Sleep Disorders in Patients with Chronic Kidney Disease

Marta Novak
Semmelweis University, Budapest, Hungary
University of Toronto, Canada
• Sleep – significance

• The most frequent sleep problems in CKD patients
• Restless legs syndrome (RLS)/Periodic limb movements in sleep (PLMS)
• Sleep disordered breathing - Obstructive sleep apnea syndrome (OSAS)
Why do we sleep?

Evolutionary theory, energy conservation

Repair and Restoration Theory
s leep enables the body and brain to repair after activity during the day – homeostatic balance
– memory
– Sleep deprivation leads to irritability, impaired concentration and hallucinations
– Sleep need is individual
Sleep disorders

• Sleep deprivation

• Individual consequences, quality of life

• Socio-economical consequences, health care utilization, accidents etc.
Consequences of Chronic Sleep Deprivation

Sleep is a vital and necessary function, and sleep needs (like hunger and thirst) must be met.
Sleepiness in residents is equivalent to that found in patients with serious sleep disorders. Mustafa and Strohl, unpublished data. Papp, 2002
Adverse Health Consequences by Average Daily Hours of Sleep*

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*Baldwin and Daugherty, 1998-9 Survey of 3604 PGY1,2 Residents

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Sleep and the Immune System

- Sleep deprivation is correlated with a significant reduction in cellular immunity
- Can cause reductions in NK cells, T-cells, and monocyte function
- Men with just four hours of sleep a night for four straight nights after receiving a flu shot produced half the antibodies as the control group (Weintraub, 2004)
Cytokines and sleep
Sleep and the Cardiovascular System

- Sleep deprivation increases concentrations of cytokines and C-reactive protein.
- This inflammation can lead to endothelial damage, leading to possible stroke or heart disease.
- Blood pressure and heart rate are higher following sleep deprived nights. (Voelker, 1999)
- Sleep deprivation increases risk of heart disease in women. (Josefson, 2003)
OSAS

Mediating processes

- Hypoxia
- Hypercapnia
- Change in the Intrathoracal pressure
- Micro-arrousals

Sympathetic nervous system activity
Endothelial dysfunction
Oxidative stress
Inflammation
Hypercoagulability

Modifying factors

- Hypertension
- Heart failure
- Arrhytmias
- CAD
- Cerebrovascular disease
- Obesity
- Gender
- Age
- Metabolic syndrome
- Smoking
- Medications

Mediating processes

- Hypertension
- Heart failure
- Arrhytmias
- CAD
- Cerebrovascular disease

Modifying factors

- Obesity
- Gender
- Age
- Metabolic syndrome
- Smoking
- Medications
Snoring and cardiovascular disease (n=12600) (Hungarostudy 2002)

**Stroke**
- men: p<0.01
- women: p<0.01

**AMI**
- men: p<0.0001
- women: p<0.005
Sleep disorders in CKD – why is it important?

- Sleep problems are one of the most common complaints of patients in the dialysis unit
- Sleep Apnea Syndrome (SAS) may contribute to the pathogenesis of hypertension, CV morbidity
- Sleep disorders may impair quality of life
- Poor sleep have been shown to be a predictor of morbidity and mortality in this patient population
- Sleep disorders are treatable – successful treatment may improve clinical outcomes
Sleep disorders in dialysis patients (30-80%)

- Insomnia
  - 4-29% vs 15-70%
- Sleep apnea syndrome (SAS)
  - 2-4% vs 20-80%
- Restless legs syndrome (RLS)
  - 5-15% vs 15-80%

Little is known about sleep problems in „predialysis” and transplanted patients
Factors contributing to sleep disturbances in patients on dialysis

Diagnostic tools to detect sleep problems

- Sleep diary
- Self-administered questionnaires
  - Insomnia: Pittsburgh Sleep Quality Index, Athen Insomnia Scale
  - SAS: Berlin Questionnaire
  - RLS: Restless Legs Syndrome Questionnaire
  - Epworth Sleepiness Scale
- Clinical interview
- Actigraphy
- Polysomnography (SAS, PLMS)
  - MSLT, MWT – daytime effects
Polysomnography

- neurophysiologic variables
- electrooculography, EEG, submental myogram – sleep stages
- Respiration
- ECG
- Limb movements
- Body position
- Video
Restless Legs Syndrome (RLS)

