FMC Sleep and Respiration Rounds

Presented By
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Director, FMC Sleep Centre
University of Calgary

Wednesday, October 2, 2019
Sleep Apnea in Patients with Renal Failure

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Wednesday, October 2, 2019
Lunch: 11:30am
Presentation: 12:00-1:00pm

Room 01500
O’Brien Centre
Health Sciences Centre

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UNIVERSITY OF CALGARY
CUMMING SCHOOL OF MEDICINE
Sleep Apnea and Kidney Disease

-A bidirectional relationship

Patrick J Hanly MD, FRCPC, DABSM

Sleep Centre, Foothills Medical Centre,
University of Calgary
## Disclosures

<table>
<thead>
<tr>
<th>Type of Potential Conflict</th>
<th>Details of Potential Conflict</th>
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<tbody>
<tr>
<td>Grant/Research Support</td>
<td>Philips Respironics (equipment and financial)</td>
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<td>Consultant</td>
<td>Dream Sleep Respiratory Services, BresoTec</td>
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<td>Speakers’ Bureaus</td>
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<td>Financial support</td>
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<td>Other</td>
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Sleep and Renal Function: Bidirectional Relationship

- Hypoxia
- OSA
- CKD
- Sleep
- Kidney
- OSA
- Sleep
- ESKD
Chronic Kidney Disease (CKD): Definition

GFR = Glomerular Filtration Rate (ml/min/1.73m²)
Sleep and Renal Function: *Bidirectional Relationship*

- Biological plausibility
- Association vs Causality
OSA is common in CKD

Nocturnal Hypoxemia

(SaO2 < 90% for ≥12% of monitoring)

<table>
<thead>
<tr>
<th>Group</th>
<th>% of Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR ≥ 60</td>
<td>16</td>
</tr>
<tr>
<td>CKD</td>
<td>47</td>
</tr>
<tr>
<td>ESRD</td>
<td>48</td>
</tr>
</tbody>
</table>

Nicholl, Chest 2012;141:1422-1430
Animal Model: Hypoxemia causes intra-renal hypoxia

- Ventilated rabbit, denervated kidney
- Systemic hypoxemia / Reduced $\text{Do}_2$
- Tissue $\text{Po}_2$ fell progressively (detected when $\text{CaO}_2$ fell 4-8%)
- $\text{Vo}_2$ remained stable despite reduced $\text{Do}_2$
- No hyperemic response to hypoxia

Kidney susceptible to tissue hypoxia, even during mild hypoxemia

Evans, Am J Physiol Regul Integr Comp Physiol 2011;300:R931-R940
OSA
- Hypoxemia

Oxidative stress
Inflammation
EDD
SNA
RAS
Insulin Resist

Atherosclerosis
CVS Disease
Renal hypoxia
HTN
Diabetes

CKD
OSA
- Hypoxemia

Renal tissue response
- Rodent models IH
- Inflamm/Ox stress
- Histological change
- Proteinuria

Renal hypoxia

Limitations
- Severity of IH
- Control for hypertension

CKD
OSA
- Hypoxemia

Renal hypoxia

Renal tissue response
- Rodent models IH
- Inflamm/Ox stress
- Histological change
- Proteinuria

Physiologic response
- Renal hemodynamics
- Renin-angiotensin system

Limitations
- Severity of IH
- Control for hypertension

CKD
OSA: Sympathetic Nervous System (SNA)

Does intermittent hypoxia effect SNA in the kidney?

Somers, J Clin Invest, 1995; 96:1896-1904
Rats: Chronic Intermittent Hypoxia (CIH) x 3 wks, 8 hr/day
- Renal SNA (RSNA) response to hypoxia

Huang, 2009: Respiratory Physiology & Neurobiology, 166, 102–106
Hypoxia: RSNA: Renal HD

- Rabbit model (ventilated)
  - Room air, Moderate hypoxia (.), Severe hypoxia
- Left kidney exposed
  - Renal nerve recording (RSNA)
  - Glomerular resistance: Pre-Glom & Post Glom

Moderate Hypoxia

Glom pressure ↑

Estimated Glomerular Capillary Pressure
(mmHg)

Estimated Pre-glomerular Resistance
(mmHg ml⁻¹ min⁻¹)

Estimated Post-glomerular Resistance
(mmHg ml⁻¹ min⁻¹)

Post Glom R ↑ 70%

Hypoxia and Renin-Angiotensin System (RAS)

