

Sleep Disturbance, Hot Flashes, and Urinary Frequency in Prostate Cancer Patients Treated with Androgen Deprivation Therapy

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ADT, Testosterone, and Prostate Cancer

- Androgen deprivation therapy (ADT) (i.e., goserelin, leuprolide) used to treat prostate cancer at intermediate or high risk of recurrence or local metastasis
- Eliminates testosterone, which slows the growth of cancer
- Associated with a number of side effects, including hot flashes and fatigue

Testosterone, Sleep, and ADT

- Testosterone may help to modulate sleep
 - Prostate cancer patients treated with ADT report sleep disturbance (Stephens et al. BJU International 2007; 99: 310-310)
 - Demonstrate average of 5.9 hours of sleep per night, frequent awakening, and report daytime sleepiness (Hanisch et al. Eur J Cancer Care 2011; 20: 549-554)
- Extent to which these problems are specific to ADT treatment is unclear
 - Sleep disturbance also common in aging men
 - May be associated with normal declines in testosterone (Anderson et al. Sleep Med Rev 2008; 12: 365-79)

Study Aims

- To compare objective sleep disturbance in prostate cancer patients treated with ADT and matched controls
 - Prostate cancer patients treated with prostatectomy
 - Men with no cancer history
- To examine symptoms of ADT which may mediate sleep disturbance
 - Hot flashes
 - Nocturia

Methods: Study Design

- Substudy of a larger study of quality of life in men treated with ADT for prostate cancer
 - Patients recruited on or before day of ADT initiation
- 3 groups of men:
 - Diagnosed with prostate cancer undergoing ADT (ADT+)
 - Diagnosed with prostate cancer treated with surgery only (ADT-)
 - Non-cancer controls (CA-)
- Matched on:
 - Age (within 3 years)
 - Education (3 levels)
 - Time since diagnosis (ADT+ & ADT-)
- ADT+ participants assessed 6 months after initiation of ADT/recruitment to larger study

Methods: Eligibility Criteria

All participants

- ≥ 18 years of age
- $\geq 6^{\text{th}}$ grade education
- Able to speak/read English
- Able to provide informed consent

ADT+

- Diagnosed with non-metastatic/asymptomatic metastatic prostate cancer
- Scheduled to be treated with ADT for at least 12 months
- No previous ADT treatment

ADT-

- Diagnosed with non-metastatic prostate cancer
- No other treatment besides a prostatectomy
- No testosterone supplementation

CA-

- No history of a cancer diagnosis besides non-melanoma skin cancer
- No testosterone supplementation

Methods: Measures

- Objective sleep disturbance was assessed using actigraphy
 - Actiwatch Score (MiniMitter, Bend, OR)
 - Worn on non-dominant wrist continuously for three consecutive days
 - Measures intensity of motion in one minute intervals
 - Validated measure of sleep
(Morgenthaler et al. Sleep 2007; 30: 519-529)
 - Real time assessment of hot flashes



Methods: Measures

- Daily diary of bedtime, rising time, urinary frequency

Daily Diary		
Dates _____ to _____		
Day: <u>Sunday</u> Date: <u>Nov. 26</u>		Notes:
Rising time: <u>7:30</u>	Number of times you urinated during the day: <u>6</u>	
Bed time: <u>11:30</u>	Number of times you urinated at night: <u>4</u>	

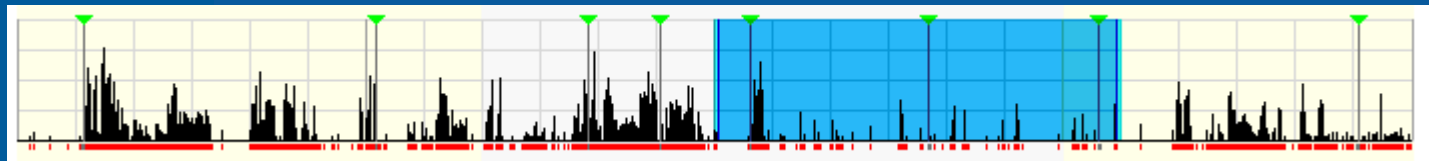
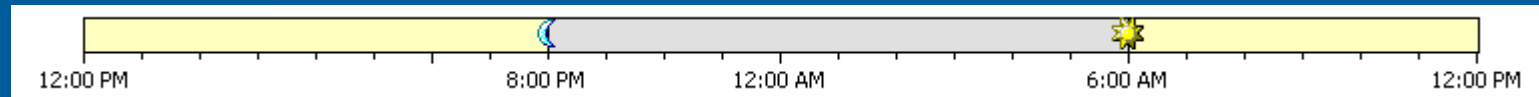
Methods: Statistical Analyses

