Chronic Kidney Disease and Nocturia

Nocturia, Nocturnal Activity, and Nondipping

Rajiv Agarwal, Robert P. Light, Jennifer E. Bills, Lindsey A. Hummel

Abstract—Patients with chronic kidney disease have less than expected decline in blood pressure during sleep (nondipping) and commonly experience the vexing symptom of nocturia. To better understand the relationship among nocturia, nighttime physical activity, and nondipping, we studied 98 patients with chronic kidney disease on 2 occasions, 1 month apart, with 24-hour ambulatory blood pressure monitoring and simultaneous activity monitoring with wrist actigraphy. Patients with nocturia had greater actigraphically recorded nighttime physical activity compared to those with no nocturia. The drop in activity from wake to sleep was reduced to a similar extent whether the patients had nocturia once or twice, but patients who had nocturia ≥3 times had the least reduction from wake to sleep activity (P<0.001 versus those with less degrees of nocturia). Those with nocturia had a lesser drop in systolic ambulatory blood pressure during sleep compared with those without nocturia. The average fall in sleep systolic blood pressure was 9.8 mm Hg (95% CI: 8.0 to 11.6 mm Hg) in those without nocturia compared with 3.4 mm Hg (95% CI: 2.7 to 4.1 mm Hg) in those with any severity of nocturia (P<0.001 for difference). Nondipping in patients with nocturia was mediated by nighttime physical activity. These differences were independent of estimated glomerular filtration rate, albuminuria, or use of diuretics. Thus, nocturia, which may reflect impaired renal tubular function, is associated with nondipping in patients with chronic kidney disease and appears to be mediated by increased nocturnal activity. Whether nocturia itself or the resulting nondipping associated with nocturia is of prognostic importance for cardiorenal events in patients with chronic kidney disease should be tested in future studies. (Hypertension. 2009;54:646-651.)

Key Words: hypertension ■ ambulatory blood pressure monitoring ■ actigraphy ■ CKD ■ physical activity ■ nocturia

Hypertension, which is a widely prevalent and treatable cardiovascular risk factor in patients with chronic kidney disease (CKD), is often difficult to assess accurately, because many patients with CKD have white-coat hypertension or masked hypertension. Out-of-clinic measured blood pressure (BP) recordings are the preferred method of BP assessment, and some studies have demonstrated that out-of-clinic measured BP may be of greater prognostic importance for predicting cardiovascular and end-stage renal disease outcomes compared with clinic-measured BP recordings. Home BP measurement and ambulatory BP monitoring are currently available tools to measure out-of-clinic BP, of which the latter has the advantage of measuring the fall in BP during sleep, a phenomenon termed “dipping.” Although the exact cause for nondipping is unclear, nondipping is associated with CKD, sleep apnea, volume overload, sympathetic activation, and other factors.

Nocturia is defined as any waking at night to void and occurs when the rate of production of urine exceeds that of bladder volume. Many factors, eg, age, benign prostatic hyperplasia, congestive heart failure, diabetes mellitus, diabetes insipidus, and CKD, are associated with nocturia. Nocturia is an early manifestation of CKD and occurs because of diminished ability of renal tubules to reabsorb salt and water. Nocturia is associated with increased daytime fatigue and increased risk of falls, especially in the elderly. Nocturia disturbs sleep, and whether this can by itself diminish dipping in patients with CKD is unknown. If so, these observations may begin to explain the association of nocturia with increased mortality.

The purpose of this study was to evaluate the association of nocturia with nondipping in patients with CKD. We hypothesized that nocturia is a cause of increased nighttime physical activity and leads to diminished fall in BP at night.

