SLEEP APNEA & ARRHYTHMIAS

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AGENDA

- **Introduction**
- **Sleep Apnea and Arrhythmias**
- **Clinical Implications**

INTRODUCTION | Sleep-Related Rhythms

Sleep

Arousal

- SN Arrhythmia
- Bradycardia
- Pauses
- Low Grade AV Block

INTRODUCTION | Sleep-Related Rhythms

Sleep

Arousal

- ↑ Heart Rate
- ↑ Blood Pressure
- ↑ Cardiac Output

INTRODUCTION | Sleep Apnea

Types (SDB)

Epidemiology

- Obstructive Sleep Apnea/ Hypopnea Syndrome
- Central Sleep Apnea
- Obesity Hypoventilation Syndrome
- Cheyne-Stokes Respiration
- Upper Airway Resistance Syndrome

INTRODUCTION | Sleep Apnea

Types (SDB)

Epidemiology

- 2-4% in adult population
- Men Twice as Women
- 82% of affected men undiagnosed
- 93% of affected women undiagnosed
- Associated with increased risk of CV morbidity

OSA & ARRHYTHMIAS | Limitations

Disease Related

Methodology

Arrhythmia Related

- Multiple Conditions
- Inconsistent Definitions
- Tracking Adherence to Treatment

OSA & ARRHYTHMIAS | Limitations

Disease Related

Methodology

Arrhythmia Related

- Non-randomization
- Self Reporting of Condition
- Self Reporting of Treatment
- Comorbid Conditions
- Short Period of Monitoring

OSA & ARRHYTHMIAS | Limitations

Disease Related

Methodology

Arrhythmia Related

Intermittent Nature

Sleep Related Arrhythmias

OSA & ARRHYTHMIAS | Proving Causation

Individual Observations

Biological Plausibility

Consistent/Strong Association

Temporal Association

Dose-Response Relation

Response to Treatment

OSA & ARRHYTHMIAS | Observations

Cardiac Arrhythmia and Conduction Disturbances During Sleep in 400 Patients With Sleep Apnea Syndrome

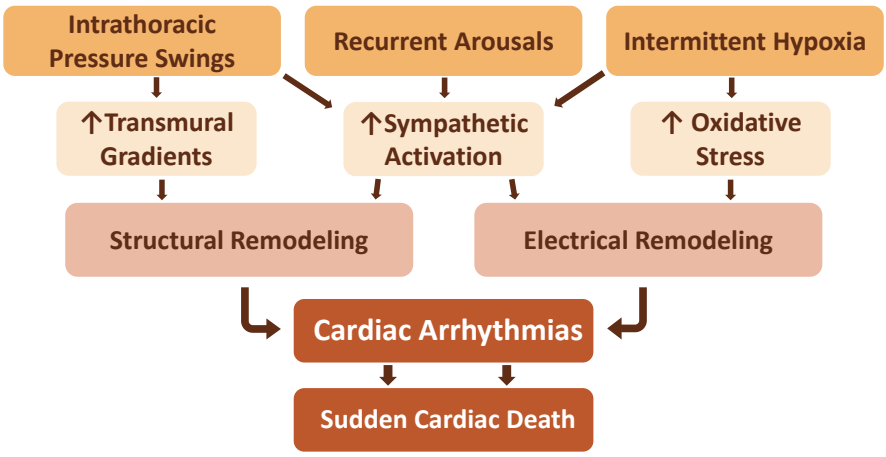
CHRISTIAN GUILLEMINAULT, MD, STUART J. CONNOLLY, MD, and ROGER A. WINKLE, MD

Cardiac Arrhythmia or Conduction Abnormality	Before Tracheostomy		After Tracheostomy	
	Awake	Asleep	Awake	Asleep
Sinus arrest 4 to 13 s	0	15	0	0
Second-degree atrioventricular block				
Mobitz type I	0	5	0	0
Mobitz type II	0	10	0	0
Ventricular tachycardia	0	8	0	0
Atrial flutter	0	2	0	0
Atrial fibrillation	0	8	0	0
Extreme sinus bradycardia	0	2	0	0
Frequent premature ventricular contractions (>2/min)	6	18*	4	4

