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Research Article

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Night shiftwork and prostate-specific antigen level in a tire manufacturing factory

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Abbreviations
BMI: body mass index; CI: confidence interval; IRB: Institutional Review Board; OR: odds ratio; PSA: prostate-specific antigen.

ABSTRACT

Background: Recent studies suggest that night shiftwork may increase the risk of prostate cancer and elevated serum prostate-specific antigen (PSA) level. The purpose of this study was to verify whether rotating night shiftwork affects serum PSA level.
Methods: This study included 3,195 male production workers who work in a large tire manufacturing factory. Serum PSA levels were measured and the data on related factors were obtained.
Results: The mean serum PSA level was 0.98 ± 0.79 ng/mL. PSA levels were significantly lower in the younger age group, the obese group, and regular exercise group. PSA levels were lower in night shift workers (n = 2,832) compared to day workers (n = 363), but the difference was not statistically significant.
Conclusions: Unlike previous studies, we did not find any evidence that night shiftwork results in an increase in serum PSA levels. Further research and consistent results are needed to elucidate the association between night shiftwork and the effect on the prostate.

Keywords: Circadian rhythm; Prostate cancer; Prostate-specific antigen; Shiftwork

BACKGROUND

The International Agency for Research on Cancer, which is part of the World Health Organization, classified shiftwork involves circadian disruption as probably carcinogenic to humans (group 2A) based on sufficient evidence [1]. While night shiftwork is known to increase the risk of breast cancer, but its association with prostate cancer is still controversial [2-4]. A previous meta-analysis performed suggests that night shiftwork increase the risk of prostate cancer [5]. Another meta-analysis found no obvious association between night shiftwork and prostate cancer, but subgroup analysis suggests that night shiftwork may increase the risk of prostate cancer in Asian men [6]. In a retrospective cohort of rotating shiftwork, a non-statistically significant elevated risk of prostate cancer was reported (odds ratio [OR]: 1.79, 95% confidence interval [CI]: 0.57–5.68) [7]. A population-based case-control study suggests that a long duration of permanent night work in combination with a long shift length or at least 6 consecutive nights may be associated with prostate cancer [8].

Competing interests
The authors declare that they have no competing interests.

Availability of data and materials
The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Authors contributions
Conceptualization: Park WJ; Data curation: Kim S; Investigation: Kang W; Validation: Moon JD; Writing - original draft: Cho S; Writing - review & editing: Park WJ, Lim DY.

Prostate-specific antigen (PSA) is often elevated in prostate disorders, especially prostate cancer. An earlier study revealed a strong positive association with current shiftwork and elevated PSA level at 4.0 ng/mL or greater (OR: 2.62, 95% CI: 1.16–5.95) [9]. This research supports the notion that sleep disturbance or circadian disruption is associated with elevated PSA. Thus, night shift workers likely have an increased risk of developing prostate cancer. But so far, there is only one study that shiftwork increase PSA level. The aim of this study was to investigate whether PSA level was associated with men performing night shiftwork.

METHODS

Study subjects

Study subjects consisted of 3,295 Korean male production workers in a large tire manufacturing factory who underwent health examinations between October 2015 and November 2015. The production process was a system that runs 24 hours a day. All night shift workers performed the same type of shift. The working schedules of the tire manufacturing factory we studied were as follows: 1) regular day work and 2) rotating shift work. The regular day work schedule started at 08:30 and ended at 17:30 hours daily. It's a schedule that works 5 days a week. Rotating shift workers performed in a four-teams-three-shift system. The rotating shift work schedule was as follows: four teams, three 8-hour shift, 5 day shifts (from 7:00 to 15:00 hours), 1 day off, 5 night shifts (from 23:00 to 7:00 hours), 2 days off, 5 swing shifts (from 15:00 to 23:00 hours), and 2 days off. It is a schedule of the 20-day cycle. And there was no difference in the tasks performed between night shift worker and day worker. We excluded 79 workers under 30 years of age. Night shift workers were defined as current night shift workers performing night shiftwork for more than 3 years. Individuals currently performing daytime work were defined as day workers. Individuals with night shiftwork experience within the last 3 years were excluded from the day workers group. Twenty-one workers who are currently receiving treated for prostate diseases, such as prostate cancer or benign prostate hyperplasia, were excluded. A total of 3,195 workers were selected as the final subjects. All subjects were Koreans.