Methods

Participants

We studied veterans between the ages of 18 and 90 years with CKD defined as an estimated glomerular filtration rate of <60 mL/min per 1.73 m² or the presence of proteinuria (spot urine:protein ratio of >200 mg/g of creatinine) or the presence of structural kidney disease (eg, adult polycystic kidney disease). We excluded patients who were morbidly obese (body mass index: ≥40 kg/m²), had an estimated glomerular filtration rate of ≥15 mL/min per 1.73 m², were hospitalized within the previous 2 months, had a seated clinic BP of ≥140/90 mm Hg, or had substantial cardiac arrhythmia (defined as ≥6 irregular heartbeats per minute).
Study Protocol
The study protocol was approved by the institutional review boards and the Veterans’ Affairs Research and Development Committee. Patients were recruited between June 2007 and March 2009 and enrolled after written informed consent. A detailed history and a focused physical examination were performed. We asked each patient if he or she had to wake up at night to pass urine. If so, we asked how many times he or she had to typically wake up to pass urine. These questions were asked only once during the period of the study. We studied each patient on 2 occasions, 1 month apart, with ambulatory BP monitoring and simultaneous actigraphy, as described below.

Ambulatory BP Monitoring
Ambulatory BP monitoring was performed in the nondominant arm for 24 hours using the SpaceLabs 90207 monitor (SpaceLabs Medical Inc), with cuff inflations every 20 minutes during the day (6:00 AM to 10:00 PM) and every 30 minutes during the night. Accuracy of ambulatory BP recordings was confirmed against auscultated BP, as described. At the time of placing the ambulatory BP monitor, 6 recordings were made, 3 each with ambulatory and auscultated methods. The recordings were sandwiched so that the auscultated reading was always followed by the ambulatory reading and vice versa. This was repeated at week 4. We used a mixed model with nested random effects to calculate the intraclass correlation coefficient and bias. Ambulatory recordings overestimated the auscultated systolic BP by 1.6 mm Hg (95% CI: 0.9 to 2.4 mm Hg) with an SD between methods of 2.6 mm Hg. The intraclass correlation coefficient between methods was 0.974. Ambulatory recordings overestimated the auscultated diastolic BP by 2.3 mm Hg (95% CI: 1.6 to 2.9 mm Hg), with an SD between methods of 2.6 mm Hg. The intraclass correlation coefficient between methods was 0.938. Hourly averages were calculated, and the average of these averages represented the mean systolic and diastolic BPs. Patients were asked to record the sleep and wake times during this recording. Dipping was defined as the change from wake to sleep in systolic ambulatory BP.

Actigraphy
Concomitant activity monitoring was performed using an Actigraph (Activwatch 64, Mini Mitter), a watch-sized device worn on the dominant wrist for the duration of ambulatory BP monitoring. The internal clocks of the ambulatory BP monitoring and Actigraph were synchronized, and activity was assessed in 15-second epochs throughout the 24-hour period. The units of activity are arbitrary but have been calibrated to metabolic equivalent of task (MET). Data were exported to a custom-designed relational database. Mean wake and sleep activities were calculated as the means of 6-minute periods for the entire duration of ambulatory BP measurement.

Statistical Analysis
Motor activity, measured by actigraphy, is strongly related to variation in measured hemodynamic variables, BP, and heart rate. We have reported previously a nonlinear relationship between actimetry and hemodynamics. Accordingly, we took the square-root transformation of the Actigraph data for descriptive and analytic evaluation.

A mixed model was used to allow for correlated data on 2 occasions within individuals. The effect of occasion was modeled as a nested effect within participants to account for the random variation. We fitted 3 models to describe the relationship of nocturia, nondipping, and nocturnal activity.

In model 1, systolic BP was analyzed as a continuous dependent variable, and nocturia was categorized as none, 1, 2, or 3 or more times for each participant. A mixed model tested the effect of nocturia category, sleep state (wake or sleep), and their interaction (all as nominal factors) on the dependent variable using the full maximal likelihood approach.

In model 2, the square-root transformation of the actigraphically recorded physical activity was analyzed as a continuous dependent variable. As in model 1, a mixed model tested the effect of nocturia category, sleep state (wake or sleep), and their interaction on the dependent variable.