Guilleminault et al. *Am J Cardiol.* 1983

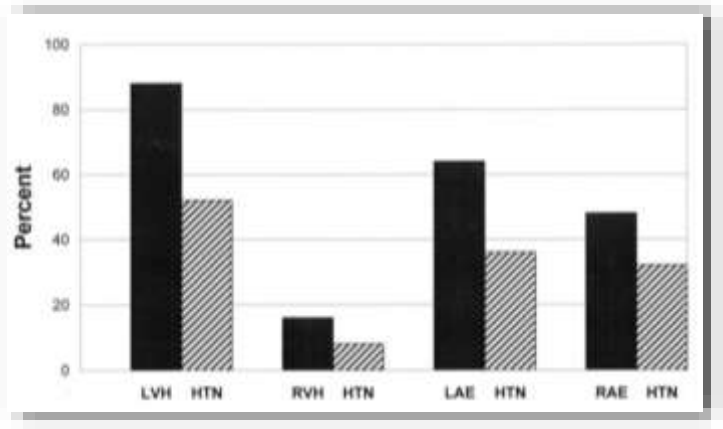
OSA & ARRHYTHMIAS | Pathophysiology

- **Intrathoracic Pressure Swings**
- **Recurrent Arousals**
- **Intermittent Hypoxia**



Structural Remodeling

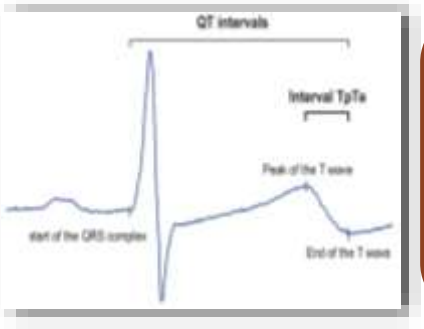
Electrical Remodeling



Cloward et al. *Chest.* 2003

Electrical Remodeling

Structural Remodeling



- 41 OSA patients on CPAP
- Divided to;
  - 21 patients stopped CPAP for 2 weeks
  - 20 patients continued therapy
- Measured;
  - QTc and T*p* T*e* intervals
  - Tp Te/QT ratio