- Sociodemographic and clinical comparisons
 - One-way ANOVA and chi-square
- Comparisons of objective sleep disturbance, hot flashes, and nocturia
 - One-way ANOVA with LSD post-hoc tests
- Relationship among symptoms
 - Pearson correlations
- Mediation
 - Linear regression in accordance with Baron and Kenny (1986)
 - Sobel tests of indirect effects

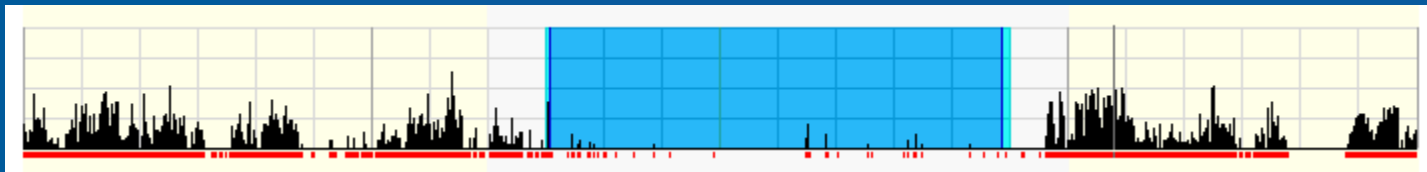
Results: Participants

	ADT+ (n=32)	ADT- (n=31)	CA- (n=28)	<i>p</i> value
Age: mean (range)	68 (49-90)	67 (56-82)	69 (55-90)	.79
College graduate	41%	42%	54%	.55
Years since diagnosis	2.68	4.52	--	.11
Caucasian	94%	97%	93%	.78
Hispanic	3%	7%	4%	.76
Annual household income (≥\$40k)	52%	70%	65%	.39

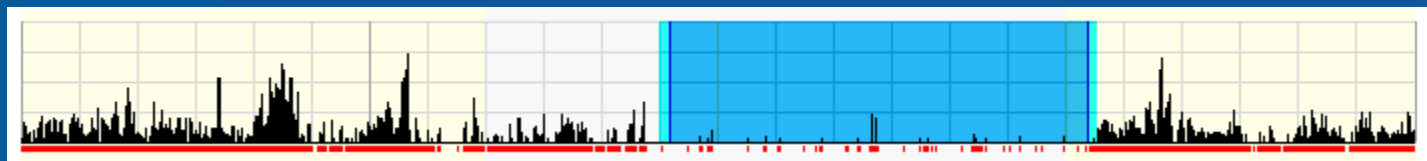
Actigraphy Data



ADT+ participant



ADT- participant



CA- participant

Results: Group Differences in Symptoms

Variable	ADT+ (n=34)	ADT- (n=32)	CA- (n=28)	F
Time in bed at night	496.67	478.34	478.82	.65
Nighttime activity	37.73	31.04	26.60	2.38
Sleep onset latency	23.51	17.00	26.20	1.38
WASO	77.16^a	60.70^b	54.29^b	5.23^{**}
Sleep efficiency	75.05^a	80.16^b	80.00^b	3.65[*]
Nighttime hot flashes	.06	.00	.01	1.00
Nighttime urinary frequency	3.34^a	1.60^b	1.48^b	10.64^{**}