Data collection

In this study, the PSA test was conducted with health examination by the Occupational Safety and Health Act, as required by the labor union. Therefore, all subjects in the factory participated in the study without exception. Information about prostate diseases was obtained through a structured questionnaire. There was no statistically significant difference in prostate diseases between the night shiftwork group and day work group per χ^2 test. All subjects fasted for 12 hours or more before undergoing measurements of serum PSA. Regular exercise was defined as performing regular exercise greater than 30 minutes per day more than twice a week. A drinker was defined as an individual who drinks more than 20 grams of alcohol more than twice a week. Their body mass index (BMI) was calculated using the following formula:

$$\text{BMI} = \text{weight (kg)}/\text{height}^2\ (\text{m}^2)$$

Cases on a current antihypertensive regimen or cases with blood pressure of ≥ 140/90 mmHg were defined as hypertensive. Subjects with diabetes mellitus were defined as those who were being treated for diabetes mellitus or had serum glucose levels ≥ 126 mg/dL. In addition, each subject provided written informed consent before participating.

Statistical analysis

We performed a cross-sectional study of 2,832 rotating night shift workers and 363 regular day workers over 30 years of age. The age range was 30 to 58 years. Since PSA levels did not show a normal distribution pattern, we carried out natural log transformation before analysis. Univariate measures of demographic characteristics were calculated for night shift workers compared to day workers. All categorical variables were compared using chi-square test, and all continuous variables were compared using Student's t-test or analysis of variance. Analyses of covariance were performed to compare the mean serum PSA levels between night shift workers and day workers after adjusting for confounders. The elevated serum PSA was defined as serum PSA ≥ 4.0 ng/mL [10]. The OR with 95% CI of elevated serum PSA for shiftwork was calculated by taking the day worker as the referent using multivariable logistic regression models. SPSS version 23.0 was used to analyze the data (SPSS Inc., Chicago, IL, USA). Statistical significance was defined as $p < 0.05$.

Ethics statement

This study protocol was approved by the Institutional Review Board (IRB) of Chonnam National University Hwasun Hospital (IRB No. CNUHH-2014-123). In addition, each subject provided written informed consent before participating.

RESULTS

The arithmetic mean of serum PSA level was 0.98 ± 0.79 ng/mL. The mean age of the night shift and day shift workers was 46.9 ± 5.5 years and 45.5 ± 7.5 years, respectively. The night shift workers' age was significantly higher than day workers ($p < 0.001$). The BMI of the night shift workers and day shift workers was 24.9 ± 2.8 and 25.3 ± 3.0, respectively. The night shift workers' BMI was significantly lower than day workers ($p = 0.003$). The night shift workers showed a higher percentage of smoking, drinking, and regular exercise, which was not statistically significant. Hypertension and diabetes mellitus were not significantly different between the 2 groups (**Table 1**).

As age increased, PSA levels increased significantly ($p < 0.001$). The PSA levels were significantly lower in the obese group (BMI ≥ 25) than in the non-obese group (BMI < 25) ($p = 0.005$). PSA levels were also significantly lower in the regular exercise group than in the group that did not exercise regularly ($p = 0.007$). There were no significant differences in PSA levels according to smoking, drinking, and night shiftwork. PSA levels were lower in night shift workers compared to day workers, but the difference was not statistically significant. There was still no significant difference after adjusting for the confounders (**Table 2**). There was no difference in PSA levels according to hypertension and diabetes mellitus in this study. OR and 95% CIs were calculated using a multiple logistic regression analysis, with a PSA of ≥ 4.0 ng/mL as the dependent variable. In all models, the OR was lower in night shift workers but not statistically significant (**Table 3**).

DISCUSSION

In this study, PSA levels were lower in night shift workers compared to day workers, but the difference was not statistically significant. There was still no significant difference after adjusting for the confounders. Contrary to previous study, we found no evidence that night shiftwork raises the level of serum PSA. Our results suggest that shiftwork may not have an effect on serum PSA levels.

