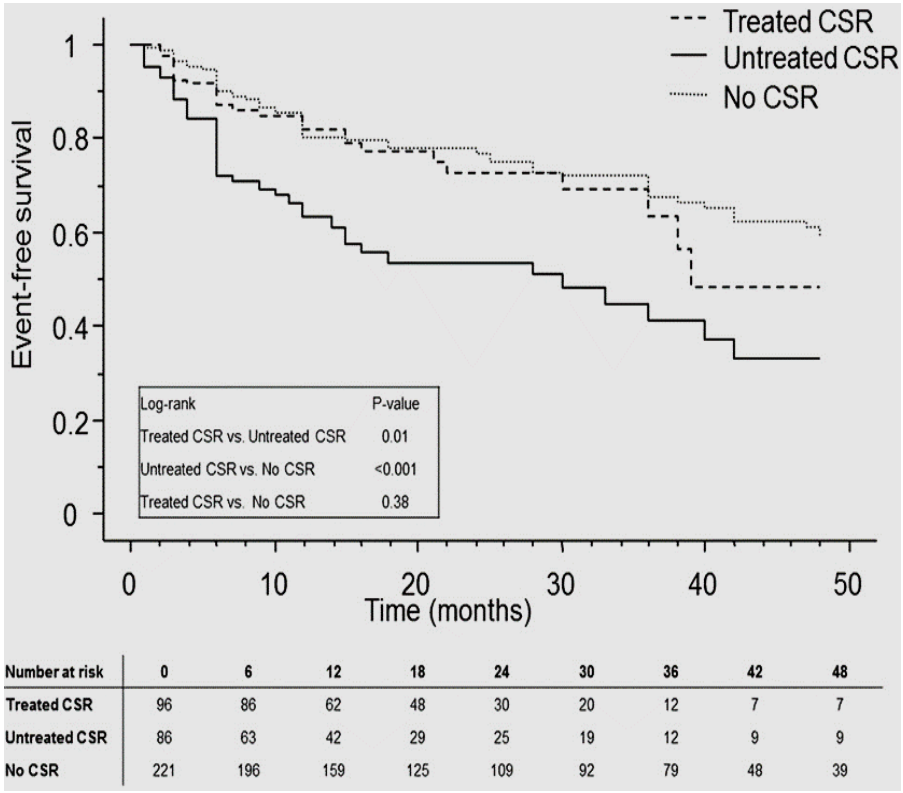
	CAI (OR, 95% CI)	CRP (OR, 95% CI)
Atrial fibrillation	1.03 (1.01–2.51)*	1.38 (0.63–3.10)
Sinus pause		
Daytime	1.09 (0.32–3.73)	2.01 (0.66–23.2)
Night-time	1.12 (1.08–1.35)*	2.96 (0.98–48.8)
VE		
Isolated		
Daytime	1.35 (0.30–6.43)	3.18 (0.80–15.6)
Night-time	3.61 (1.00–15.8)*	2.74 (0.93–9.41)
NSVT		
Daytime	1.22 (1.00–6.92)*	5.82 (2.58–56.1)*
Night-time	3.57 (1.06–13.1)*	10.7 (3.30–44.4)**