Camen et al. *Eur J Appl Physiol.* 2013

OSA & ARRHYTHMIAS | Spectrum

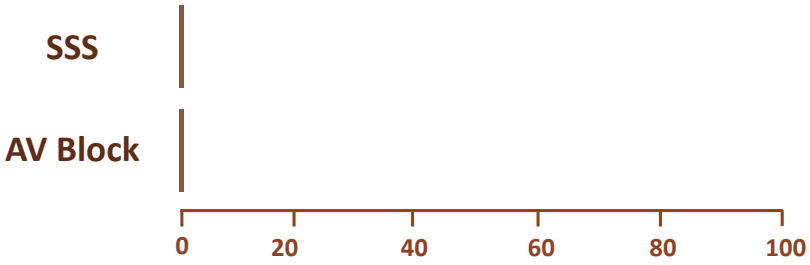
Bradyarrhythmias

Atrial Fibrillation

Sudden Cardiac Death

BRADYARRHYTHMIA | Observations

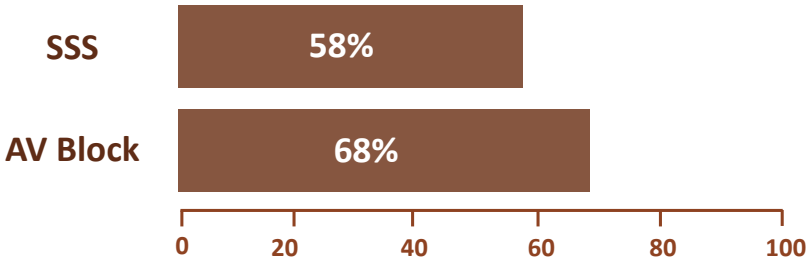
OSA among PM patients



Garrigue et al. *Circulation*. 2007

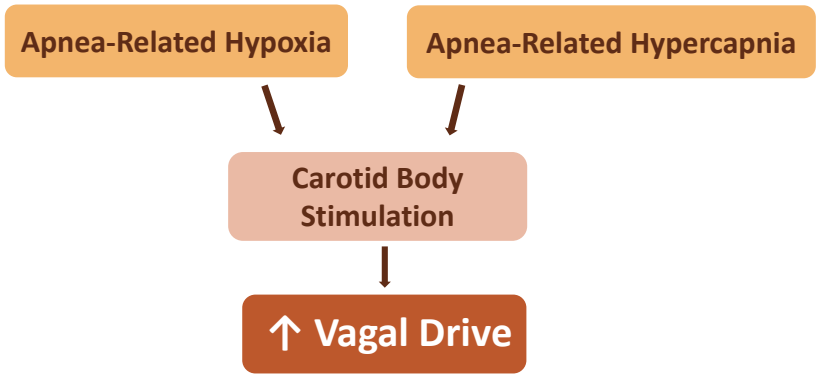
BRADYARRHYTHMIA | Observations

OSA among PM patients



Garrigue et al. *Circulation*. 2007

BRADYARRHYTHMIA | Mechanisms



BRADYARRHYTHMIA | Association

Ref.	Design	Patients	Diagnostic method	Cardiac monitoring	Results
Becker et al[84]	Observational, prospective	336 unselected OSAH	PSG	24-h Holter ECG	Second and third-degree AV block and/or sinus arrest in 7.8%
Simantirakis et al[85]	Observational, prospective	23 moderate–severe OSAH	PSG	Implantable loop recorder	Cardiac pauses (>3 s) and bradycardia (<40 bpm) in 47%, abolished by CPAP
Guilleminault et al[81]	Uncontrolled	400 severe OSAH	PSG	24-h Holter ECG	Sinus arrest in 10%, AV block in 3%
Miller[86]	Uncontrolled	23 unselected OSAH	PSG	24-h Holter ECG	Sinus bradycardia (<38 bpm) and pauses (>1.8 s) in 9%, first and second-degree AV block in 4%
Mehra et al[71]	Case–control	228 severe OSAH vs. 338 healthy	PSG	12-lead ECG during PSG	No significant difference in sinus pauses (>3 s), AV blocks, intraventricular conduction delay
Rocha et al[87]	Case–control	66 OSAH vs. 61 healthy	PSG	Holter ECG during PSG	Pauses and bradycardia significantly different; vinculin and second-degree AV blocks not
Ahn et al[74]	Nonrandomized, prospective	197 mild, 368 moderate, 785 severe OSAH, 44 healthy (316 CPAP therapy)	PSG	12-lead ECG during PSG	Sinus bradycardia and pauses (>2 s) significantly different, reduced by CPAP
Hetland et al[88]	Observational, prospective	45 unselected OSAH	PSG	48-h Holter ECG before and after 2–3 days of CPAP	Sinus pauses and second-degree AV block resolved in 97.5%
Koehler et al[89]	Nonrandomized, prospective	16 OSAH with nocturnal heart block without electrophysiological abnormalities	PSG	24h Holter ECG before and after CPAP/BiPAP	AV blocks and sinus arrest completely eliminated in 56%, reduced in 31% patients, unchanged in 13%
Becker et al[90]	Observational, prospective	17 unselected OSAH patients with heart block	PSG	ECG before and after CPAP	Significantly decrease of heart block, completely abolished in 70.6%

BRADYARRHYTHMIA | Association

Guilleminault et al.[91]	Uncontrolled	400 severe OSAH	PSG	24-h Holter ECG	Sinus arrest in 10%, AV block in 7%
Miller[92]	Uncontrolled	23 unselected OSAH	PSG	24-h Holter ECG	Sinus bradycardia (<30 bpm) and pauses (>1.8s) in 9%, first and second-degree AV block in 4%

