Sorin Group Satellite Symposium

Advances in cardiac pacing and arrhythmia management

Chairmen: M.G. Bongiorni / Pisa, Italy – H. Burri / Geneva, Switzerland

Long-lasting ECG monitoring for syncope and palpitations, what else?
E. Locati / Milan, Italy

Multidisciplinary approach for sleep apnea syndrome in paced patients
A. Capucci / Ancona, Italy

20 years in CRT therapy: what’s more?
R. Mantovan / Cesena, Italy

Relevance of ICD longevity in clinical practice
L. Calò / Rome, Italy

Strategies to reduce inappropriate shocks: which options?
S. Reif / Munich, Germany
Multidisciplinary approach for Sleep Apnea Syndrome in paced patients

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NO CONFLICT OF INTEREST TO DECLARE
Apnea and Hypopnea

• Apneic episodes are defined by complete cessation of airflow for $\geq 10$ s

• Hypopnea episodes are characterized by either $\geq 30\%$ reduction in airflow and $\geq 4\%$ reduction in blood oxygen saturation from baseline for at least 10 s or $50\%$ reduction in airflow and $\geq 3\%$ reduction in oxygen saturation from baseline for at least 10 s or arousal from sleep

• AHI: n° of apneas and hypopnea per hour of total sleep

• Sleep Apnea Syndrome (SAS): $\text{AHI} > 5$ with symptoms

*American Academy of Sleep Medicine Task Force (Sleep 1999; 22: 667-689)*
Symptoms of OSA

**DAY TIME:**

- Early morning headaches,
- Fatigue, Daytime sleepiness,
- Poor memory,
- concentration or motivation,
- Unproductive at work,
- Falling asleep driving,
- Depression

**NIGHT TIME:**

- Frequent nocturnal awakenings, Waking up choking or gasping for air,
- Restless sleep, nocturia, Unrefreshed sleep,
- decreased libido, Loud snoring, Witnessed apnoea
- reported by bed partner

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*Patil SP, Schneider H & al. CHEST 2007;132:325-37*
Two main categories of SAS

1. Obstructive Sleep Apnea (OSA)
   - Most common form of SAS
   - More than 90% of SAS patients
   - Obstruction of upper airway despite increased ventilatory effort

2. Cheyne-Stokes Respiration (CSR) and Central Sleep Apnea (CSA)
   - More prevalent in some patient groups
   - Less than 10% of SAS patients
   - Absence of brain signal to the muscle to breathe
Sleep apnea and comorbidities correlations

Sleep apnea is a systemic disease. It is not a local disease.
Managing SAS is important for cardiovascular co-morbidities

- The risk of HF is 58% higher in severe Sleep Apnea patients

- The risk of AF is 4 times higher in Sleep Apnea patients

- Sleep Apnea patients show resistance to pharmacological treatment

- More recurrence of AF after AF ablation and cardioversion

- The severity of Sleep Apnea is an independent predictor of mortality

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[References]
CSA increases risk of HF patient readmissions

More than 50% of HF patients with CSA were readmitted at 6 months

Almost 25% of HF patients with CSA had 2 or more readmissions within 6 months

As a consequence CSA monitoring can be very useful for HF monitoring

Screening and Diagnosing Sleep Apnea

**Polysomnography (PSG):** gold standard for the diagnosis of SDB

- Using multiple channels to record sleep quality, disturbances of breathing and oxygen desaturation during sleep

- Assessment of the severity of sleep apnea measuring AHI (apnea/hypopnea index)

**BUT**....

- Limited number of sleep laboratories available/waiting list

- Need specific training, laborious task, high costs

- Expensive & time-consuming
SAS Treatment

Treatment of OSA by CPAP virtually eliminates the increased risk for Cardiovascular Events

CRT improves cardiac function and CSA


Sleep Apnea is highly prevalent... in general population

**OSA prevalence** = 2 – 4 % of US adult population
- Risk factors double for men
- increases with age and is at least 20% in patients over 65 years old
- Increased with BMI and is 3-fold higher in high BMI than in low BMI

**CSA prevalence**: less than 1% in adult population.
- Higher in population subsets: CSB-CSA has been reported in 25-50% of patients with heart failure and in 10% of patients who have had a stroke