Hypoxia

Hypotension or hypovolemia → Renal hypoperfusion →
- Afferent arteriolar stretch
- NaCl delivery to macula densa

Renin release

Renin substrate → Angiotensin I → Angiotensin II

- Aldosterone secretion
- Renal Na⁺ reabsorption
- Extracellular volume expansion
- Systemic blood pressure
- Renin release

Sympathetic neural tone

Converting enzyme
Glomerular Hypertension - Hyperfiltration Theory

Tubulointerstitial injury - Chronic Hypoxia Hypothesis
Glomerular Hypertension - *Hyperfiltration Theory*

- **OSA**

- **RAS**

- **Tubulointerstitial injury - Chronic Hypoxia Hypothesis**
Renal Hemodynamics & Renal RAS: Study Protocol

**High Salt Diet**

-3 days 0 days

**Fasting**

0 days

**Time**

-90 min

**Continuous inulin and PAH infusion**

0 min 30 min 60 min 90 min

**Ang II**

3 ng/kg/min

6 ng/kg/min

**Ang II stopped**

**RECOVERY**

Renal Hemodynamics

Renal RAS
Renal Hemodynamics & Renal RAS

• Renal hemodynamics
  – Baseline RPF, GFR, FF (GFR/RPF)
    • $FF = \textit{Surrogate marker of glomerular pressure}$

• Renal RAS
  – RPF response to AngII
    • $\Delta RPF = \textit{Surrogate marker of renal RAS activity}$
## Filtration Fraction in OSA Patients & Obese Controls

![Image](https://via.placeholder.com/720x720)

**Zalucky, 2015; Am J Respir Crit Care Med 192:873-80**

### Table: Filtration Fraction in OSA Patients & Obese Controls

<table>
<thead>
<tr>
<th></th>
<th>Severe</th>
<th>Moderate</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td># patients</td>
<td>14</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>47 ± 11</td>
<td>49 ± 10</td>
<td>42 ± 11</td>
</tr>
<tr>
<td>Men (%)</td>
<td>57</td>
<td>71</td>
<td>33</td>
</tr>
<tr>
<td>% Caucasian</td>
<td>93</td>
<td>59</td>
<td>100</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>43 ± 5.5*</td>
<td>33 ± 6.7</td>
<td>39 ± 7.5</td>
</tr>
<tr>
<td>RDI (/hr)</td>
<td>64 ± 26*</td>
<td>40.4 ± 18.6†</td>
<td>5 ± 2.3</td>
</tr>
<tr>
<td>Mean SaO₂ (%)</td>
<td>84 ± 4.4*</td>
<td>91 ± 0.2†</td>
<td>93 ± 1.4</td>
</tr>
<tr>
<td>SaO₂&lt;90% (%)</td>
<td>77 ± 14.7*</td>
<td>24.6 ± 0.3†</td>
<td>2.2 ± 3.8</td>
</tr>
<tr>
<td>ERPF (ml/min)</td>
<td>674 ± 88</td>
<td>689 ± 121</td>
<td>805 ± 221</td>
</tr>
<tr>
<td>GFR (ml/min)</td>
<td>106 ± 9.6</td>
<td>126 ± 37.8</td>
<td>107 ± 15.2</td>
</tr>
<tr>
<td>FF</td>
<td>16 ± 1.5†</td>
<td>19 ± 6.6†</td>
<td>14 ± 2.6</td>
</tr>
</tbody>
</table>

**OSA is associated with Glomerular Hypertension**
Renal RAS in OSA Patients & Obese Controls

- Response of RPF to AngII infusion

Renal RAS is up-regulated in OSA independent of obesity, and in proportion to the severity of hypoxia.
Impact of CPAP: Filtration Fraction

Reduced FF = Decreased Glomerular Pressure

Nicholl, Am J Respir Crit Care Med 2014;190:572-580
Impact of CPAP: Renal RAS
- Response of RPF to AngII infusion

Greater response to AngII (post CPAP)
= Renal RAS down-regulated by CPAP

Nicholl, Am J Respir Crit Care Med 2014;190:572-580
Effect of OSA on the Kidney

Sleep and Renal Function: *Bidirectional Relationship*

- Biological plausibility
- Association vs Causality
Is OSA associated with CKD progression?

Sleep Centre Database

Diagnostic Sleep Test

≥ 2 Serum Cr measurements

Alberta Kidney Disease Network

Nocturnal Hypoxemia
- \( \text{SaO}_2 < 90\% \) for ≥ 12% recording time

Renal Function
- Rapid Decline GFR
  \( \geq 4\text{ml/min/1.73m}^2/\text{yr} \)

Is OSA associated with CKD progression?