BRADYARRHYTHMIA | Effect of Treatment

Harbison et al.[94]	Observational, prospective	45 unselected OSAH	PSG	18 h Holter ECG before and after 2–3 days of CPAP	Sinus pauses and second-degree AV block resolved in 87.5%
Koehler et al.[95]	Nonrandomized, prospective	16 OSAH with nocturnal heart block without electrophysiological abnormalities	PSG	24h Holter ECG before and after CPAP/BiPAP	AV blocks and sinus arrest completely eliminated in 56%, reduced in 31% patients, unchanged in 13%
Becker et al.[96]	Observational prospective	17 unselected OSAH patients with heart block	PSG	ECG before and after CPAP	Significantly decrease of heart block, completely abolished in 70.6%

BRADYARRHYTHMIA | Effect of Treatment

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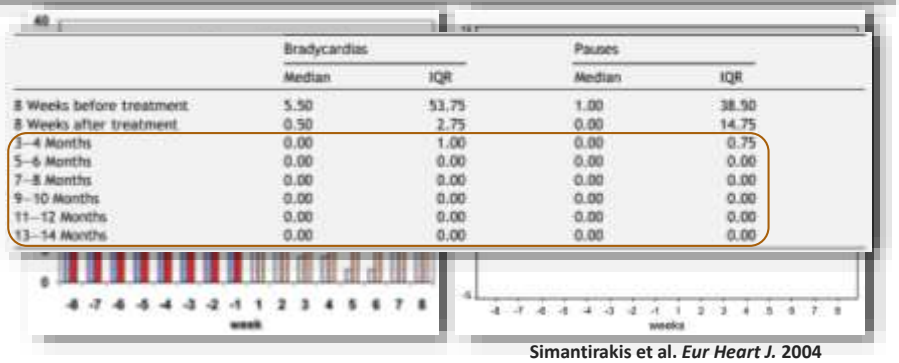
	Bradycardias		Pauses	
	Median	IQR	Median	IQR
8 Weeks before treatment	5.50	53.75	1.00	38.50
8 Weeks after treatment	0.50	2.75	0.00	14.75
3–4 Months	0.00	1.00	0.00	0.75
5–6 Months	0.00	0.00	0.00	0.00
7–8 Months	0.00	0.00	0.00	0.00
9–10 Months	0.00	0.00	0.00	0.00
11–12 Months	0.00	0.00	0.00	0.00
13–14 Months	0.00	0.00	0.00	0.00



Simantirakis et al. *Eur Heart J.* 2004

ATRIAL FIBRILLATION | Observations

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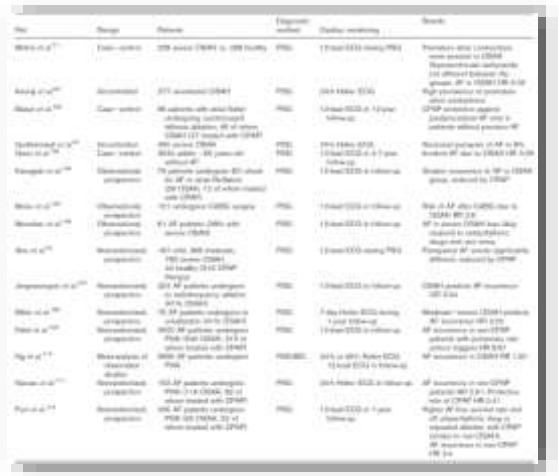
Guilleminault et al. *Am J Cardiol.* 1983

ATRIAL FIBRILLATION | Mechanisms

- **Vagal Tone**
- **Pro-inflammatory state**
- **Co-Morbidities**
- **↑ LA & LV masses**

ATRIAL FIBRILLATION | Associations



ATRIAL FIBRILLATION | Associations

Guilleminault *et al*[91]	Uncontrolled	400 severe OSAH	PSG	24 h Holter ECG	Nocturnal paroxysm of AF = 8%
Gami *et al*[133]	Case–control	3642 adults < 65 years old without AF	PSG	12-lead ECG in 4.7-year follow-up	Incident AF due to OSAH HR 3.29