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Table 1. General characteristics of subjects

Variables	Day worker (n = 363)	Night shift worker (n = 2,832)	*p*-value[a]
Age (years)	45.5 ± 7.5	46.9 ± 5.5	< 0.001
30–39	86 (23.7)	242 (8.5)	< 0.001
40–44	53 (14.6)	738 (26.1)	
45–49	94 (25.9)	887 (31.3)	
50–54	93 (25.6)	698 (24.6)	
55–59	37 (10.2)	267 (9.4)	
Tenure (years)	20.4 ± 9.2	21.5 ± 6.2	0.030
BMI (kg/m^2)	25.3 ± 3.0	24.9 ± 2.8	0.003
< 25	153 (42.1)	1,284 (45.3)	0.263
≥ 25	210 (57.9)	1,548 (54.7)	
Smoking			0.104
Non-smoker	107 (29.5)	700 (24.7)	
Ex-smoker	118 (32.5)	924 (32.6)	
Current smoker	138 (38.0)	1,208 (42.7)	
Drinking			0.667
No	281 (77.4)	2,159 (76.2)	
Yes	82 (22.6)	673 (23.8)	
Regular exercise			0.549
No	270 (74.4)	2,060 (72.7)	
Yes	93 (25.6)	772 (27.3)	
Hypertension			0.216
No	315 (86.8)	2,521 (89.0)	
Yes	48 (13.2)	311 (11.0)	
Diabetes mellitus			0.922
No	332 (91.5)	2,581 (91.1)	
Yes	31 (8.5)	251 (8.9)	
PSA levels (ng/mL)			0.073
< 1.0	219 (60.3)	1,868 (66.0)	
≥ 1.0, < 2.0	123 (33.9)	791 (27.9)	
≥ 2.0, < 3.0	14 (3.9)	116 (4.1)	
≥ 3.0, < 4.0	1 (0.3)	28 (1.0)	
≥ 4.0	6 (1.7)	29 (1.0)	

Values are presented as number (%), arithmetic mean ± standard deviation or *p*-value.
BMI: body mass index; PSA: prostate-specific antigen.
[a]Comparison by Student's t-test or Pearson χ^2 test.

The epidemiological evidence examining the relationship between night shiftwork and breast cancer is now appreciable. Furthermore, possible association between night shiftwork and prostate cancer was also examined. According to the conclusions of a recently published review article, the evidence for prostate cancer is strong, but still insufficient to allow any firm conclusions to be made [11]. There is still debate, but several studies have shown a significant relationship between prostate cancer and shiftwork [6,7,9,12-15]. The mechanisms are also unclear, but there are the following hypotheses. According to the potential causality pathway, artificial light at night, reaching the human retina, suppresses nocturnal production of melatonin, an anti-oncogenic agent, resulting in the increased risk of cancer development [16]. Disruption of circadian rhythm is responsible for the loss of regulatory function of cells. Vitamin D deficiency, a decline in immunity due to sleep deprivation, and harmful lifestyle factors (such as poor-quality diets, altered mealtimes, less physical activity, and higher BMI) are suggested as causes [17,18]. Sleep deprivation suppresses natural killer-cell activity and changes the T-helper 1/T-helper 2 cytokine balance, reducing cellular immune defense and surveillance. Sleep in the modulation of immunity and demonstrate that even a modest disturbance of sleep produces a reduction of natural immune responses and T cell cytokine production [19-21].

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Table 2. Serum prostate-specific antigen levels (ng/mL) by variables