1. Young T, Palta M (Wisconsin, US), NEJM 1993 Apr, Vol 328 Nr 17
Sleep Apnea is highly prevalent... 
*in paced patients*

11 European centers
n = 98 patients

Bradycardia
67±6 years
BMI 27±4

Bradycardia
37%

Heart failure
62±6 years
BMI 26±6

Heart failure
24%

AV Block
68±10 years
BMI 26±4

AV Block
35%

1 out of 4 SND or AVB patients suffers from severe SAS

<table>
<thead>
<tr>
<th>Variables</th>
<th>AV Block n=36</th>
<th>Brady n=31</th>
<th>HF n=21</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 ≥ AHI &lt; 30</td>
<td>41%</td>
<td>31%</td>
<td>45%</td>
</tr>
<tr>
<td>AHI ≥ 30</td>
<td>27%</td>
<td>27%</td>
<td>05%</td>
</tr>
<tr>
<td>Total</td>
<td>63%</td>
<td>58%</td>
<td>50%</td>
</tr>
</tbody>
</table>

| | Obstructive apnea | Central apnea | Hypopnea |
| | 15±19% | 07±09 % | 78±19 % |
| | 13±17 | 08±07 | 79±17 |
| | % | % | % |

| | 19±23 | 08±12 | 73±25 |
| | % | % | % |

80% of patients with moderate to severe Obstructive sleep Apnea (OSA) are underdiagnosed\(^1\)

CSA is “silent” for patients with multiple comorbidities (in particular diabetes & HF patients)\(^2\)

50% to 90% of patients are undiagnosed and therefore untreated\(^1\)

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Fast Track Publication

Estimation of the Clinically Diagnosed Proportion of Sleep Apnea Syndrome in Middle-aged Men and Women

Terry Young, Linda Evans, Laurel Finn and Mari Palta

Sleep and Respiration Research Group, Department of Preventive Medicine, University of Wisconsin-Madison, Madison, Wisconsin, U.S.A.

Summary: The proportion of sleep apnea syndrome (SAS) in the general adult population that goes undiagnosed was estimated from a sample of 4,925 employed adults. Questionnaire data on doctor-diagnosed sleep apnea were followed up to ascertain the prevalence of undiagnosed sleep apnea. In-laboratory polysomnography on a subset of 1,090 participants was used to estimate screen-detected sleep apnea. In this population, without obvious barriers to healthcare for sleep disorders, we estimate that 93% of women and 82% of men with moderate to severe SAS have not been clinically diagnosed. These findings provide a baseline for assessing healthcare resource needs for sleep apnea. Key Words: Sleep apnea—Epidemiology—Sleep disorders—Prevalence.
SAS is a common clinical problem in patients with implantable cardiac devices

- High prevalence pathology among pacemaker patient, under-diagnosed, with heavy cardiovascular (CV) consequences
- Costly therapies are less efficient on untreated Sleep Apnea patients
- Diagnostic methods expensive and time-consuming
- SAS therapy effective on symptoms, and on reduction of CV morbi-mortality

Problem: how to diagnose SAS at CV-care level?
Which effective and “easy to use” screening tools are today available for cardiologists?
Reliability of SA screening tool: the “DREAM” study

Main objective: to validate a transthoracic impedance signal with advanced algorithm (Sleep Apnea Monitoring) for identifying severe SA in an unselected patient population with indication for permanent cardiac pacing.
... SAS screening by the Pacemaker

Transthoracic impedance measurement

\[ Z_{th} (\Omega) = \frac{dV (V)}{I (A)} \]

- \( Z_{th} \) is the transthoracic impedance
- \( I \) is the value of a fixed current injected between the can and the distal atrial electrode
- \( dV \) is the voltage measured between the can and the proximal atrial electrode

Calculation of MV signal

\[ VM (\Omega \cdot s^{-1}) = \frac{Z_{th} (\Omega)}{\text{Time period (s)}} \]
SAM (Sleep Apnea Monitoring)

A specific software dedicated to automatically identify apneas and hypopneas, to make an automatic screening of pacemaker patients (SR, DR or CRT) for the risk of severe Sleep Apnea

- **Definition of **RDI (Respiratory Disturbance index):

  \[ \text{RDI} \text{ defines the severity of Sleep Apnea} \]

\[ \text{Number of Ventilation Pauses & Reductions} \]
\[ \text{Number of Hours of Monitoring} \]
**Apnea / Hypopnea detection**