- Restless legs syndrome (RLS) is characterized by an urge to move the legs that is often hard to resist and is usually but not always associated with disagreeable leg sensations.
- Main symptoms:
  - 1. An urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs.
  - 2. The unpleasant sensations begin or worsen during rest or inactivity.
  - 3. The unpleasant sensations are partially or totally relieved by movement.
  - 4. The unpleasant sensations are worse in the evening or night than during the day or only occur in the evening or night.
## Restless Legs Syndrome

### Predictors, etiology
- Altered CNS dopamin metabolism
- Iron deficiency (cerebral versus peripheral)
- Uremia – uremic toxins?
- Anemia
- Neuropathy

### Consequences
- Fragmented sleep, „intitiation” insomnia
- Fatigue, tiredness
- Daytime sleepiness
- Impaired QoL
- Incr. mortality?
• Prevalence of RLS: 12-20% in dialysed\textsuperscript{1,2} and 4.5% in kidney transplanted populations\textsuperscript{3}

• RLS is associated with increased risk of

• insomnia and impaired quality of life (QoL) in dialysed patients\textsuperscript{4}

• There is no data regarding the association of RLS, poor sleep and QoL after renal transplantation

\textsuperscript{1} Winkelman et al. (1995)
\textsuperscript{2} Mucsi et al. (2004)
\textsuperscript{3} Molnar et al. (2005)
\textsuperscript{4} Unruh et al. (2004)
RLS in dialysis patients predicts mortality

Table 3. Adjusted Hazards of Severe Symptoms of Restless Legs and by Category of Restless Legs Symptom

<table>
<thead>
<tr>
<th></th>
<th>Severe Restless Legs Symptoms</th>
<th>Category of Restless Legs Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted hazard</td>
<td>1.31 (1.00-1.73)</td>
<td>1.06 (0.97-1.15)</td>
</tr>
<tr>
<td>Model 1, adjusted for age and race</td>
<td>1.42 (1.07-1.97)</td>
<td>1.07 (0.98-1.16)</td>
</tr>
<tr>
<td>Model 2, model 1 and adjusted for ICD, Karnofsky</td>
<td>1.39 (1.05-1.84)</td>
<td>1.06 (0.98-1.16)</td>
</tr>
<tr>
<td>Model 3, model 2 adjusted for clustering of clinics</td>
<td>1.30 (1.08-1.79)</td>
<td>1.06 (0.98-1.16)</td>
</tr>
</tbody>
</table>

Adjusted Differences in Quality of Life by Restless Legs Symptoms

Fig 2. Crude cumulative mortality according to severe symptoms of restless legs.

Unruh et al; AJKD; 2004
Restless legs syndrome, insomnia and quality of life in patients on maintenance dialysis

Istvan Mucić1−3, Miklos Zsolt Molnar1,2,4, Csaba Ambrus2,4, Lilla Szeifert1, Agnes Zsofia Kovacs1, Rezső Zoller1, Szabolcs Barótfi1, Adam Remport5 and Marta Novak1,6

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Prevalence of sleep disorders in Hungarian dialysis and transplanted patients

* Transplanted
Wait-listed

*: P<0.001, Khi-square test
Restless Legs Syndrome in Patients After Renal Transplantation

Miklos Zsolt Molnar, MD, Marta Novak, MD, Csaba Ambrus, MD, Lilla Szeifert, Agnes Kovacs, Judit Pap, Adam Remport, MD, and Istvan Mucsi, MD, PhD