In model 3, the systolic BP was analyzed as a continuous dependent variable, and a mixed model tested the effect of nocturia category, sleep state (wake or sleep), the average overall activity during the day or night, and their 3-way interaction on the dependent variable.

Statistical analysis was performed using Stata 10.1 (StataCorp), and the nominal level of statistical significance was set at a 2-sided P value of <0.05.

Results
A total of 103 patients were recruited, of which 98 provided adequate recordings of paired ambulatory and actigraphy recordings. Of a total of 196 expected ambulatory BP measurements, 83% were adequate, of which 89 (91%) were adequate on the first visit and 74 (76%) on the second visit.

Baseline characteristics of the 98 patients are listed in Table 1. Nocturia was present in 87% of the participants who were mostly older men, 84% being white, 13% being black, and the remaining being of other ethnicities. The clinical and laboratory characteristics among the 4 categories of nocturia were well balanced, and the clinic-obtained BP measurements indicated good control. Only 4 patients were not taking antihypertensive drugs and estimated glomerular filtration rate averaged 38.7 mL/min per 1.73 m², with little differences between nocturia categories. Geometric mean of 24-hour urine albumin:creatinine ratio on an overnight collection was 56 mg/g of creatinine. There were no statistical differences in the prescription of diuretic drugs between nocturia categories.

Sixty-five patients had paired recordings of ambulatory BP, and dipping was defined as a drop from awake to sleep in systolic BP of ≥10 mm Hg. Forty patients were nondippers at the initial and final visit, and 10 were dippers on both occasions. Six patients became dippers, and 9 became nondippers. Agreement was 76%, with a κ statistic of 0.415 (P<0.001). McNemar’s test for discordant pairs was not significant (P=0.60).

Sixty-five patients had paired recordings of activity during day and night. A ratio of activity was calculated as a mean square-root transformed activity recording from awake to sleep on each of the 2 occasions. The Bland-Altman difference between ratios was −0.117, with the 95% limits of agreement being −3.567 to 3.333. Lin’s concordance correlation coefficient between ratios was 0.425 (P<0.001). The relationship between mean differences and differences in ratios was −0.09 and was not significant.

Table 2 shows the unadjusted relationship between the fall in activity during sleep and the severity of nocturia. Wake activity levels between nocturia categories were similar, but the sleep activity levels were lower in patients who did not have nocturia compared with those who had nocturia. Thus, the average fall in activity during night was 5.6 U in those with no nocturia and was only a 4.3-U fall in those who had nocturia of ≥3 times. The drop in activity from wake to sleep was reduced to a similar extent whether the patient had nocturia once or twice, but patients who had nocturia ≥3 times had the least reduction from wake to sleep activity (P<0.001 versus those with lesser degrees of nocturia).

Table 3 shows the unadjusted relationship between the fall in systolic BP during sleep (dipping) and the severity of nocturia. Wake BP levels between nocturia categories were...
Table 1. Baseline Characteristics by Frequency of Nocturia