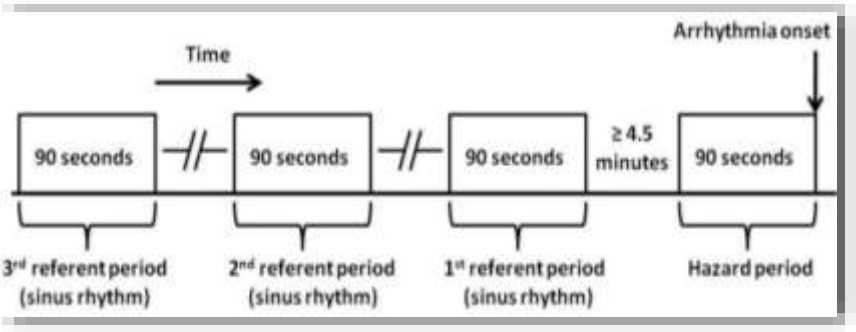
ATRIAL FIBRILLATION | Associations

Mooe *et al*[135]	Observational, prospective	121 undergone CABG surgery	PSG	12-lead ECG in follow-up	Risk of AF after CABG due to OSAH RR 3.8
Monahan *et al*[136]	Observational, prospective	61 AF patients (38% with severe OSAH)	PSG	12-lead ECG in follow-up	AF in severe OSAH less likely respond to antiarrhythmic drugs and vice versa

ATRIAL FIBRILLATION | Associations

Jongnarangsin et al.[111]	Nonrandomized, prospective	324 AF patients undergoing to radiofrequency ablation (41% OSAH)	PSG	12-lead ECG in follow-up	OSAH predicts AF recurrence OR 3.04
Bitter et al.[109]	Nonrandomized, prospective	75 AF patients undergoing to cryoablation (41% OSAH)	PSG	7-day Holter ECG during 1-year follow-up	Moderate–severe OSAH predicts AF recurrence HR 3.20

ATRIAL FIBRILLATION | Temporal Association



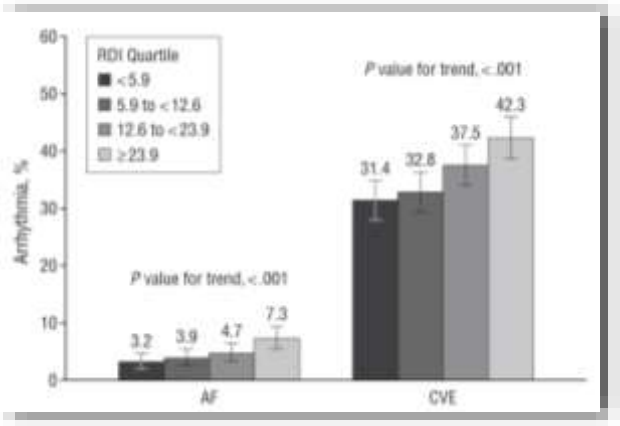
Monahan et al. *J Am Coll Cardiol.* 2009

ATRIAL FIBRILLATION | Temporal Association

		Number of arrhythmias included in each analysis	Odds Ratio (95% CI)
Primary Overall Analysis		62	17.5 (5.3–58.4)
Sub-Analyses			
By Arrhythmia type			
	PAF	15	17.9 (2.2–144.2)
	NSVT	47	17.4 (4.0–75.7)