- 858 patients, 44% had nocturnal hypoxemia
- Rapid Decline GFR (≥4ml/min/1.73m²/yr)

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted Model OR [95% CI]</th>
<th>Multivariate adjusted model† OR [95% CI]</th>
<th>Multivariate adjusted model‡ OR [95% CI]</th>
</tr>
</thead>
</table>

*‡ Adjusted for RDI, age, BMI, diabetes and heart failure

OSA: Risk of Incident CKD

• Cohort definition
  – eGFR > 60 without a diagnosis of OSA

• Exposure (Oct 2004 – Sept 2006)
  – Incident OSA ± CPAP

• Outcomes
  – *Incident CKD*: eGFR<60 twice, and >25% decrease vs baseline
  – *Rate of decline in renal function*
    – Slope of change in eGFR
    – Rapid deterioration in eGFR (>5 ml/min/1.73m²/y)

• Follow up period (median 7.74 yrs)

*Molnar, Thorax 70:888-895, 2015*
OSA: Risk of Incident CKD

- Three groups: No OSA  OSA  OSA+CPAP

- Incident CKD
  - Event rate 10%  25%  29%
  - HR (OSA, no tx) 2.27 (CI 2.19-2.36)
  - HR (OSA+CPAP) 2.79 (CI 2.48-3.13)

- Decline in renal function
  - eGFR slope -0.41 -0.61 -0.87

- Rapid decline
  - OR (OSA, no tx) 1.3 (CI 1.24-1.35)
  - OR (OSA+CPAP) 1.28 (CI 1.09-1.5)

Molnar, Thorax 70:888-895, 2015
CPAP: Impact on renal function

- Sub-study of SAVE (Sleep Apnea & Cardiovascular Endpoints) trial
  - 200 pts, AHI 15-29: randomized CPAP vs usual care
  - Follow up: 4.3 (CPAP) and 4.5 (usual care) years
  - Primary outcome: Annual rate of decline of eGFR

- Analysis
  - Intention to treat: CPAP adherence 4±2.6 hrs/night
  - Per protocol: Good CPAP adherence (≥4 hrs/night)
    Poor CPAP adherence (<4 hrs/night)
    No CPAP (usual care)

Loeffler, Am J Respir Crit Care Med, 2017;
ΔGFR: Annual Rate of Decline

Annual Change in eGFR (ml/min/1.73m²)

Baseline

Exit

Loffler, Am J Respir Crit Care Med, 2017;
Sub-study of SAVE: Limitations

- Patient population
  - Underpowered for primary outcome
  - Majority (≈ 90%) patients did not have CKD

- Risk for progression of renal failure was low
  - Low prevalence of diabetes (≈ 25%)
  - Low prevalence albuminuria (≈ 10%)

- Renal insult modest
  - Nocturnal hypoxemia mild (rarely < 85%)
  - ACEI’s (≈ 90%) and ARB’s (≈ 70%)
OSA: Risk of CKD

- Are we studying the right population?

• Sleep clinic OSA cohort
  – More symptomatic (sleepiness)
  – More severe hypoxemia ± hypoventilation

• Nephrology clinic
  – More risk factors for CKD
  – Established and active kidney disease
Prevalence of OSA patients *at risk* of CKD progression - CSCN OSA Cohort (n=727)

<table>
<thead>
<tr>
<th>GFR ml/min/1.73m²</th>
<th>A1: Normal-to-Mild increase &lt;3 mg/mmol</th>
<th>A2: Moderate increase 3-30 mg/mmol</th>
<th>A3: Severe increase &gt;30 mg/mmol</th>
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<tbody>
<tr>
<td>≥90</td>
<td>237 (32.6)</td>
<td>52 (7.2)</td>
<td>8 (1.1)</td>
</tr>
<tr>
<td>60-89</td>
<td>306 (42.1)</td>
<td>44 (6.1)</td>
<td>7 (1.0)</td>
</tr>
<tr>
<td>45-59</td>
<td>40 (5.5)</td>
<td>6 (0.8)</td>
<td>3 (0.4)</td>
</tr>
<tr>
<td>30-44</td>
<td>9 (1.2)</td>
<td>5 (0.7)</td>
<td>2 (0.3)</td>
</tr>
<tr>
<td>15-29</td>
<td>2 (0.3)</td>
<td>3 (0.4)</td>
<td>2 (0.3)</td>
</tr>
<tr>
<td>&lt;15</td>
<td>1 (0.1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