Table 2. Characteristics of Patients With or Without RLS in the Tx Group

<table>
<thead>
<tr>
<th></th>
<th>RLS (n = 39)</th>
<th>No RLS (n = 777)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>51 ± 11</td>
<td>48 ± 13</td>
<td>NS</td>
</tr>
<tr>
<td>Male</td>
<td>59</td>
<td>59</td>
<td>NS</td>
</tr>
<tr>
<td>eGFR (mL/min)</td>
<td>42 ± 19</td>
<td>50 ± 23</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Number of comorbid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>conditions, median (range)</td>
<td>3 (0-7)</td>
<td>2 (0-7)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Immunosuppressive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>drugs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steroids</td>
<td>74</td>
<td>87</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Cyclosporin A</td>
<td>77</td>
<td>69</td>
<td>NS</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>18</td>
<td>18</td>
<td>NS</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>56</td>
<td>64</td>
<td>NS</td>
</tr>
<tr>
<td>Imuran</td>
<td>13</td>
<td>12</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes</td>
<td>11</td>
<td>17</td>
<td>NS</td>
</tr>
<tr>
<td>Serum albumin (g/dL)</td>
<td>4.08 ± 0.37</td>
<td>4.16 ± 0.33</td>
<td>NS</td>
</tr>
<tr>
<td>Serum phosphorus (mg/dL)</td>
<td>3.4 ± 1.3</td>
<td>3.4 ± 0.8</td>
<td>NS</td>
</tr>
<tr>
<td>Serum Hb (g/dL)</td>
<td>12.7 ± 2.0</td>
<td>13.3 ± 1.9</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Serum transferrin</td>
<td>243 ± 52</td>
<td>247 ± 52</td>
<td>NS</td>
</tr>
<tr>
<td>Iron deficiency TSAT &lt;20%</td>
<td>26</td>
<td>11</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Time since transplantation (mo)</td>
<td>69 ± 53</td>
<td>58 ± 45</td>
<td>NS</td>
</tr>
</tbody>
</table>

RLS and Overall Sleep Quality

Proportion of patients with RLS (%)

Tertiles of Athens score

M. Zs. Molnar et al. (in press, JPR)

Restless Legs Syndrome, Insomnia and Quality of Life after Renal Transplantation
SF-36 QoL Scores with and without RLS*

M. Zs. Molnar et al. (in press, JPR)
Restless legs syndrome is associated with mortality in kidney transplanted patients

M. Zs. Molnar et al. (AJKD 2007)
Restless legs syndrome is associated with mortality in kidney transplanted patients

Multivariate Cox-model

<table>
<thead>
<tr>
<th>Presence of RLS</th>
<th>HR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>1.03-3.95</td>
<td>0.04</td>
<td></td>
</tr>
</tbody>
</table>

Adjusted for: age, gender, eGFR, albumin, hemoglobin, CRP, diabetes, hypertonia and transplant vintage

M. Zs. Molnar et al. (AJKD 2007)
Periodic limb movements in sleep

Overlap with RLS

Regular leg movements during sleep

Sleep fragmentation

Hypersomnia

Predictor of mortality in dialysis patients (Benz et al; AJKD; 2000)
Clinical management of RLS in CKD

- Adequate dialysis/ renal transplantation
- Iv iron/ anemia management (Dose?)
- Drugs
  - Ropirinole, pramipexole, carbidopa/levodopa, Pergolide – side eff., safety??
  - Benzodiazepines - efficacy??
  - Gabapentin, carbamazepine – efficacy??
Sleep apnea syndrome

- intermittent episodes of breathing cessation during sleep,
  - airway collapse (obstructive sleep apnoea, OSA)
  - cessation of respiratory effort (central SA)
  - or both (mixed SA)

- The severity of the SAS is usually characterized by the number of apneic events per hour of sleep (AHI, RDI) (RDI>5 is considered pathological), severity of desaturation and by the presence and severity of daytime sleepiness.

- SAS is associated with disturbances of sleep initiation and maintenance as well as daytime sleepiness.

- A potential link is suggested between SAS and HTN, CAD, CHF and arrhythmias
OSAS

- Upper airway obstruction
- Anatomical problems
- Decreased muscle tone ↓
  + weakness of pharyngeal wall

\[ \text{Dynamic collapse during inspiration} \]
Apnea leads to micro-arousals and fragmented sleep
Clinical features of sleep apnea

- Snoring and daytime sleepiness
- Non-restorative sleep and other sleep-related symptoms
- Daytime consequences: daytime sleepiness, tiredness, headaches, naps, neuropsych symptoms
- Medical consequences: cardiovasc, sex, diab.
Sleep Apnoe Syndrome

Predictors, correlates

- Age
- Obesitas (BMI, neck circumference)
- Male gender/menopause
- Alcohol
- Uremic toxins?
- Anemia
- Altered metabolic state

Consequences

- Daytime sleepiness
- Accidents
- Cognitive impairment
- Depression
- Sexual dysfunction
- Hypertension, LVH, CAD, arrhythmias
- Impaired QoL
- Increased morbidity, mortality?
CKD specific factors potentially contributing to the pathogenesis of SAS

- Hypocapnia, acid-base disorders
- Uremic toxins – effects on CNS
- Soft tissue edema
- Anemia
- Endocrine problems (menopause – gender difference)
- Dialysis modality (HD-cytokines, type of PD)
Sleep-Disordered Breathing in Nondialyzed Patients with Chronic Renal Failure