Monahan et al. *J Am Coll Cardiol.* 2009

ATRIAL FIBRILLATION | Dose-Response



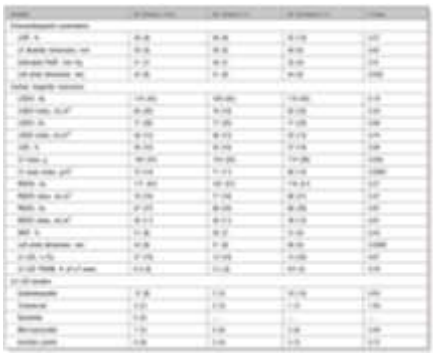
Mehra et al. *Arch Intern Med.* 2009

ATRIAL FIBRILLATION | Effect of Treatment

- ↓ Hypoxia-Related Vagal Activation
- ↓ Inflammation
- ↓ LV Mass and LA size

ATRIAL FIBRILLATION | Effect of Treatment

- ↓ LV Mass and LA size



Neilan et al. *J Am Heart Assoc.* 2013

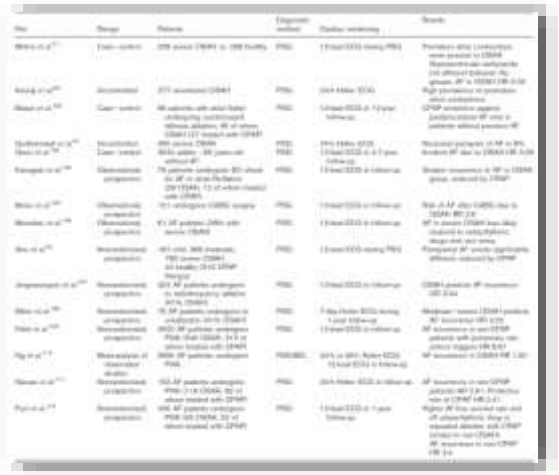
ATRIAL FIBRILLATION | Effect of Treatment

↓ LV Mass and LA size

LV mass, g	164 (34)	154 (29)	174 (36)	0.005
LV mass index, g/m^2	75 (14)	71 (11)	80 (14)	0.0002
RVEDV, mL	171 (44)	167 (37)	176 (51)	0.27
RVEDV index, mL/m^2	78 (18)	77 (16)	80 (21)	0.47
RVESV, mL	87 (27)	86 (24)	88 (29)	0.97
RVESV index, mL/m^2	40 (11)	40 (11)	39 (12)	0.67
RVEF, %	51 (8)	50 (7)	51 (8)	0.24
Left atrial dimension, mm	44 (6)	41 (6)	46 (8)	0.0008

Neilan et al. *J Am Heart Assoc.* 2013

ATRIAL FIBRILLATION | Effect of Treatment



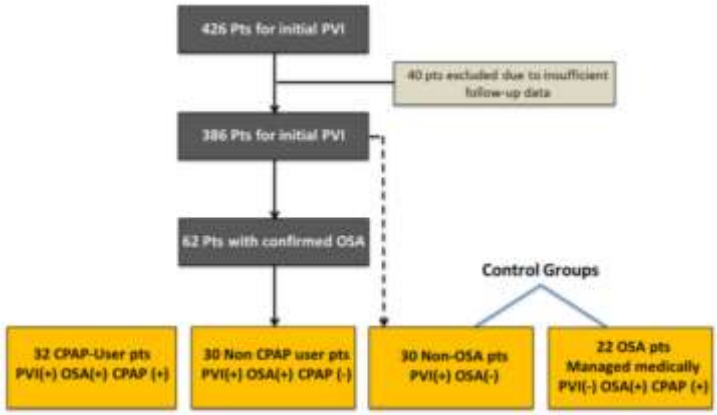
ATRIAL FIBRILLATION | Effect of Treatment

Kanagala *et al*[138]	Observational, prospective	79 patients undergone DC shock for AF or atrial fibrillation (39 OSAH, 12 of whom treated with CPAP)	PSG	12-lead ECG in follow-up	Greater recurrence of AF in OSAH group, reduced by CPAP

ATRIAL FIBRILLATION | Effect of Treatment

Jongnarangsin *et al*[137]	Nonrandomized, prospective	324 AF patients undergone to radiofrequency ablation (41% OSAH)	PSG	12-lead ECG in follow-up	OSAH predicts AF recurrence OR 3.04
Bitter *et al*[139]	Nonrandomized, prospective	75 AF patients undergone to cryoablation (41% OSAH)	PSG	7-day Holter ECG during 1-year follow-up	Moderate–severe OSAH predicts AF recurrence HR 3.20
Patel *et al*[136]	Nonrandomized, prospective	3000 AF patients undergone PVAI (840 OSAH, 315 of whom treated with CPAP)	PSG	12-lead ECG in follow-up	AF recurrence in non-CPAP patients with pulmonary vein antrum triggers HR 8.81