Variables	No.	Arithmetic (mean ± SD)	Geometric (mean ± GSD)	*p*-value[a]	Adjusted geometric mean	*p*-value[b]
Age (years)				< 0.001		< 0.001
30–39	328	0.89 ± 0.50	0.78 ± 1.65		0.78	
40–44	791	0.90 ± 0.61	0.77 ± 1.76		0.77	
45–49	981	0.96 ± 0.87	0.80 ± 1.76		0.80	
50–54	791	1.06 ± 0.91	0.85 ± 1.88		0.86	
55–59	304	1.11 ± 0.83	0.91 ± 1.85		0.91	
BMI (kg/m^2)				0.004		0.005
< 25	1,437	1.01 ± 0.78	0.84 ± 1.78		0.84	
≥ 25	1,758	0.95 ± 0.81	0.79 ± 1.79		0.79	
Smoking				0.642		0.737
Non-smoker	807	0.96 ± 0.71	0.80 ± 1.84		0.80	
Ex-smoker	1,042	0.99 ± 0.89	0.82 ± 1.77		0.82	
Current-smoker	1,346	0.98 ± 0.76	0.81 ± 1.78		0.82	
Drinking				0.768		0.740
No	2,440	0.97 ± 0.71	0.81 ± 1.79		0.81	
Yes	755	0.99 ± 1.01	0.81 ± 1.79		0.81	
Regular exercise				0.006		0.005
No	2,330	0.99 ± 0.83	0.83 ± 1.78		0.83	
Yes	865	0.93 ± 0.69	0.78 ± 1.82		0.77	
Night shiftwork				0.192		0.067
No	363	1.04 ± 1.14	0.84 ± 1.87		0.86	
Yes	2,832	0.97 ± 0.74	0.81 ± 1.78		0.81	

Values are presented as mean ± standard deviation or *p*-value.
BMI: body mass index; GSD: geometric standard deviation; SD: standard deviation.
[a]Comparison by Student's t-test and analysis of variance; [b]Comparison by analysis of covariance adjusted for age, BMI, and exercise.

Table 3. Night shiftwork and risk for elevated serum prostate-specific antigen (≥ 4.0 ng/mL)

Variables	Adjusted OR	95% CI	β	SE	*p*-value
Day work[a]	Reference				
Night shiftwork[b]					
Model 1	0.584	0.24–1.47	−0.539	0.453	0.235
Model 2	0.596	0.25–1.45	−0.520	0.454	0.255
Model 3	0.563	0.23–1.38	−0.579	0.457	0.209

Model 1: adjusted for age. Model 2: adjusted for age, body mass index, and exercise. Model 3: adjusted for age, body mass index, exercise, smoking, drinking, hypertension, and diabetes mellitus.
CI: confidence interval; OR: odds ratio; SE: standard error.
[a]Workers who have never worked night shiftwork in last 3 years; [b]Workers who have been on night shiftwork for the last 3 years.

Unlike previous studies, we show that PSA was lower in the night shiftwork group. Although we could not determine the exact cause, there are possibilities as to why. First, our results suggest that there may be no association between night shiftwork and prostate cancer, or PSA increasing may not be involved in the mechanism in which night shiftwork causes prostate cancer. Second, the effect of including strong healthy workers could reverse the association between shiftwork and serum PSA level. Those who are vulnerable to health hazards are likely to quit night shiftwork and move to day work. And tire manufacturing is a physically burdensome job. So only physically healthy workers are likely to remain in the production workplace, especially night shiftwork. The average work experience of the subjects in this study exceeded 20 years. It is possible that the surviving workers have been adapted to long-term regular night duty schedules. Shift workers' sleep-wake disturbances can be minimized through ergonomic proper scheduling [22]. Third, occupational and recreational physical activity may help reducing prostate diseases. Physical activity may have an inverse association with prostate cancer and benign prostatic hyperplasia risk [23,24]. In this study, PSA levels were also significantly lower in the regular exercise group than in the group that did not exercise regularly. There may have been differences in occupational physical activity between

day and shift workers. In the future study, objective evaluation of physical activity may be necessary. Fourth, another reason is the possibility of publication bias. Publication bias is defined as the tendency on the parts of investigators, reviewers, and editors to submit or accept manuscripts for publication based on the direction or strength of the study findings. Publishing only results that show a significant finding disturbs the balance of findings and inserts bias in favor of positive results [25]. It is possible that insignificant studies, such as this study, have not been published. More research results should be accumulated to elucidate the impact of night shiftwork on the prostate.