**PSG recording and PMK transthoracic impedance signal**

**A:** 2 apnea events concurrent reduction of the amplitude of the thoracic impedance signal from the PMK

**B:** 3 hypopnea events simultaneous reduction of the amplitude of the thoracic impedance signal from the PMK
DREAM study\textsuperscript{1}: SAM-RDI vs PSG-AHI

- SAM-RDI is correlated with gold standard Apnea-Hypopnea Index (AHI-PSG)
- An optimal cutoff of 20 events/h for the SAM-RDI value was validated to identify severe SA (AHI-PSG > 30) with a sensitivity of 88.9\%, a PPV of 88.9\%, and a specificity of 84.6\%.

\begin{itemize}
  \item [No or mild SAS] \hspace{1cm} [Moderate SAS] \hspace{1cm} [Severe SAS]
  \item [1. Defaye P, J & al. Heart Rhythm 2014]\
\end{itemize}
Reliability of SA screening tool: the “DREAM” Study
Main findings and conclusions

- Prevalence of SA in the DREAM study unselected pacemaker population (evaluated by PSG-AHI)
  - 78% moderate to severe SA
  - 56% severe SA

- An optimal cut-off of 20 events/hour for SAM-RDI value was validated to identify severe SA with
  - 88.9% Sensitivity – 88.9% PPV
  - 84.6% Specificity

The DREAM study showed that a transthoracic impedance sensor with an advanced algorithm (SAM) could be used to identify severe SA in PMK patients
SAM: Not only screening but also monitoring
Clinical case showing the practical use of the screening detection of the cardiac device
Clinical Case

Introduction

• Male, 57 yr old
• Ischemic Cardiomyopathy
• Indication: High degree AVB
• No known SAS
• No AF
• Hypertension/Dyslipidemia

▸ Dual-chamber PM *(REPLY 200 DR)* implanted Sep 12\(^{\text{th}}\), 2013
  
  FU at 1 month: October 23\(^{\text{rd}}\) 2013
  
  FU at 4 month: January 11\(^{\text{th}}\) 2014

By courtesy of Dr. J. Martí Almor – Hospital del Mar, Barcelona (Sp)
FU – 4 weeks - October 23rd 2013

Severe SAS suspected by PM diagnostics

Automatic alerts on Programmer screen when patients are at risk of severe SAS
Early screening for severe sleep apnea

Overnight respiratory polygraphy results

- Severe OSAS
- **AH Index = 55.6/hour**
- 254 Apnea events and 137 Hypopnea events
- Apnea events: average = 17.2s, longest = 29s

→ REPLY 200 diagnostics confirmed
RDI since implant

The night after night measurements after implantation help to monitor and understand the evolution of severe SA, together with different therapeutic interventions

• CPAP treatment started just after previous FU
• Over the first month, the RDI decreases with CPAP treatment
• Over the next 3 weeks, the RDI increases again: there was a leak on the mask?!!
• To be continued....

By courtesy of Dr. J. Martí Almor – Hospital del Mar, Barcelona (Sp)
Correlation between the patient's disturbed respiratory events and nocturnal AVB

SAM is a valuable diagnostic tool for monitoring patient clinical status

Before CPAP treatment

Nocturnal AVB confirmed
Apneic patients treated by pneumologists…

… many of them are similar to patients treated by cardiologists!
Paced Patient Management
Multidisciplinary approach

Pacemaker patients
Sleep Apnea patients

Electrophysiology Cardiology

Pneumology Neurology Sleep Centers

Poor collaboration in managing SA / Heart diseases & co-morbidities
Paced Patient Management Multidisciplinary approach

Conditions to activate a Multidisciplinary Approach:
• Reliable SA screening tool
• Patients’ compliance
• Cardiology / Pneumology reciprocal commitment

Electrophysiology Cardiology
SA screening of undiagnosed patients
SA therapy impact on cardiovascular comorbidity
Long-term monitoring of applied SA therapies

Pneumology Neurology Sleep Centers
potential mutual benefits
Towards a new clinical management model ...