184 patients (25%) at moderate to high risk of CKD progression

Beaudin, 2019, WSS, Sept 23:5:30-7:00
RCT: Treatment of OSA in patients with CKD: *Impact on kidney function*

- CKD Stage 3 or 4
  - Patient Consent
    - Chart Review
    - Questionnaire
    - HSAT
  - Inclusion and Exclusion criteria
  - Recruitment: Nephrology Clinics
  - Randomization

CONTROL Group
- Medical Tx

CPAP Group
- CPAP + Medical Tx

1 month
- Confirm CPAP Adherence
- Confirm correction of OSA and hypoxemia
- Health Questionnaires

3, 6, 9, 12 months
- CPAP Adherence
- Renal Function: eGFR, ACR
- Health Questionnaires
- Co-morbidities: BP, HbA1C, BMI, Meds

Follow up

*Rimke, BMJ Open, 2019:9:e024632*
Why is this important?
- Impact of CKD/ESRD on CVS outcomes

**Normal kidney function** → **CKD** → **ESRD**

- Sleep apnea/nocturnal hypoxemia

- CVS disease
CKD associated with worse Outcomes

Death Rate

CVS Events

Hospitalizations

Go AS, NEJM 2004;351:1296-305
eGFR & ACR: All-Cause and CVS Mortality

- Meta-analysis, 21 gen population cohorts
  - >1000 pts, baseline eGFR and ACR/dipstick
  - Mortality (all-cause and CVS)
  - Excluded studies CVS disease or risk factors

- 14 studies with ACR: 105,872 pts
  - Median age 61 yrs
  - Median follow up 7.9 years

CKD Prognosis Consortium, Lancet 2010, 375:2073-81
All-cause Mortality

**eGFR**

All-cause Mortality

**ACR**

All-cause Mortality

---

**CVS Mortality**

---

**CVS Mortality**

---

CKD Prognosis Consortium, Lancet 2010, 375:2073-81
eGFR and categorical albuminuria (ACR)

All-cause Mortality

CVS Mortality

eGFR and albuminuria associated with mortality independently of each other (no evidence of interaction) independently of traditional CVS risk factors (excluded)

CKD Prognosis Consortium, Lancet 2010, 375:2073-81
Albuminuria (UACR) and All-Cause Mortality
-Adjusted for co-morbidities

Kovesdy, J Am Coll Cardiol 2013;61:1626-33
CKD: Life expectancy per eGFR and ACR stage

**eGFR stage**

- Stage 1-2
- Stage 5

**ACR stage**

- Stage 1
- Stage 3

Dx CKD 4,5 in middle age reduces life expectancy by approx 15 yrs
Dx DM ............... approx 8 yrs

Gansevoort, Lancet 2013;382:339-52
CKD: Cause of death per eGFR and ACR stage

Gansevoort, Lancet 2013;382:339-52
Why is this important?

- *Impact of CKD/ESRD on CVS outcomes*

Normal kidney function → CKD → ESRD → Sleep apnea/nocturnal hypoxemia → CVS disease
ESRD: OSA and CVS morbidity/mortality
- Hemodialysis

- 94 CHD pts, 64±1 yr, BMI 22±1, 53% male

- Overnight oximetry with sleep log
  - SDB: 3% ODI>5

- Primary outcome
  - First CVS event (fatal or non-fatal)
  - All cause mortality

Masuda, Nephrol Dialy Transplant 2011;26:2289-2295
ESRD: OSA and CVS morbidity/mortality
-Nocturnal Hypoxemia

<table>
<thead>
<tr>
<th>3% ODI (events/h)</th>
<th>Normal ODI, /hr</th>
<th>SDB ODI, /hr</th>
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<tr>
<td>&lt;5</td>
<td>2.0±0.2</td>
<td>12.3±1.3</td>
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<tr>
<td>5-15</td>
<td>6.7±2.8</td>
<td>27.5±3.9</td>
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<tr>
<td>15-30</td>
<td></td>
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<tr>
<td>30≤</td>
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<table>
<thead>
<tr>
<th>3% ODI</th>
<th>n (%)</th>
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<tbody>
<tr>
<td>&lt;5</td>
<td>50 (53.2)</td>
</tr>
<tr>
<td>5-15</td>
<td>33 (35.1)</td>
</tr>
<tr>
<td>15-30</td>
<td>10 (10.6)</td>
</tr>
<tr>
<td>30≤</td>
<td>1 (1.1)</td>
</tr>
</tbody>
</table>