In this study, PSA levels were significantly low in the younger age group, the obese group, and regular exercise group. These results are consistent with previous studies. As age increases, serum PSA level increases. For every unit increase in age, PSA increased by 0.034 ng/mL [26]. Previous studies have shown an inverse relationship between BMI and PSA level. Lower levels of PSA in obese and overweight men could potentially mask prostate cancer. Evidence suggests that prostate cancer screening by serum PSA may be adversely affected by increased BMI. Higher BMI was associated with higher plasma volume, and hemodilution may therefore be responsible for the lower serum PSA concentrations. High BMI has been directly associated with risk of aggressive or fatal prostate cancer [27-30]. Individuals who engage in more sedentary behavior and lower levels of physical activity have higher PSA concentrations [31,32].

The limitations of this study are as follows. First, we could not exclude the effect of unknown confounders in this study. PSA is not cancer specific. Serum PSA levels are also increased in various conditions. The tire manufacturing factory uses a variety of chemical hazards including organic solvents and various rubber components, which many workers are exposed to. Previous studies have shown the possibility of chemical exposure and its association with PSA level. Exposure to either dichloro-diphenyl-trichloroethane or dichloro-diphenyl-dichloroethylene may produce a false-negative PSA test when screening for prostate cancer, resulting in an inaccurate clinical diagnosis. And tetrachlorodibenzodioxin exposure might be associated with more aggressive prostate cancer [33,34]. Other confounding variables include the effect of ejaculation or constipation on the serum total PSA, which we did not examine [35,36]. Future studies will need to consider detailed occupational and personal information. Owing to the limitations of cross-sectional studies, it was not possible to determine if there was a precise causal relationship. In this study, only about 1% (35 out of 3,195) of the total were those with PSA levels of 4.0 ng/mL or higher. It may not be suitable for performing multiple logistic regression models. Therefore, we attempted various analyses, such as Poisson regression analysis, but could not produce other significant results. And, this study focused exclusively on a specific occupation working in a factory and may not generalize to the entire population. Another limitation is the fact that only the total PSA is measured, and the free PSA is not measured. Use of the percentage of free PSA show better improves the specificity in predicting prostate cancer compared with using total PSA alone [37]. Individual differences in internal time (chronotype) is an important factor in shiftwork research. Chronotype plays a key role in a worker's ability to adjust to night shiftwork [38,39]. However, there is a limitation in this study that we did not consider it.

CONCLUSIONS

We compared the serum PSA levels of night shift workers and day workers employed in a large manufacturing factory. PSA level was lower in night shift worker compared to the day

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worker, but it was not statistically significant. Our results suggest that night shiftwork may not influence serum PSA levels. Additional research and consistent results are needed to elucidate the association between night shiftwork and prostate cancer.

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REFERENCES

1. International Agency for Research on Cancer (IARC). Paintings, firefighting, and shiftwork. IARC monographs on the evaluation of carcinogenic risks to humans. Volume 98. 2010. https://monographs.iarc.fr/ENG/Monographs/vol98/mono98.pdf. Accessed 15 Aug 2019.
2. Hansen J. Night shift work and risk of breast cancer. Curr Environ Health Rep 2017;4(3):325-39. PUBMED | CROSSREF
3. Wegrzyn LR, Tamimi RM, Rosner BA, Brown SB, Stevens RG, Eliassen AH, et al. Rotating night-shift work and the risk of breast cancer in the nurses' health studies. Am J Epidemiol 2017;186(5):532-40. PUBMED | CROSSREF
4. Lee HE, Lee J, Jang TW, Kim IA, Park J, Song J. The relationship between night work and breast cancer. Ann Occup Environ Med 2018;30:11. PUBMED | CROSSREF
5. Rao D, Yu H, Bai Y, Zheng X, Xie L. Does night-shift work increase the risk of prostate cancer? a systematic review and meta-analysis. Onco Targets Ther 2015;8:2817-26. PUBMED
6. Du HB, Bin KY, Liu WH, Yang FS. Shift work, night work, and the risk of prostate cancer: a meta-analysis based on 9 cohort studies. Medicine (Baltimore) 2017;96(46):e8537. PUBMED | CROSSREF
7. Kubo T, Oyama I, Nakamura T, Kunimoto M, Kadowaki K, Otomo H, et al. Industry-based retrospective cohort study of the risk of prostate cancer among rotating-shift workers. Int J Urol 2011;18(3):206-11. PUBMED | CROSSREF
8. Wendeu-Foyet MG, Bayon V, Cénée S, Trétarre B, Rébillard X, Cancel-Tassin G, et al. Night work and prostate cancer risk: results from the EPICAP Study. Occup Environ Med 2018;75(8):573-81. PUBMED | CROSSREF
9. Flynn-Evans EE, Mucci L, Stevens RG, Lockley SW. Shiftwork and prostate-specific antigen in the National Health and Nutrition Examination Survey. J Natl Cancer Inst 2013;105(17):1292-7. PUBMED | CROSSREF
10. Catalona WJ, Smith DS, Ratliff TL, Dodds KM, Coplen DE, Yuan JJ, et al. Measurement of prostate-specific antigen in serum as a screening test for prostate cancer. N Engl J Med 1991;324(17):1156-61. PUBMED | CROSSREF
11. Crawford JO, Cherrie JW, Davis A, Dixon K, Alexander C, Cowie H, et al. A review of the impact of shift work on occupational cancer: part 2–mechanistic and health and safety evidence. Policy Pract Health Saf 2018;16(1):109-44. CROSSREF
12. Conlon M, Lightfoot N, Kreiger N. Rotating shift work and risk of prostate cancer. Epidemiology 2007;18(1):182-3. PUBMED | CROSSREF
13. Parent MÉ, El-Zein M, Rousseau MC, Pintos J, Siemiatycki J. Night work and the risk of cancer among men. Am J Epidemiol 2012;176(9):751-9. PUBMED | CROSSREF
14. Behrens T, Rabstein S, Wichert K, Erbel R, Eisele L, Arendt M, et al. Shift work and the incidence of prostate cancer: a 10-year follow-up of a German population-based cohort study. Scand J Work Environ Health 2017;43(6):560-8. PUBMED