<table>
<thead>
<tr>
<th>Clinical Characteristic</th>
<th>0</th>
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<th>2</th>
<th>≥3</th>
<th>Total</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (%)</td>
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<td>23</td>
<td>33</td>
<td>29</td>
<td>98</td>
<td>0.34</td>
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<tr>
<td>Age, mean±SD, y</td>
<td>67±8</td>
<td>69±14</td>
<td>71±11</td>
<td>67±11</td>
<td>69±11</td>
<td></td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>13</td>
<td>22</td>
<td>32</td>
<td>28</td>
<td>95</td>
<td>0.91</td>
</tr>
<tr>
<td>Race, n (%)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>White</td>
<td>11</td>
<td>19</td>
<td>27</td>
<td>25</td>
<td>82</td>
<td>0.88</td>
</tr>
<tr>
<td>Black</td>
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<td>3</td>
<td>5</td>
<td>4</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Other/unknown</td>
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<td>1</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Weight, mean±SD, kg</td>
<td>98.2±18.4</td>
<td>90±15.3</td>
<td>86.2±16.5</td>
<td>93.5±15.1</td>
<td>90.8±16.4</td>
<td>0.10</td>
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<td>Body mass index, mean±SD, kg/m²</td>
<td>30.8±4</td>
<td>30.3±5.1</td>
<td>28.8±4.4</td>
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<td>Etiology of CKD, n (%)</td>
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<td>Diabetes mellitus</td>
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<td>6</td>
<td>11</td>
<td>7</td>
<td>25</td>
<td></td>
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<tr>
<td>Hypertensive nephrosclerosis</td>
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<td>7</td>
<td>9</td>
<td>6</td>
<td>25</td>
<td></td>
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<tr>
<td>Ischemic nephropathy</td>
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<td>2</td>
<td>2</td>
<td>8</td>
<td>13</td>
<td></td>
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<tr>
<td>Polycystic kidney disease</td>
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<td>3</td>
<td>0</td>
<td>3</td>
<td></td>
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<tr>
<td>Nephritic glomerulonephritis</td>
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<td>1</td>
<td>2</td>
<td>1</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Nephrotic glomerulonephritis</td>
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<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td></td>
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<tr>
<td>Obstructive uropathy</td>
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<td>2</td>
<td>0</td>
<td>1</td>
<td>4</td>
<td></td>
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<td>0</td>
<td>1</td>
<td>3</td>
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<td>1</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction, n (%)</td>
<td>2</td>
<td>10</td>
<td>13</td>
<td>12</td>
<td>37</td>
<td>0.32</td>
</tr>
<tr>
<td>Heart failure hospitalization, n (%)</td>
<td>0</td>
<td>4</td>
<td>4</td>
<td>7</td>
<td>15</td>
<td>0.19</td>
</tr>
<tr>
<td>Stroke, n (%)</td>
<td>1</td>
<td>4</td>
<td>7</td>
<td>12</td>
<td>24</td>
<td>0.08</td>
</tr>
<tr>
<td>Peripheral vascular bypass surgery, n (%)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>10</td>
<td>0.91</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>7</td>
<td>15</td>
<td>25</td>
<td>16</td>
<td>63</td>
<td>0.40</td>
</tr>
<tr>
<td>Gout, n (%)</td>
<td>2</td>
<td>8</td>
<td>8</td>
<td>5</td>
<td>23</td>
<td>0.49</td>
</tr>
<tr>
<td>Hemoglobin, mean±SD, g/dL</td>
<td>13.6±1.4</td>
<td>12.6±1.8</td>
<td>12.4±1.8</td>
<td>13.4±1.9</td>
<td>12.9±1.8</td>
<td>0.06</td>
</tr>
<tr>
<td>Cholesterol, mean±SD, mg/dL</td>
<td>159±41</td>
<td>161±57</td>
<td>148±29</td>
<td>167±46</td>
<td>158±44</td>
<td>0.38</td>
</tr>
<tr>
<td>Blood urea nitrogen, mean±SD, mg/dL</td>
<td>32±17</td>
<td>39±18</td>
<td>38±13</td>
<td>30±12</td>
<td>35±15</td>
<td>0.07</td>
</tr>
<tr>
<td>Serum creatinine, mean±SD mg/dL</td>
<td>1.9±0.6</td>
<td>1.8±0.6</td>
<td>2±0.5</td>
<td>1.7±0.4</td>
<td>1.9±0.5</td>
<td>0.13</td>
</tr>
<tr>
<td>Estimated GFR, mean±SD, mL/min per 1.73 m²</td>
<td>39.8±15.2</td>
<td>42.9±23.1</td>
<td>33.2±9.8</td>
<td>41.1±12.9</td>
<td>38.7±15.7</td>
<td>0.09</td>
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<tr>
<td>Log e urine albumin:creatinine ratio, mean±SD, mg/g</td>
<td>4.37±2.06</td>
<td>3.85±2.02</td>
<td>3.78±1.77</td>
<td>4.25±2.31</td>
<td>4.02±2.02</td>
<td>0.72</td>
</tr>
<tr>
<td>Systolic BP/diastolic BP, mean±SD, mm Hg</td>
<td>124.2±9.4/68.5±10.8</td>
<td>121.7±12.6/67.6±11.1</td>
<td>121±11.7/66±8.2</td>
<td>125.2±13.3/68.8±8.3</td>
<td>122.8±12.1/67.6±9.2</td>
<td>0.53/0.67</td>
</tr>
</tbody>
</table>