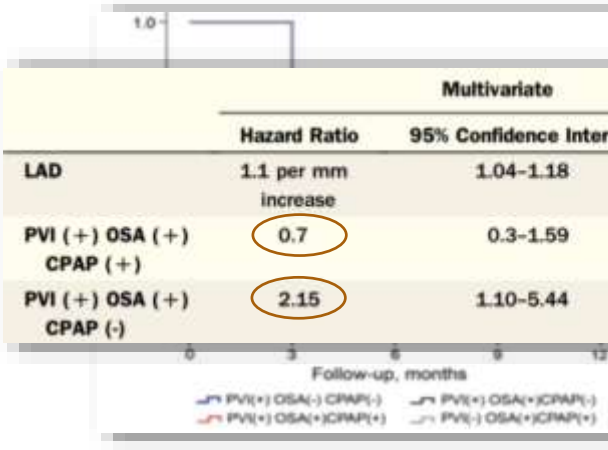
ATRIAL FIBRILLATION | Effect of Treatment



Fein et al. *J AM Coll Cardiol.* 2013

ATRIAL FIBRILLATION | Effect of Treatment

	Multivariate		
	Hazard Ratio	95% Confidence Interval	p Value
LAD	1.1 per mm increase	1.04–1.18	0.003
PVI (+) OSA (+) CPAP (+)	0.7	0.3–1.59	0.39
PVI (+) OSA (+) CPAP (-)	2.15	1.10–5.44	0.02