15. Kubo T, Ozasa K, Mikami K, Wakai K, Fujino Y, Watanabe Y, et al. Prospective cohort study of the risk of prostate cancer among rotating-shift workers: findings from the Japan collaborative cohort study. Am J Epidemiol 2006;164(6):549-55.
PUBMED | CROSSREF

16. Rybnikova NA, Haim A, Portnov BA. Is prostate cancer incidence worldwide linked to artificial light at night exposures? Review of earlier findings and analysis of current trends. Arch Environ Occup Health 2017;72(2):111-22.
PUBMED | CROSSREF

17. Stewart LV, Weigel NL. Vitamin D and prostate cancer. Exp Biol Med (Maywood) 2004;229(4):277-84.
PUBMED | CROSSREF

18. Fritschi L, Glass DC, Heyworth JS, Aronson K, Girschik J, Boyle T, et al. Hypotheses for mechanisms linking shiftwork and cancer. Med Hypotheses 2011;77(3):430-6.
PUBMED | CROSSREF

19. Straif K, Baan R, Grosse Y, Secretan B, El Ghissassi F, Bouvard V, et al. Carcinogenicity of shift-work, painting, and fire-fighting. Lancet Oncol 2007;8(12):1065-6.
PUBMED | CROSSREF

20. Irwin M, McClintick J, Costlow C, Fortner M, White J, Gillin JC. Partial night sleep deprivation reduces natural killer and cellular immune responses in humans. FASEB J 1996;10(5):643-53.
PUBMED | CROSSREF

21. Dimitrov S, Lange T, Tieken S, Fehm HL, Born J. Sleep associated regulation of T helper 1/T helper 2 cytokine balance in humans. Brain Behav Immun 2004;18(4):341-8.
PUBMED | CROSSREF

22. Sallinen M, Kecklund G. Shift work, sleep, and sleepiness - differences between shift schedules and systems. Scand J Work Environ Health 2010;36(2):121-33.
PUBMED | CROSSREF

23. Dal Maso L, Zucchetto A, Tavani A, Montella M, Ramazzotti V, Polesel J, et al. Lifetime occupational and recreational physical activity and risk of benign prostatic hyperplasia. Int J Cancer 2006;118(10):2632-5.
PUBMED | CROSSREF

24. Friedenreich CM, Thune I. A review of physical activity and prostate cancer risk. Cancer Causes Control 2001;12(5):461-75.
PUBMED | CROSSREF