(Continued)
similar, but the sleep BPs were lower in patients who did not have nocturia compared with those who had nocturia. Thus, the average fall in systolic BP was 9.8 mm Hg in those with no nocturia, but the fall was only 2.6 mm Hg in those who had nocturia of ≥3 times. After adjustment for the level of activity between nocturia categories, there were no differences in the extent of dipping (P = 0.14).

The Figure shows the unadjusted relationship between nondipping and the severity of nocturia. Dipping was reduced to a similar extent in those who had nocturia once, twice, or ≥3 times. Thus, increasing severity of nocturia was not associated with increasing severity of nondipping (P = 0.2). The average fall in sleep systolic BP in those with any severity of nocturia was 3.4 mm Hg (95% CI: 2.7 to 4.1 mm Hg; P < 0.001 versus those without nocturia). The Figure also shows the unadjusted relationship between the change in activity level from day to night and the severity of nocturia. These changes in activity level from wake to sleep paralleled the changes in wake to sleep systolic BP. Accordingly, adjustment for activity level removed the effect of nocturia on the dipping phenomenon, as shown in Table 3.

Table 1. Continued

<table>
<thead>
<tr>
<th>Clinical Characteristic</th>
<th>0</th>
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<th>2</th>
<th>≥3</th>
<th>Total</th>
<th>P</th>
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<tbody>
<tr>
<td>No. of antihypertensive drugs</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Blockers, n (%)</td>
<td>9 (69)</td>
<td>16 (70)</td>
<td>24 (73)</td>
<td>16 (55)</td>
<td>65 (66)</td>
<td>0.50</td>
</tr>
<tr>
<td>α-Blockers, n (%)</td>
<td>2 (15)</td>
<td>3 (13)</td>
<td>11 (33)</td>
<td>9 (31)</td>
<td>25 (26)</td>
<td>0.25</td>
</tr>
<tr>
<td>ACE inhibitors, n (%)</td>
<td>9 (69)</td>
<td>8 (35)</td>
<td>20 (61)</td>
<td>18 (62)</td>
<td>55 (56)</td>
<td>0.12</td>
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<tr>
<td>ARBs, n (%)</td>
<td>3 (23)</td>
<td>4 (17)</td>
<td>8 (24)</td>
<td>5 (17)</td>
<td>20 (20)</td>
<td>0.88</td>
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<tr>
<td>Centrally acting agents, n (%)</td>
<td>0 (0)</td>
<td>2 (9)</td>
<td>2 (6)</td>
<td>4 (14)</td>
<td>8 (8)</td>
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<td>Loop diuretics, n (%)</td>
<td>2 (15)</td>
<td>9 (39)</td>
<td>16 (48)</td>
<td>12 (41)</td>
<td>39 (40)</td>
<td>0.23</td>
</tr>
<tr>
<td>Thiazide diuretics, n (%)</td>
<td>5 (38)</td>
<td>2 (9)</td>
<td>12 (36)</td>
<td>6 (21)</td>
<td>25 (26)</td>
<td>0.07</td>
</tr>
<tr>
<td>K-sparing diuretics, n (%)</td>
<td>1 (8)</td>
<td>2 (9)</td>
<td>3 (9)</td>
<td>1 (3)</td>
<td>7 (7)</td>
<td>0.83</td>
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<tr>
<td>Dihydropyridines, n (%)</td>
<td>5 (38)</td>
<td>7 (30)</td>
<td>17 (52)</td>
<td>18 (62)</td>
<td>47 (48)</td>
<td>0.12</td>
</tr>
<tr>
<td>Nondihydropyridines, n (%)</td>
<td>0 (0)</td>
<td>2 (9)</td>
<td>2 (6)</td>
<td>1 (3)</td>
<td>5 (5)</td>
<td>0.67</td>
</tr>
<tr>
<td>Vasodilators, n (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>4 (12)</td>
<td>2 (7)</td>
<td>6 (6)</td>
<td>0.22</td>
</tr>
</tbody>
</table>