Fein et al. *J AM Coll Cardiol.* 2013

SCD | Mechanisms

Apneic Spells

High Vagal Tone

Hypertension

↑ Sympathetic Activation

Pro-inflammatory State

Pro-coagulant State

SCD | Mechanisms

Apneic Spells

High Vagal Tone

Hypertension

Sinus Arrest

High Grade AV Block

SCD | Mechanisms

Apneic Spells

High Vagal Tone

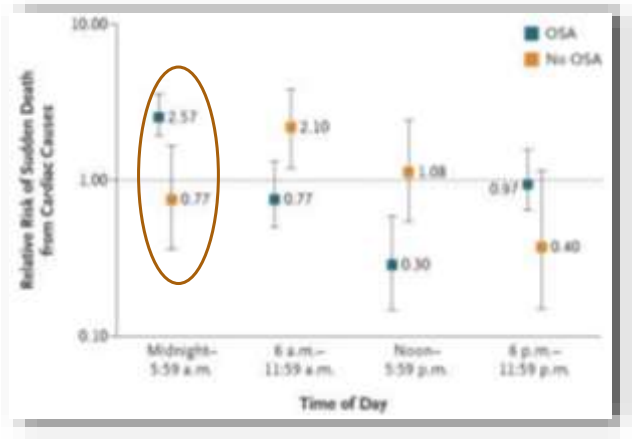
Hypertension

Concentric Hypertrophy

Myocardial Ischemia

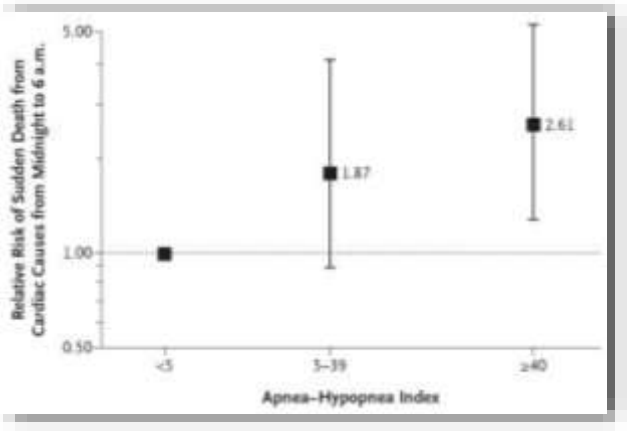
Fibrosis & Wall Stress

SCD | Associations



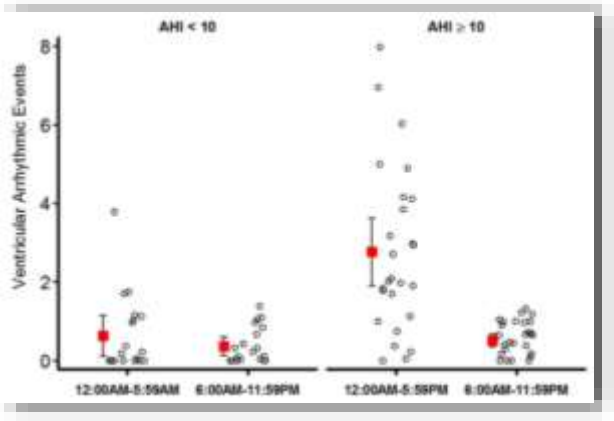
Gami et al. *N Eng J Med.* 2005

SCD | Associations



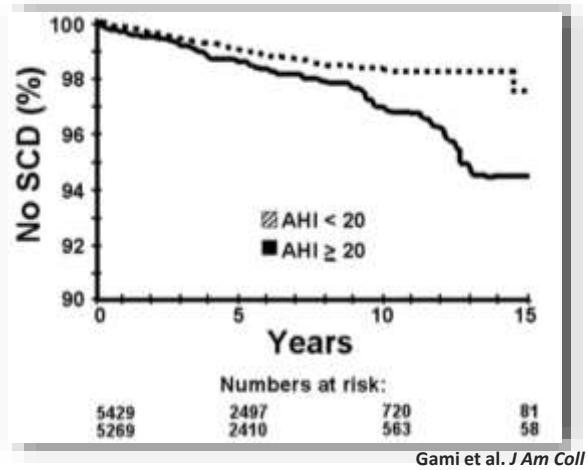
Gami et al. *N Eng J Med.* 2005

SCD | Temporal Association



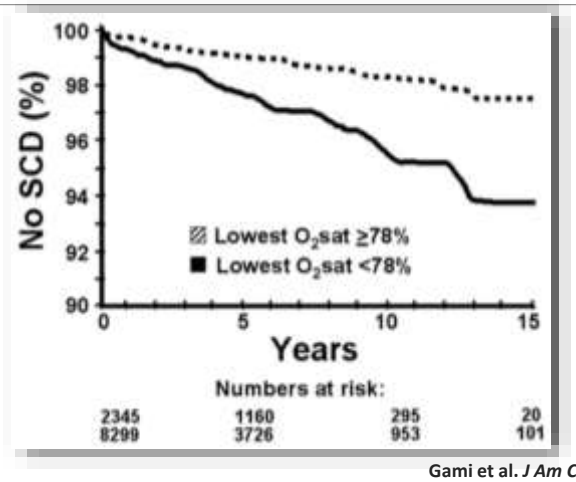
Zeidan-Shwiri et al. *Heart Rhythm.* 2011

SCD | Dose-Response Relation



Gami et al. *J Am Coll Cardiol.* 2013

SCD | Dose-Response Relation



Gami et al. *J Am Coll Cardiol.* 2013

SCD | Effect of Treatment

CLINICAL IMPLICATIONS | Screening

STOP Questionnaire

- Snoring
- Tiredness
- Observed you stop breathing
- Blood Pressure

BANG

- BMI >35
- Age >50
- Neck circumference >40 cm (>15.7")
- Gender male

High risk: Yes to ≥3 items → Refer for sleep testing

CLINICAL IMPLICATIONS | SCD & Brady

Recommendations	Class[a]	Level[b]
Sleep apnoea syndrome should be considered in the differential diagnosis of bradyarrhythmias.	IIa	B
The presence of sleep apnoea and reduced oxygen saturation may be considered as a risk factor for SCD in subjects with sleep disordered breathing.	IIb	C

CLINICAL IMPLICATIONS | Atrial Fibrillation

Recommendations	Class[a]	Level[b]
Correction of hypoxaemia and acidosis should be considered as initial management for patients who develop AF during an acute pulmonary illness or exacerbation of chronic pulmonary disease.	IIa	C
Interrogation for clinical signs of obstructive sleep apnoea should be considered in all AF patients.	IIa	B
Obstructive sleep apnoea treatment should be optimized to reduce AF recurrences and improve AF treatment results.	IIa	B


Thank
you


ANY
QUESTIONS
?