25. Song F, Parekh S, Hooper L, Loke YK, Ryder J, Sutton AJ, et al. Dissemination and publication of research findings: an updated review of related biases. Health Technol Assess 2010;14(8):iii, ix-xi, 1-193.
PUBMED | CROSSREF

26. Pater LE, Hart KW, Blonigen BJ, Lindsell CJ, Barrett WL. Relationship between prostate-specific antigen, age, and body mass index in a prostate cancer screening population. Am J Clin Oncol 2012;35(5):490-2.
PUBMED | CROSSREF

27. Bonn SE, Sjölander A, Tillander A, Wiklund F, Grönberg H, Bälter K. Body mass index in relation to serum prostate-specific antigen levels and prostate cancer risk. Int J Cancer 2016;139(1):50-7.
PUBMED | CROSSREF

28. Baillargeon J, Pollock BH, Kristal AR, Bradshaw P, Hernandez J, Basler J, et al. The association of body mass index and prostate-specific antigen in a population-based study. Cancer 2005;103(5):1092-5.
PUBMED | CROSSREF

29. Barqawi AB, Golden BK, O'Donnell C, Brawer MK, Crawford ED. Observed effect of age and body mass index on total and complexed PSA: analysis from a national screening program. Urology 2005;65(4):708-12.
PUBMED | CROSSREF

30. Freedland SJ, Platz EA, Presti JC Jr, Aronson WJ, Amling CL, Kane CJ, et al. Obesity, serum prostate specific antigen and prostate size: implications for prostate cancer detection. J Urol 2006;175(2):500-4.
PUBMED | CROSSREF

31. Loprinzi PD, Kohli M. Effect of physical activity and sedentary behavior on serum prostate-specific antigen concentrations: results from the National Health and Nutrition Examination Survey (NHANES), 2003–2006. Mayo Clin Proc 2013;88(1):11-21.
PUBMED | CROSSREF

32. Kim SH, Jang KH, Park WJ, Kwon DH, Kang WY, Lim HM, et al. Serum prostate-specific antigen levels and type of work in tire manufacturing workers. Ann Occup Environ Med 2014;26(1):50.
PUBMED | CROSSREF

33. Shah SR, Freedland SJ, Aronson WJ, Kane CJ, Presti JC Jr, Amling CL, et al. Exposure to Agent Orange is a significant predictor of prostate-specific antigen (PSA)-based recurrence and a rapid PSA doubling time after radical prostatectomy. BJU Int 2009;103(9):1168-72.
PUBMED | CROSSREF

34. Wong LI, Labrecque MP, Ibuki N, Cox ME, Elliott JE, Beischlag TV. p,p′-Dichlorodiphenyltrichloroethane (p,p′-DDT) and p,p′-dichlorodiphenyldichloroethylene (p,p′-DDE) repress prostate specific antigen levels in human prostate cancer cell lines. Chem Biol Interact 2015;230:40-9.
PUBMED | CROSSREF

35. Tarhan F, Demir K, Orcun A, Madenci OC. Effect of ejaculation on serum prostate-specific antigen concentration. Int Braz J Urol 2016;42(3):472-8.
PUBMED | CROSSREF

36. Bayraktar Z, Inan EH, Bayraktar V. Effect of constipation on serum total prostate-specific antigen levels in men. Int J Urol 2012;19(1):54-9.
PUBMED | CROSSREF

37. Catalona WJ, Partin AW, Slawin KM, Brawer MK, Flanigan RC, Patel A, et al. Use of the percentage of free prostate-specific antigen to enhance differentiation of prostate cancer from benign prostatic disease: a prospective multicenter clinical trial. JAMA 1998;279(19):1542-7.
PUBMED | CROSSREF

38. Kantermann T, Juda M, Vetter C, Roenneberg T. Shift-work research: Where do we stand, where should we go? Sleep Biol Rhythms 2010;8(2):95-105.
CROSSREF

39. Papantoniou K, Castaño-Vinyals G, Espinosa A, Aragonés N, Pérez-Gómez B, Burgos J, et al. Night shift work, chronotype and prostate cancer risk in the MCC-Spain case-control study. Int J Cancer 2015;137(5):1147-57.
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