Nikolaos Markou · Maria Kanakaki · Pavlos Myrianthefs · Dimitrios Hadjiyanakos · Dimosthenis Vlassopoulos · Anastasios Damianos · Konstantinos Siamopoulos · Miltiadis Vasiliou · Stavros Konstantopoulos

Sleep Apnea in Patients on Conventional Thrice-Weekly Hemodialysis: Comparison with Matched Controls from the Sleep Heart Health Study

Mark L. Unruh,* Mark H. Sanders,† Susan Redline,‡ Beth M. Piraino,* Jason G. Umans,§ Terese C. Hammond,‖ Imran Sharief,¶ Naresh M. Punjabi,** and Anne B. Newman††

<table>
<thead>
<tr>
<th>Variable</th>
<th>HD Population (n = 46)</th>
<th>Matched Controls (n = 137)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep time (min)</td>
<td>319.5 ± 106.3</td>
<td>378.9 ± 67.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sleep efficiency (sleep time/total time in bed)</td>
<td>78.1 ± 15.3</td>
<td>81.3 ± 10.4</td>
<td>NS</td>
</tr>
<tr>
<td>Stage 1 sleep (%)</td>
<td>5.0 ± 3.4</td>
<td>5.5 ± 3.65</td>
<td>NS</td>
</tr>
<tr>
<td>Stage 2 sleep (%)</td>
<td>57.6 ± 14.3</td>
<td>58.4 ± 11.5</td>
<td>NS</td>
</tr>
<tr>
<td>Stage 3 to 4 sleep (%)</td>
<td>23.4 ± 12.2</td>
<td>14.3 ± 10.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>REM sleep (%)</td>
<td>13.6 ± 8.2</td>
<td>21.7 ± 6.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Arousal index (arousals/h)</td>
<td>25.1 ± 14.6</td>
<td>17.1 ± 8.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Respiratory disturbance index</td>
<td>27.2 ± 19.3</td>
<td>15.2 ± 14.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypoxemic index</td>
<td>7.2 ± 20.8</td>
<td>1.84 ± 8.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lowest oxygen saturation, NREM</td>
<td>83.6 ± 7.1</td>
<td>86.7 ± 5.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Lowest oxygen saturation, REM</td>
<td>81.2 ± 9.7</td>
<td>85.9 ± 6.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Epworth Sleepiness Scale</td>
<td>9.0 ± 4.7</td>
<td>8.0 ± 4.3</td>
<td>NS</td>
</tr>
</tbody>
</table>
SAS - HTN


SAS - LVH

SAS and quality of life in dialysis patients

(A)

Social Functioning

(B)

Emotional Reactions

Sanner et al.: NDT, 2002
Clinical management of SAS in CKD

• Weight loss life style changes
• CPAP
  – Long term effects?
  – Compliance?
• Oral devices, Sx
• Transplantation?
• Intensified dialysis

photo courtesy of the American Sleep Apnea Association
SAS and Nocturnal Home Hemodialysis

Alleviation of Sleep Apnea in Patients with Chronic Renal Failure by Nocturnal Cycler-Assisted Peritoneal Dialysis Compared with Conventional Continuous Ambulatory Peritoneal Dialysis

Sydney C.W. Tang,†† Bing Lam,† Pui Pui Ku,‡ Wah Shing Leung,§ Chung Ming Chu,§ Yiu Wing Ho,‡ Mary S.M. Ip,‡ and Kar Neng Lai*
Prevalence of sleep disorders in Hungarian dialysis and transplanted patients

* *:

*: P<0.001, Khi-square test
High risk of OSAS and renal function in Tx patients

Molnar et al: NDT 2007
Outcome during 4 years

High risk of OSAS
- Living with graft: 74%
- Died: 16%
- Living on dial: 10%

Low risk of OSAS
- Living with graft: 83%
- Died: 10%
- Living on dial: 7%
High risk of OSAS and graft failure

Graft survival

Cumulative survival

Follow up (months)
Insomnia

- Difficulties falling or staying asleep, poor sleep quality, short sleep duration
- Multi-causal
- Lifestyle important
- Role of psychological disturbances (anxiety, depression)
- Depression – early morning awakening
- Other sleep disturbances?
Treatment of insomnia