ACE indicates angiotensin-converting enzyme; ARBs, angiotensin receptor blockers; GFR, glomerular filtration rate.

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Table 2. Relationship Between Nocturia and Physical Activity

<table>
<thead>
<tr>
<th>Variable</th>
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<tbody>
<tr>
<td>Nocturia, Frequency per Night</td>
<td></td>
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</tr>
<tr>
<td>Wake activity*</td>
<td>7.4</td>
<td>6.4</td>
<td>7.0</td>
<td>6.9</td>
</tr>
<tr>
<td>Sleep activity*</td>
<td>1.8</td>
<td>1.7</td>
<td>2.3</td>
<td>2.6</td>
</tr>
<tr>
<td>Wake-sleep activity, mean (95% CI)</td>
<td>5.6 (5.5 to 5.7)</td>
<td>4.7 (4.6 to 4.8)</td>
<td>4.7 (4.6 to 4.8)</td>
<td>4.3 (4.2 to 4.4)</td>
</tr>
<tr>
<td>Difference from reference category, mean (95% CI)</td>
<td>Reference</td>
<td>0.9 (0.8 to 1.1)</td>
<td>0.9 (0.8 to 1.1)</td>
<td>1.3 (1.2 to 1.4)</td>
</tr>
</tbody>
</table>

*Activity was averaged every 6 minutes throughout the day and square-root transformed before analysis.

Discussion

The major findings of our study are as follows: (1) patients with CKD who have nocturia have impaired dipping in systolic BP; (2) patients with nocturia have greater sleep-time activity compared with wake-time activity; (3) this increase in nocturnal physical activity appears to mediate the nondipping phenomenon in these patients; and (4) impaired dipping does not appear to be attributable to differences in estimated glomerular filtration rate, albuminuria, or the use of diuretics.

The prevalence of nocturia, defined as waking at night to pass urine, was present in 87% of our patients. It has been reported previously that 60% of people 65 years of age have nocturia.12 Given that all of our patients had concomitant CKD and were mostly elderly, it is not surprising to find such a high prevalence of nocturia.

Patients with CKD often have nondipping BP pattern. The causes of nondipping in these patients are not clear, but many factors have been proposed, eg, sodium sensitivity, autonomic activation, and endocrine dysfunction.13,14 Mansoor et al15 found that, in patients with untreated hypertension,
nondippers have similar wake activity but higher sleep activity compared with dippers. We have reported previously in a separate cohort of patients that sleep activity was increased in patients with nondipping, which raises the question of whether patients with nondipping have poor sleep quality. This study found nocturia as an obvious cause for disturbed sleep in these patients. Patients with CKD often have poor renal tubular concentrating ability; this results in nocturnal increase in physical activity presumably as a result of nocturia.

The above findings are relevant for the interpretation of ambulatory BP dipping patterns. Verdecchia et al reported that perceived quantity of sleep during overnight ambulatory BP recording influenced the dipping pattern. Overall, 30% of the patients reported sleep duration <2 hours less than usual, 10% between 2 to 4 hours less than usual, and 4% >4 hours less than usual. The independent prognostic value of nighttime BP for total cardiovascular end points and all-cause mortality was lost in the 14% of the patients who had sleep disturbance of >2 hours. Given that nocturia is a potent cause of sleep disturbance, as noted by the increased nocturnal physical activity in our study, it is possible that some of the prognostic value contained in the nocturnal BP may simply be because of nocturia, underlying CKD, or a combination thereof.