* p<0.05 ** p<0.01

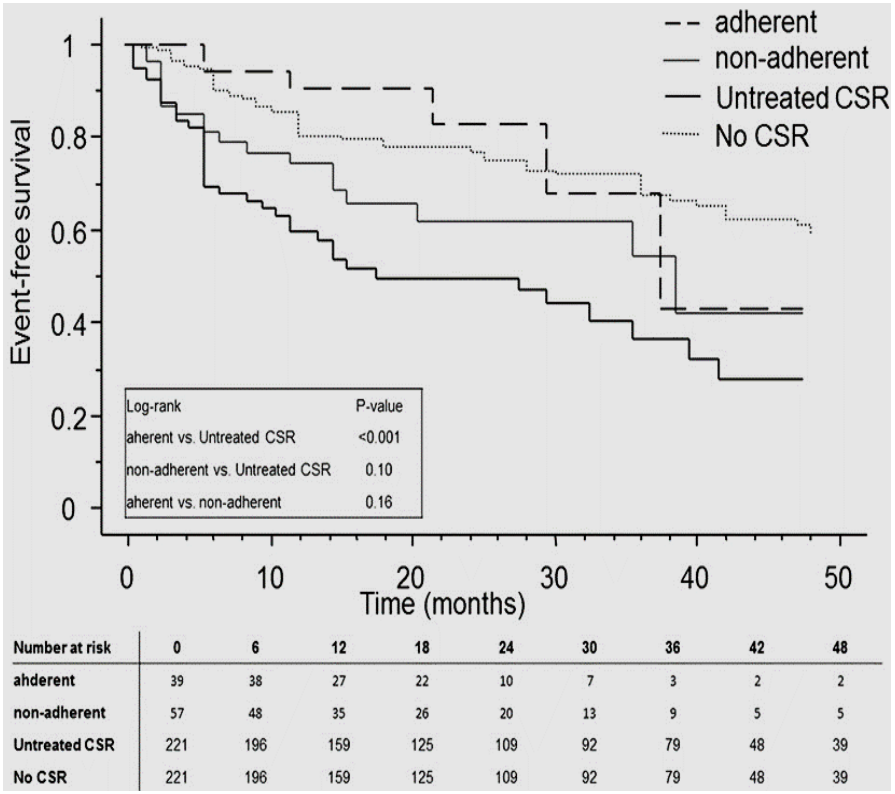
Sano K et al., Eur J Heart Fail 2013; 15: 1003–1010

Treatment of Cheyne-Stokes Respiration Reduces Arrhythmic Events in Chronic HF

403 pts with CHF (LVEF ≤45%, NYHA-class ≥2) and implanted ICD; 221 had mild or no CSR (apnea-hypopnea index [AHI]<15/h), and 182 had moderate to severe CSR (AHI>15/h). Latter ones were offered therapy with adaptive servoventilation (ASV), which 96 patients accepted and 86 rejected.



Number at risk	0	6	12	18	24	30	36	42	48
Treated CSR	96	86	62	48	30	20	12	7	7
Untreated CSR	86	63	42	29	25	19	12	9	9
No CSR	221	196	159	125	109	92	79	48	39