- Sleep hygiene, lifestyle
- Combined approach
- Pharmacotherapy
- Non-pharmacological treatment: psychotherapy, relaxation, cognitive-behavioral therapy, light therapy
Our research
• Sleep disorders in dialysis patients (n=78)
• Sleep disorders – HRQoL in the FMC Hungary network (n=cca 1000)
• Transqol-HU (WL – Tx): cross-sectional and prospective
• Hungarostudy 2002 (nationally representative survey)
• Sleep disorders – HRQoL in CKD patients (HRRH: 130 pts; DOPPS Canada; Budapest 340 pts)
• OSAS and hypertension in the family practice (Ontario: 60 pts; Hungary: recruiting)
• Malnutrition-inflammation complex syndrome, anemia, depression and sleep disorders in kidney transplanted patients (in progress: cca. 500 pts enrolled, 57 PSG)
HUNGAROSTUDY 2002

$N=12.643$

Cross-sectional survey enrolling a large, nationally representative sample of the Hungarian population

• clustered, stratified sampling
• Home interview with a battery of questionnaires
• Athens Insomnia Scale for insomnia
• Sociodemographic characteristics
TransQol-Hu 2002

- Waitlisted dialysis patients vs kidney transplanted patients in Budapest

- RLS - RLS Questionnaire (Allen and Earley, 2001)
- Insomnia - Athens insomnia scale (Soldatos et al., 2000)
- OSAS - Berlin Questionnaire (Netzer et al., 1999)
- Depression - CES-D (Radloff, 1977)
- QoL - KDQoL-SF (Hays et al., 1995)

- Baseline in 2002 – 4 yrs follow up since
<table>
<thead>
<tr>
<th>Transplanted</th>
<th>Waiting list</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N=959</strong></td>
<td><strong>N= 214</strong></td>
</tr>
<tr>
<td>• age: 49±12 years (18-76 years)</td>
<td>• age: 49±12 years (23-79 years)</td>
</tr>
<tr>
<td>• Median Tx time: 61 mos (1-311 months)</td>
<td>• Median dial time: 35 mos (3-213 mos)</td>
</tr>
<tr>
<td>• male: 59%</td>
<td>• male: 62%</td>
</tr>
<tr>
<td>• diabetes: 17%</td>
<td>• diabetes: 14.5%</td>
</tr>
<tr>
<td>• Hb: 132 ±19 g/l</td>
<td>• Hb: 113 ±15 g/l</td>
</tr>
<tr>
<td>• albumin: 42 ±3 g/l</td>
<td>• albumin: 41 ±4 g/l</td>
</tr>
<tr>
<td>• eGFR 50 ±22 ml/min</td>
<td>• Kt/V: 1.27 ± 0.26</td>
</tr>
</tbody>
</table>
MICS-Sleep 2007

- Cca 1100 kidney transplanted patients in Budapest

- Malnutrition, inflammation – alb, pre-albumin, cholesterol, CRP, SGA, IL1, IL4, IL6, IL10, TNF-alpha, leptin, adiponectin

- Depression - CES-D (Radloff, 1977) + structured interview in a sample of consecutive patients

- Sleep – PSG in cca 100 pts +
  - Athens insomnia scale (Soldatos et al., 2000)
  - Berlin Questionnaire (Netzer et al., 1999)
  - RLS Questionnaire (Allen and Earley, 2001)

- Baseline in 2007 – 5 yrs follow up planned
Sleep problems in predialysis patients
(Humber River Regional Hospital, Toronto; n=128)

Prevalence of specific sleep problems

Frequency of sleep problems

- Insomnia
- SAS
- RLS
The presence of sleep problems and Health Related Quality of Life in predialysis patients (n=128)
Daytime sleepiness and Health Related Quality of Life in dialysis patients (n=908)

The diagram shows the KDQoL score across different QoL domains: Burden of Kidney Dis, Sleep, Overall health, Physical fctn, and Emotional WB.
Sleep complaints in transplanted vs dialysis patients vs the general population

- Problems with:
  - Falling asleep
  - Maintaining sleep
  - Early awakening
  - Daytime sleepiness

Legend:
- General pop. (12400)
- Tx (920)
- Dial (908)
Sleep problems and renal function in transplant patients (n=920)

![Graph showing prevalence of sleep problems across different CKD stages. The graph indicates a significant difference (p<0.001) between SAS, RLS, and Insomnia across CKD stages.](image-url)

- **Prevalence (%)**: The prevalence of sleep problems increases with CKD stage.
- **CKD stages**: 1+2, 3, 4, 5.
- **Sleep Problems**: SAS, RLS, Insomnia.
- **Statistical Significance**: p<0.001 for the comparison between SAS and RLS across CKD stages.
Sleep disorders in CKD patients - summary

• The prevalence of sleep disorders is much higher in patients with CKD than in the average population.