The strengths of our study are measurements of ambulatory BP and concomitant activity on 2 predetermined occasions in a population of CKD patients with well-controlled clinic BP. Furthermore, nearly all of the patients were on antihypertensive drugs and generally had well-controlled BP, as is the standard of care. The repeated measurements on the same patient reduced the probability of chance associations. A limitation of our work was that it was restricted to older male veterans. Furthermore, the case-control approach of our study does not permit us to draw a cause-and-effect relationship between nocturia and nondipping. Tubulointerstitial damage is related to sodium sensitivity and may also be associated with nocturia; therefore, common factors that lead to both nondipping and increased nocturnal activity may falsely draw a causal relationship between nocturnal activity and nondipping. Finally, whether the nocturnal activity in our patients was related to sleep apnea needs clarification. Obesity is the

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nocturia, Frequency per Night</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
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<tr>
<td>Unadjusted model</td>
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<tr>
<td>Wake systolic BP, mm Hg</td>
<td>125.5</td>
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<tr>
<td>Sleep systolic BP, mm Hg</td>
<td>115.8</td>
</tr>
<tr>
<td>Dipping (wake-Sleep BP), mean (95% CI)</td>
<td>9.8 (8.0 to 11.6)</td>
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<tr>
<td>Difference from reference category, mean (95% CI)</td>
<td>Reference</td>
</tr>
<tr>
<td>P for difference from reference</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model adjusted for physical activity (at rest)</td>
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<tr>
<td>Wake systolic BP, mm Hg</td>
<td>123.7</td>
</tr>
<tr>
<td>Sleep systolic BP, mm Hg</td>
<td>115.8</td>
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<tr>
<td>Dipping (wake-Sleep BP), mean (95% CI)</td>
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<tr>
<td>Mean difference from reference category</td>
<td>Reference</td>
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<tr>
<td>Difference from reference category, mean (95% CI)</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Figure. Unadjusted relationship among nondipping, nocturnal activity, and severity of nocturia. Dipping was reduced in those with nocturia. Increasing severity of nocturia was not associated with increasing severity of nondipping (P>0.2). The average fall in sleep systolic BP in those with any severity of nocturia was 3.4 mm Hg (95% CI: 2.7 to 4.1 mm Hg; P<0.001 versus those without nocturia). The change in activity level from wake to sleep was greatest in those without nocturia. These changes in activity level from wake to sleep paralleled the changes in wake to sleep systolic BP. Those with nocturia of ≥3 times per night had the least reduction from wake to sleep activity.
most important risk factor for obstructive sleep apnea. We excluded patients with morbid obesity from our study. Body mass index distribution was similar between nocturia categories (see Table 1). However, given that we did not perform polysomnography, we cannot exclude the possibility of obstructive sleep apnea causing nondipping in our study.

**Perspectives**

If nocturia is attributed to prostate hyperplasia, then treatment of the condition, eg, with transurethral resection of the prostate, may regress nocturia and restore dipping. However, nocturia in patients with CKD may be associated with impaired renal tubular function. To dissect the independent effect of nocturia from nighttime wakening on nondipping, several strategies can be considered, eg, placement of an indwelling bladder catheter, restriction of sodium and water intake, or avoidance of the nighttime dose of diuretic may be appropriate strategies. We conclude that nocturia in patients with CKD may be more than an inconvenience. Other than indicating impaired tubular function and/or reduced bladder capacity, nocturia may impair nocturnal dipping, which is a potent cardiovascular risk factor, and may begin to explain the increased mortality associated with nocturia in these patients. Long-term studies are required to determine whether nocturia elevates the mortal risk through nondipping or whether it does so independent of nocturnal dipping.

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**Disclosures**

None.

**References**

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