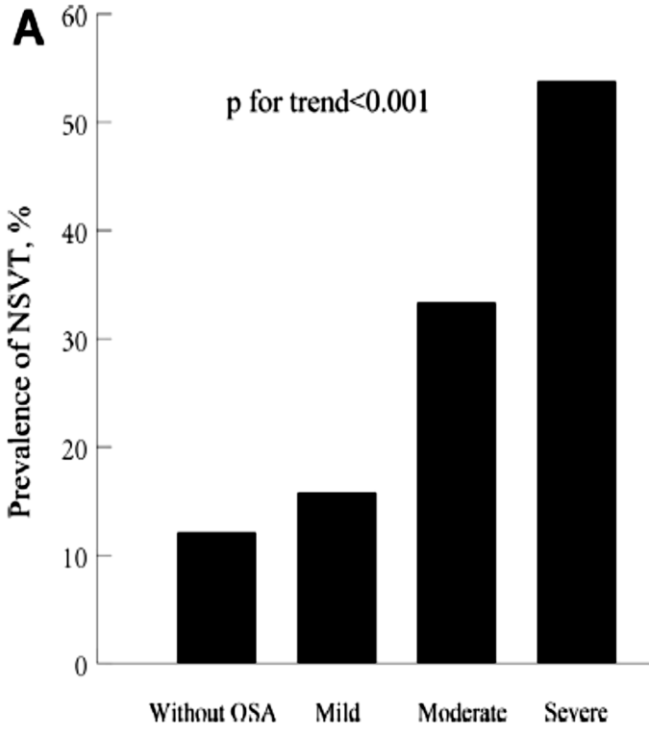


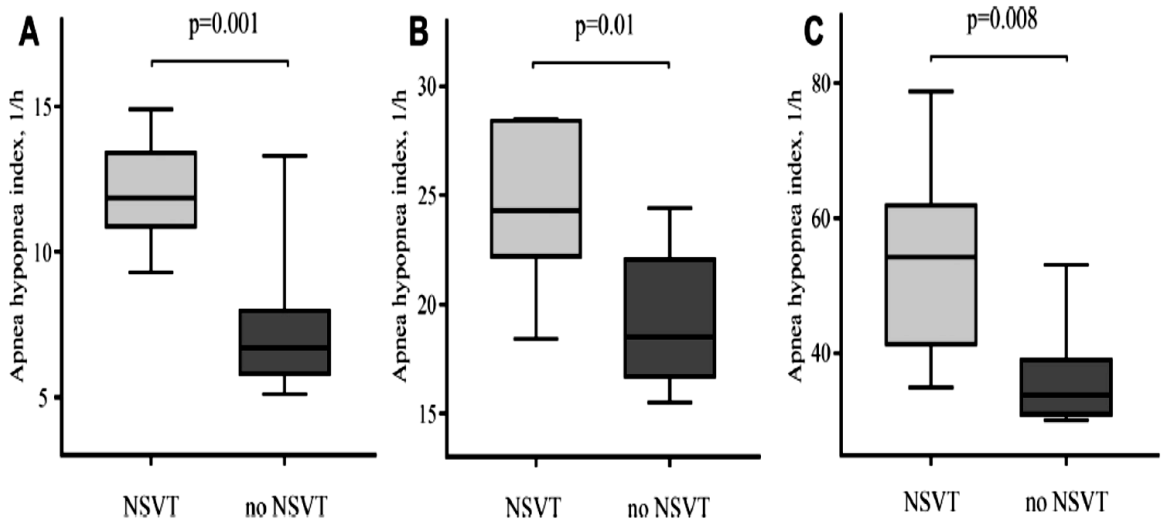
Number at risk	0	6	12	18	24	30	36	42	48
ahderent	39	38	27	22	10	7	3	2	2
non-adherent	57	48	35	26	20	13	9	5	5
Untreated CSR	221	196	159	125	109	92	79	48	39
No CSR	221	196	159	125	109	92	79	48	39

Bitter T et al., J Cardiovasc Electrophysiol 2013; 24: 1132-1140

Obstructive sleep apnea is associated with NSVT in pts with hypertrophic obstructive cardiomyopathy

Of 130 pts, 72 (55%) were diagnosed with OSA, including 38 with mild, 21 with moderate, and 13 with severe OSA, and 27 pts (21%) had NSVT. Mild OSA, moderate OSA, and severe OSA were defined as AHI > 5 events/h, AHI ≥ 15 events/h, and AHI ≥ 30 events/h, respectively





The value of AHI according to the presence of NSVT among the different OSA groups: (A) mild OSA, (B) moderate OSA, and (C) severe OSA.

Wang S et al., Heart Rhythm 2019; 16: 694–701

Sleep-Disordered Breathing in Patients With the Brugada Syndrome

Twenty patients were included (50 ± 15 years old, 75% men). Despite their normal BMI (24.7 ± 2.7 kg/m2), 45% had sleep-disordered breathing (SDB), with a mean apnea-hypopnea index of 17.2 ± 14 events/hour. In patients with a high risk of arrhythmias, 5 (63%) had SDB. Spontaneous ST-segment changes occurred in 2 patients. Most ST-segment changes were observed during rapid eye movement sleep (31%) or within 1 minute of arousals (44%). Regarding respiratory events, 25 (56%) of ST-segment changes were related to occurrence of apnea or hypopnea.

