

Supplementary Material

Urinary melatonin-sulfate / cortisol ratio and the presence of prostate cancer: A case-control study

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Running title: Melatonin and the Prostate Cancer

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Supplementary Table S1. Joint risks of urinary melatonin or cortisol level and the PSA level associated with the presence of prostate cancer.

| Factor/category | | Controls | Cases | | | | |
|------------------------------|------------------|-----------|-----------|-------------|-------------------|------------------|-------------------|
| | | N=240 | N=120 | | | | |
| | | N (%) | | OR | 95% CI | aOR ¹ | 95% CI |
| Melatonin² | PSA level | | | | | | |
| High | < 10 | 70 (30.6) | 12 (10.1) | 1.0 | (Ref) | 1.0 | (Ref) |
| Low | < 10 | 50 (21.8) | 14 (11.7) | 1.63 | 0.70-3.83 | 1.63 | 0.69-3.88 |
| High | ≥ 10 | 54 (23.6) | 34 (28.6) | 3.67 | 1.74-7.76 | 3.71 | 1.73-7.94 |
| Low | ≥ 10 | 55 (24.0) | 59 (49.6) | 6.26 | 3.06-12.78 | 6.58 | 3.16-13.71 |
| Cortisol² | PSA level | | | | | | |

| | | | | | | | |
|------|------|-----------|-----------|-------------|-------------------|-------------|-------------------|
| Low | < 10 | 61 (26.6) | 11 (9.2) | 1.0 | (Ref) | 1.0 | (Ref) |
| High | < 10 | 59 (25.8) | 15 (12.6) | 1.41 | 0.60-3.32 | 1.42 | 0.60-3.39 |
| Low | ≥ 10 | 62 (27.1) | 39 (32.8) | 3.49 | 1.64-7.43 | 3.71 | 1.71-8.04 |
| High | ≥ 10 | 47 (20.5) | 54 (45.4) | 6.37 | 3.00-13.51 | 6.33 | 2.94-13.61 |

¹Adjusting for age (< 65 vs. ≥ 65 yr), personal habits of smoking, alcohol, betel nut, family history of prostate cancer, and prostate-specific antigen level (<10 vs. ≥ 10 ng/ml).

²Medians of 43.23 ng/mg creatinine for melatonin, 24.06 ng/mg creatinine for cortisol, and 1.76 for MT/C ratio.

Supplementary Table S2. Joint risks of urinary melatonin or cortisol level and the PSA level associated with clinical staging of prostate cancer.

| Factor/category | | Control | Localized ¹ | Advanced ¹ | Localized ¹ vs. | Advanced ¹ vs. | Advanced ¹ vs. Localized ¹ | | | |
|------------------------------|--------------|-----------|------------------------|-----------------------|----------------------------|---------------------------|--|-------------------|------------------|-------------------|
| | | N=240 | N=51 | N=69 | control | control | | | | |
| | | N (%) | | | aOR ² | (95%CI) | aOR ² | (95%CI) | aOR ² | (95%CI) |
| | PSA | | | | | | | | | |
| Melatonin³ | level | | | | | | | | | |
| High | < 10 | 70 (30.6) | 9(18.0) | 3 (2.5) | 1.0 | (Ref) | 1.0 | (Ref) | 1.0 | (Ref) |
| Low | < 10 | 50 (21.8) | 9 (18.0) | 5 (4.2) | 1.38 | 0.51-3.77 | 2.34 | 0.53-10.35 | 1.69 | 0.30-9.42 |
| High | ≥ 10 | 54 (23.6) | 14 (28.0) | 20 (16.8) | 2.24 | 0.91-5.55 | 8.11 | 2.25-29.33 | 3.62 | 0.82-15.95 |
| Low | ≥ 10 | 55 (24.0) | 18 (36.0) | 41 (34.5) | 2.92 | 1.21-7.04 | 18.06 | 5.19-62.85 | 6.19 | 1.47-25.97 |

| Cortisol ³ | PSA | | | | | | | | | |
|-----------------------|-------|-----------|-----------|-----------|-------------|------------------|--------------|-------------------|-------------|-------------------|
| | level | | | | | | | | | |
| Low | < 10 | 61 (26.6) | 7 (14.0) | 4 (5.8) | 1.0 | (Ref) | 1.0 | (Ref) | 1.0 | (Ref) |
| High | < 10 | 59 (25.8) | 11 (22.0) | 4 (5.8) | 1.61 | 0.58-4.48 | 1.05 | 0.25-4.47 | 0.66 | 0.12-3.57 |
| Low | ≥ 10 | 62 (27.1) | 17 (34.0) | 22 (31.9) | 2.87 | 1.11-7.42 | 5.11 | 1.61-16.22 | 1.78 | 0.44-7.22 |
| High | ≥ 10 | 47 (20.5) | 15 (30.0) | 39 (56.5) | 2.91 | 1.09-7.75 | 12.74 | 4.17-38.91 | 4.38 | 1.10-17.36 |

PSA = prostate-specific antigen.

¹Localized PCa defined as stage T1 or T2 at diagnosis; Advanced PCa defined as stage T3 or T4 and or LN or distant metastases at diagnosis

²Adjusting for the same variables in Table 2.

³Medians of 43.23 ng/mg creatinine for melatonin, 24.06 ng/mg creatinine for cortisol, and 1.76 for MT/C ratio.