Note: Differing subscripts indicate statistically significant group differences

*p<.05, **p<.01

Results: Relationships Among Symptoms in ADT Patients

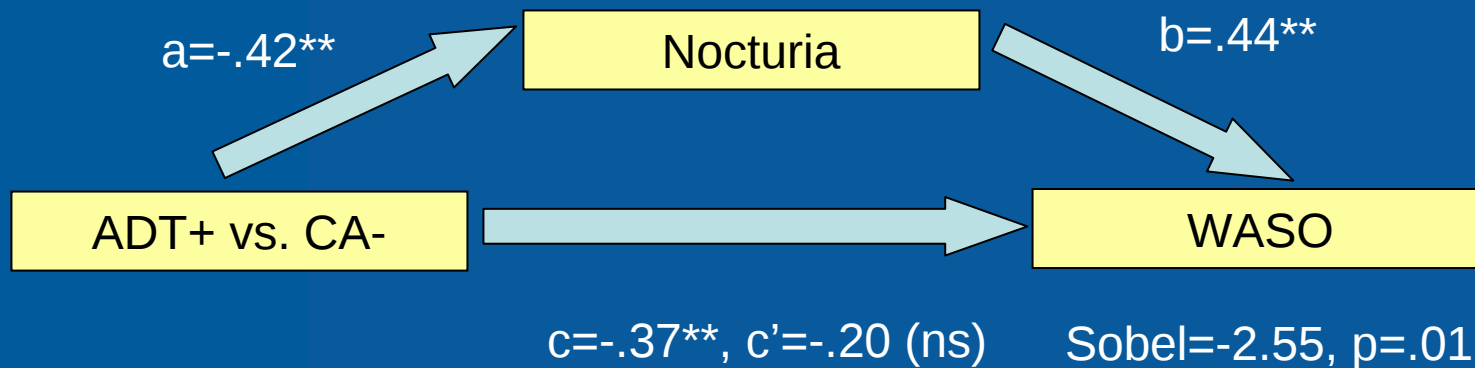
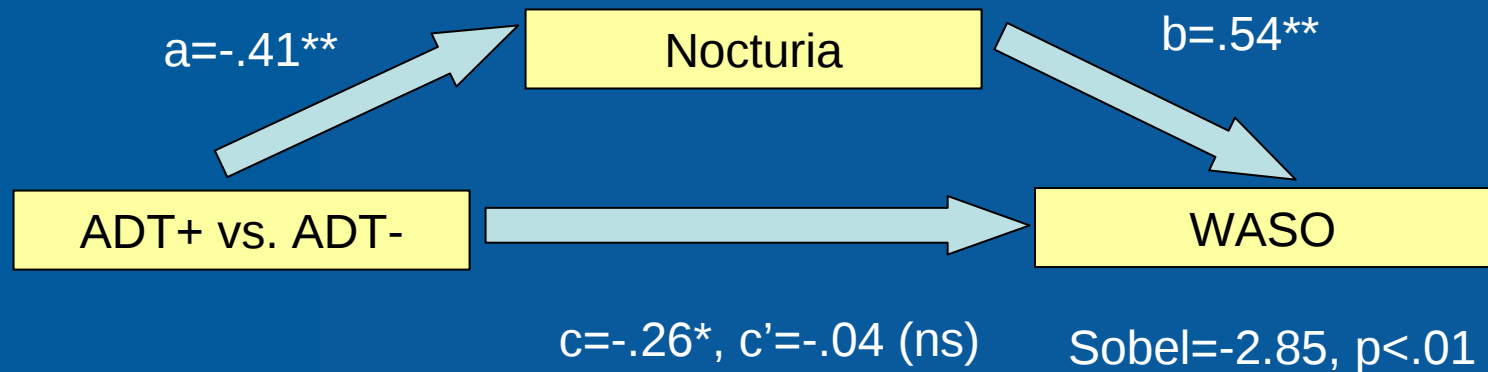
	WASO	Sleep efficiency	Nighttime hot flashes	Nighttime urinary frequency
WASO	1.00			
Sleep efficiency	-.70**	1.00		
Nighttime hot flashes	.04	.05	1.00	
Nighttime urinary frequency	.55**	-.50**	-.03	1.00

**p<.01

Results: Mediation models

- Because WASO and sleep efficiency were highly correlated in ADT+ patients ($r^2=.70$), we selected one (i.e, WASO) to test in mediation model
- Compared ADT+ to ADT-, ADT+ to CA-
- Models tested: Group $\rightarrow$ Nocturia $\rightarrow$ WASO

Results: Mediation models



Summary of Findings

- Patients treated with ADT displayed significantly greater WASO, worse sleep efficiency, and more nocturia than patients treated with prostatectomy and men without cancer
- No differences were found among groups in real-time assessment of hot flashes
- Greater sleep disturbance was associated with greater nocturia but not hot flashes
- Nocturia mediated the relationship between ADT treatment and sleep disturbance

Discussion

- Findings on poor sleep, nocturia among patients treated with ADT consistent with previous literature (Hanisch et al. Eur J Cancer Care 2011; 20: 549-554)
 - First study to our knowledge comparing these symptoms in ADT patients to matched controls
 - Suggests that symptoms are not the result of cancer itself or normal aging
- Suggests that poor sleep is not the result of hot flashes
 - Consistent with self-report measures of sleep and hot flashes in the same study
 - Limitations of real-time hot flash data collection
- Patients should be educated regarding sleep disturbance and nocturia as side effects of cancer
 - Treatment for urinary frequency (e.g., tolterodine, oxybutynin) may improve sleep in patients treated with ADT

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