Masuda, Nephrol Dialy Transplant 2011;26:2289-2295
ESRD: OSA and CVS morbidity/mortality
- Median follow up 55±2 months

CVS event free survival

Overall survival

Log-Rank

P = 0.002

P = 0.001

Time (months)

Time (months)

Masuda, Nephrol Dialy Transplant 2011;26:2289-2295
Sleep and Renal Function: Bidirectional Relationship

Hypoxia
OSA

CKD

Sleep
OSA
Sleep

Kidney
ESKD
ESKD: Renal Replacement Therapy (RRT) - *Impact on sleep apnea*

- **Standard RRT**
  - Conventional hemodialysis (CHD)
  - Chronic ambulatory peritoneal dialysis (CAPD)

- **Intensive RRT**
  - Nocturnal hemodialysis (NHD)
  - Nocturnal peritoneal dialysis (NPD)
  - Kidney transplant

*Kennedy 2018, J Nephrol;31:61-70*
CHD: Rostral fluid shift

- 26 ESKD pts, CHD, 45±15 yrs, BMI 27±8

- Overnight PSG
  - AHI≥15: 12 pts (46%)

- Overnight change
  - Leg fluid volume (LFV)
  - Neck circumference (NC)

Elias 2012, Nephrol Dial Transplant;27:1569-1573
CHD: Rostral fluid shift

Elias 2012, Nephrol Dial Transplant;27:1569-1573
CHD: Rostral fluid shift
- Dependent on fluid overload

CHD: Rostral fluid shift
- Dependent on fluid overload

<table>
<thead>
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<th>Factor</th>
<th>Multivariate Linear Regression</th>
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<tbody>
<tr>
<td></td>
<td>Change in OAHI (no./h) β (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>OAHI pre-HD (no./h)</td>
<td>0.3 (0.0 to 0.5)</td>
<td>0.05</td>
</tr>
<tr>
<td>Fluid overload pre-HD (L)</td>
<td>6.5 (1.6 to 11.4)</td>
<td>0.01</td>
</tr>
<tr>
<td>ΔFluid overload (L)</td>
<td>2.1 (−5.1 to 9.2)</td>
<td>0.54</td>
</tr>
<tr>
<td>ΔNocturnal rostral fluid shift (L)</td>
<td>3.1 (−15.3 to 21.6)</td>
<td>0.72</td>
</tr>
</tbody>
</table>

Fluid overload pre-hemodialysis strongest predictor of reduction in AHI following CHD

CHD: Ultrafiltration

- 15 pts, CHD, 54±10 yrs, BMI 25±5
- PSG: AHI 44±20; 10 OSA, 5 CSA
- Bioelectrical impedance: ECFV

- Ultrafiltration without dialysis
  - 2.17±0.45 L removed
  - No change in urea

Lyons 2015, Am J Respir Crit Care Med;11:1287-1294
CHD: Ultrafiltration (UF)

Change in AHI

Baseline: 44±20
Post UF: 28±18

Correlation ΔECFV and ΔAHI

ΔAHI post UF

ΔECFV post UF

Lyons 2015, Am J Respir Crit Care Med;11:1287-1294
Nephrotic syndrome: *Rostral fluid shift*

- 23 pts, 45±19 yrs, BMI 25±6, eGFR 94±45

- Proteinuria, hypo-albuminemia, leg edema
  - Steroid responsive
  - Hydration fraction (TBW, % body wt) fell 14±12%

- Baseline PSG: 11 pts had OSA (RDI 35±8)
- Follow up PSG 8.1±2.6 mths later

Nephrotic syndrome: Rostral fluid shift

RDI (all patients)

RDI (patients with OSA)

Tang 2012, Nephrol Dial Transplant;27:2788-2794
ESRD: Renal Replacement Therapy (RRT) - Impact on sleep apnea

• Standard RRT
  – Conventional hemodialysis (CHD)
  – Chronic ambulatory peritoneal dialysis (CAPD)

• Intensive RRT
  – Nocturnal hemodialysis (NHD)
  – Nocturnal peritoneal dialysis (NPD)
  – Kidney transplant

Kennedy 2018, J Nephrol;31:61-70
Nocturnal hemodialysis (NHD) vs CHD

14 pts, CHD, 45±9 yrs, BMI 26±6
- OSA (7 pts), CSA (1 pt)
Nocturnal hemodialysis (NHD) vs CHD