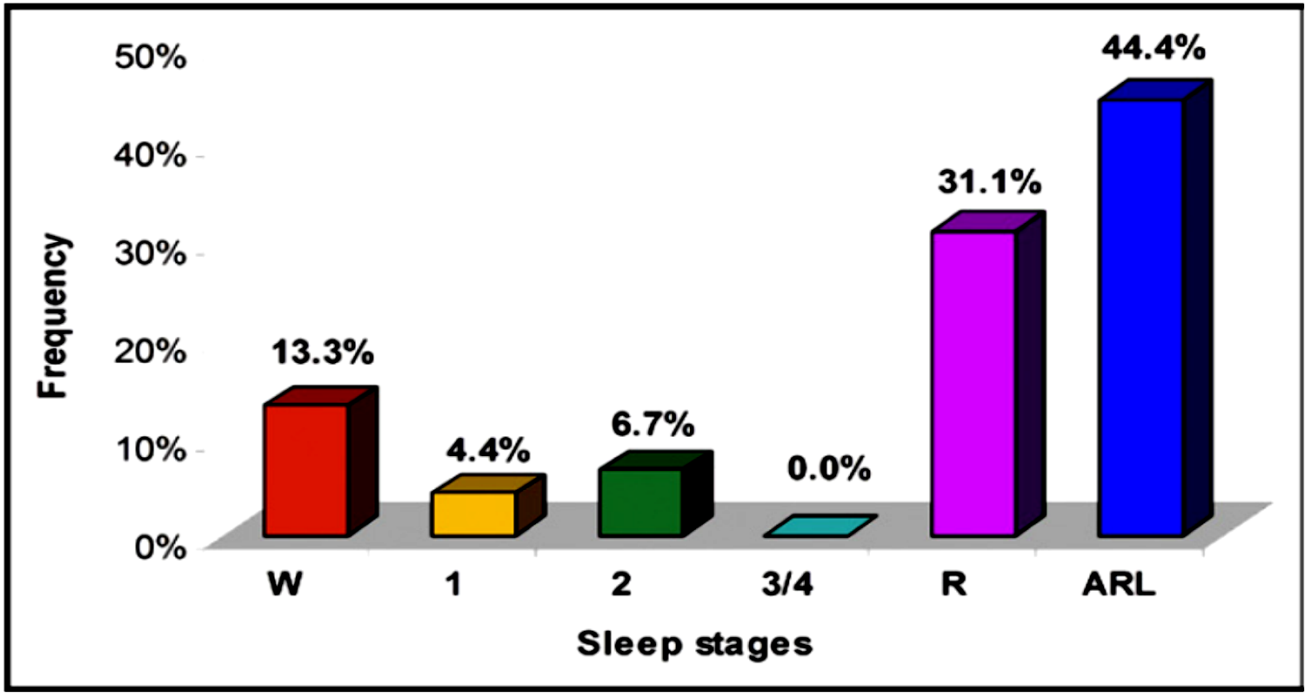


Figure 2. Distribution of ST-segment changes in 2 patients according to changes in sleep stages. 1 = stage 1; 2 = stage 2; 3/4 = stage 3 and 4; ARL = arousals; R = REM; W = wakefulness.

Macedo PG et al., Am J Cardiol 2011;107:709 –713

Conclusions

- A substantial body of evidence exists that support a link between the sleep disorder breathing and cardiac arrhythmias
- There are many mechanisms leading to arrhythmogenesis in HF and OSA, such as metabolic derangement, remodeling, inflammation, and autonomic imbalance. These mechanisms lead to the generation of arrhythmic triggers and substrates, resulting in ventricular arrhythmias that cause significant morbidity and mortality.
- In heart failure patients, OSA and CSA are both independently associated with a shorter event-free survival period until first monitored ventricular arrhythmia or appropriate ICD therapy occurs
- Whether adequate therapy of SDB is accompanied by a superior event-free survival needs to be determined