Moving from these premises and keeping in mind the strict interactions between heart and sleep a group of clinical researchers, began to work about an idea:

a) To develop a “Clinical Management Model” dedicated to diagnose / treat paced patients virtually affected by Sleep Apnea

b) To improve multidisciplinary collaboration [ Cardiologist ↔ Lung Specialist / Neurologist ]

In order to realize these aims, a Multicenter Prospective Observational Registry (“UPSTREAM”) was conceived, to follow-up PMK patients (devices featuring Sleep Apnea screening tools) with a Systematic Multidisciplinary Approach involving Cardiologist/Lung Specialists (and/or Neurologist)
The basic idea of the “Multidisciplinary Approach”

“Heart Center” Tasks
- Pacemaker implant
- PM/patient follow-up
- CV assessment

“Sleep Center” Tasks
- Sleep Apnea diagnosis
- SA treatment evaluation
- SA therapy adjustment

Clinical info (SA pacemaker index)
- Sleep Apnea screening
- SA therapy monitoring

Clinical info
- Sleep Apnea patient profile
- SA therapy decision

To assess the CLINICAL IMPACT of this Multidisciplinary Approach, a protocol was developed for a Multicenter Prospective Observational Registry (UPSTREAM), to follow-up PMK patients clinical outcomes
UPSTREAM Registry: Flowchart

Pacemaker implant SR/DR/CRT (Guidelines), including device replacements (AV node ablated pts excluded)

Patient inclusion period: within 2 months following the implant procedure

During 1st year of FU, the protocol suggests a PGF performed by the reference Sleep-Center (Pneumology/Neurology)

The Sleep-Center will evaluate the need for SA therapy (i.e. CPAP)

Analysis of PGF outcomes (Core Lab) to assess Sensitivity, Specificity, NPV / PPV of Pacemaker index vs PGF (secondary objective)
UPSTREAM Registry: Primary Objectives

**Primary Clinical objective**
Impact of Multidisciplinary Approach on MACE* endpoint (Major Adverse Cardiov. Events)
VS standard paced patient management (ANSWER study cohort, n = 320 DC-PM pts)

**Primary Clinical objective**
Pilot assessment of Multidisciplinary Approach impact on MACE endpoint

**Study size**
510 pts [ 2-4 yrs FU ]

- Subgroup 1 Dual Chamber pacemaker (# 355 pts)
- Subgroup 2 Single Chamber pacemaker (# 125 pts)
- Subgroup 3 CRTP (# 30 pts)

* MACE (Major Adverse Cardiovascular Events)
  - all-cause mortality
  - CV mortality
  - HF events
  - urgent visits for Arrhythmia Cardioversions (A/V), coronary ischemia, or stroke;
  - recurrence of Atrial Arrhythmias after electrical / pharmacological cardioversion
UPSTREAM Registry: Secondary Objectives

**Study size**
510 pts [2-4 yrs FU]

- **Subgroup 1**
  Dual Chamber pacemaker (# 355 pts)

- **Subgroup 2**
  Single Chamber pacemaker (# 125 pts)

- **Subgroup 3**
  CRTP (# 30 pts)

**RDI pacemaker index vs PGF outcomes**
Evaluation of PM-index Sensitivity, Specificity, NPP, PPV compared with SA diagnostic gold standards (PGF) (Pneumology Core-Lab)

**Adverse Events**

**Cardiovascular Therapy changes**

(for DC pacemaker pts): *Resource consumption & Multidisciplinary Approach cost/effectiveness*
(vs standar approach; ANSWER study cohort)

(for DC pacemaker & CRTP pts): *AF burden*
Tot time in AF (pacemaker diagnostics) and SA therapy impact on AF burden
Each investigator created a link with a referential lung specialist/neurologist, and a reciprocal commitment has been established to manage paced patient virtually affected by Sleep Apnea.
Conclusions

• There is an extremely high prevalence of undiagnosed SAS in paced patients.

• SAS should be sistematically searched to avoid additional detrimental effectcs on cardiovascular condition of these patients.

• A specific and advanced algorithm (SAM) included in a new generation of pacemakers has been found able to identify paced patients with SAS, with an excellent correlation with classical PSG.

• The feasibility of a new model of managing paced patients with SAS has also been demonstrated.

• On the strenght of these considerations, the observational registry «UPSTREAM» was conceived, with the aim of developing a multidisciplinary approach for the diagnosis and treatment of paced patients potentially affected by SAS.
Thank you for your attention