ESRD/OSA: Ventilatory instability

- 24 pts, CHD, 31-68 yrs
  - PSG: Apneic (AHI ≥ 15) vs non-apneic (AHI < 15)

- CHD converted to NHD
  - Apneic “responders”: AHI fell > 50% and/or < 15
  - Apneic “non-responder”

- Ventilatory response to hypercapnia
  - Modified Read rebreathing technique

Beecroft 2009, Sleep Medicine; 10:47-54
Ventilatory response to Hypercapnia
-Apneic responders vs non-responders

Responders
AHI: 43±20 to 10±7

Non-responders
AHI: 39±21 to 31±11

Ventilatory sensitivity to hypercapnia reduced following conversion from CHD to NHD in apneic responders

Beecroft 2009, Sleep Medicine;10:47-54
Change in ventilatory sensitivity
- Correlated with change in AHI

Beecroft 2009, Sleep Medicine;10:47-54

$r = 0.528, p = 0.029$
NHD reduced ventilatory sensitivity
- *Potential mechanisms*

- **Uremia**
  - Better clearance of toxins, middle molecules

- **Sympathetic nervous system activation**
  - Reduced by NHD

- **Ultrafiltration**
  - Resolution of interstitial pulmonary edema
Nocturnal Peritoneal Dialysis (NPD) vs CAPD

• 24 ESKD pts, 51±13 yrs, BMI 21±4
  – Cycler-assisted NPD (8 wks) vs CAPD

• PSG on NPD vs CAPD

• Bioelectrical impedance analysis
  – Change in hydration fraction (HF=TBW, % wt)

## Nocturnal Peritoneal Dialysis (NPD) vs CAPD


<table>
<thead>
<tr>
<th></th>
<th>NPD</th>
<th>CAPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHI</td>
<td>3.4±1.3</td>
<td>14±4</td>
</tr>
<tr>
<td>HF</td>
<td>-3.6±0.6</td>
<td>-0.7±0.5</td>
</tr>
</tbody>
</table>

![Graph showing comparison between NPD and CAPD](image)
Nocturnal Peritoneal Dialysis (NPD) vs CAPD

Nasopharynx (NP)
Oropharynx (OP)
Hypopharynx (HP)
Tongue
MPXA

% Volumetric change after conversion to CAPD

Reduction in volume ≈ Δ AHI (r=-0.565, p=0.035)

Kidney Transplantation

<table>
<thead>
<tr>
<th>Reference</th>
<th>All n</th>
<th>Apneic n</th>
<th>AHI Pre TP</th>
<th>AHI Post TP</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jurado-Gamez 2008</td>
<td>9</td>
<td>3</td>
<td>10±11</td>
<td>4.9±6.1</td>
<td></td>
</tr>
<tr>
<td>Beecroft 2009</td>
<td>18</td>
<td>11</td>
<td>20±15</td>
<td>24±21</td>
<td>27% “responders”*</td>
</tr>
<tr>
<td>Rodrigues 2010</td>
<td>34</td>
<td>9</td>
<td>5.3±7.3</td>
<td>3.1±4.5</td>
<td></td>
</tr>
<tr>
<td>Lee 2011</td>
<td>20</td>
<td>12</td>
<td>13.5 (2-40)</td>
<td>4.5 (0-20)</td>
<td>66% “responders”</td>
</tr>
</tbody>
</table>

* Responder = AHI reduced >50% and/or AHI <10/hr

- No consistent benefit
  - Heterogenous group
    - Pre-existing SDB not related to ESKD
    - New risk factors for SDB post TP eg weight gain
- No mechanistic studies
  - Phenotype
Implications for Management

- Consider whether un-recognized OSA is contributing to symptoms
  - *Overlapping symptoms*

- Awareness of potential for OSA/hypoxemia to injure the kidney
  - *Benefit of OSA treatment to kidney function not established*

- Consider treatment of OSA/hypoxemia in specific phenotypes
  - *Resistant hypertension in patient with co-existing CKD*
  - *Accelerated decline in kidney function despite conventional CKD Tx*
Implications for Management

- Optimize correction of volume overload
  - *Predominant mechanism for pathogenesis of OSA in ESKD*

- Consider CPAP trial in symptomatic patient
  - *May require management of co-existing insomnia, RLS*

- Intensification of RRT does not guarantee correction of OSA
  - *Clinical and objective monitoring follow up required*
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