• The prevalence of RLS and insomnia these conditions is the lower in transplanted patients (not OSAS)

• Age, gender, renal function and co-morbidity is associated with sleep disorders in kidney transplanted patients
Sleep disorders in CKD patients - summary

- Patients with sleep disorders have more fatigue/daytime sleepiness, increased illness intrusiveness and impaired QoL
- OSAS is a predictor of graft loss, RLS is associated with mortality in transplanted patients
Conclusions

- Sleep disorders are frequent in the CKD population
- Sleep disorders underdiagnosed and un(der)treated
- Effect of sleep disorders on quality of life and other outcomes (co-morbidity?, survival?)
- Management of these treatable disorders and may improve QoL of renal patients
Yawning Apprentice
Mihály Munkácsy
(1844 – 1900)

THANK YOU!
Sleep Heart Health Study

• Multicentrikus, populáció szintű vizsgálat
• N=6,132 (életkor >=40 év, 52.8% nő)
• Kardiovaszkuláris morbiditás és mortalitás közti kapcsolat elemzése
• Hypertonia prevalenciája és a vérnyomás az AHI index-szel arányosan nőtt

JAMA 2000;283:1829-1836
Hypertonia és AHI index: Sleep Heart Health Study, 1995-1998

<table>
<thead>
<tr>
<th>Variables</th>
<th>No. of Subjects</th>
<th>OR Adjusted for Demographics†</th>
<th>OR (95% CI)</th>
<th>OR (95% CI)</th>
<th>OR (95% CI)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apnea-hypopnea index per hour</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1.5</td>
<td>1691</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>1.5-4.9</td>
<td>1598</td>
<td>1.25 (1.08-1.44)</td>
<td>1.12 (0.96-1.30)</td>
<td>1.11 (0.95-1.29)</td>
<td>1.07 (0.91-1.26)</td>
<td></td>
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<tr>
<td>5-14.9</td>
<td>1751</td>
<td>1.57 (1.35-1.81)</td>
<td>1.28 (1.09-1.48)</td>
<td>1.24 (1.06-1.45)</td>
<td>1.20 (1.01-1.42)</td>
<td></td>
</tr>
<tr>
<td>15-29.9</td>
<td>719</td>
<td>1.73 (1.43-2.10)</td>
<td>1.32 (1.08-1.61)</td>
<td>1.26 (1.03-1.55)</td>
<td>1.25 (1.00-1.56)</td>
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</tr>
<tr>
<td>≥30</td>
<td>373</td>
<td>2.27 (1.76-2.92)</td>
<td>1.60 (1.23-2.08)</td>
<td>1.47 (1.12-1.92)</td>
<td><strong>1.37 (1.03-1.83)</strong></td>
<td></td>
</tr>
<tr>
<td>P (trend)</td>
<td></td>
<td>.0001</td>
<td>.0001</td>
<td>.0008</td>
<td>.005</td>
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</tr>
</tbody>
</table>
## Sleep Heart Health Study
Korrigált esély hányados az AHI quartilisek szerint

<table>
<thead>
<tr>
<th>Quartile range</th>
<th>AHI Quartile</th>
<th>p Value</th>
</tr>
</thead>
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<tr>
<td></td>
<td>I</td>
<td>II</td>
</tr>
<tr>
<td></td>
<td>0-1.3</td>
<td>1.4-4.4</td>
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<tr>
<td>Coronary heart disease</td>
<td>1.0</td>
<td>0.92</td>
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<tr>
<td></td>
<td>(0.71-1.20)</td>
<td>(0.93-1.54)</td>
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<tr>
<td>Heart failure</td>
<td>1.0</td>
<td>1.13</td>
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<tr>
<td></td>
<td>(0.54-2.39)</td>
<td>(0.99-3.83)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>1.0</td>
<td>0.98</td>
</tr>
<tr>
<td></td>
<td>(0.77-1.24)</td>
<td>(1.02-1.61)</td>
</tr>
</tbody>
</table>
Fig. 1 Kaplan–Meier analysis: event-free survival in the groups with and without treatment for obstructive sleep apnea.