TESTOSTERONE AND THE PROSTATE

BIBLIORAPHIE AND REFERENCES

1. Is testosterone treatment good for the prostate? Study of safety during long-term treatment. Feneley MR, Carruthers M. J Sex Med. 2012 Aug;9(8):2138-49. doi: 10.1111/j.1743-6109.2012.02808.x. Epub 2012 Jun 6.

1,365 men diagnosed with secondary testosterone deficiency syndrome in the UK Androgen Study were treated with testosterone replacement therapy (TRT) and monitored for up to 20 years. The prostate cancer incidence in the treated group did not differ from that of the general population. Testosterone therapy did not cause significant changes in free or total PSA; and PSA change was not predictive of of cancer diagnosis

2. Testosterone Replacement Therapy in Patients with Prostate Cancer After Radical Prostatectomy. Pastuszak A, Pearlman A, ShunLai W, Godoy G, Sthyamoorthy K, Liu J, Miles B, Lipschultz L, Khera M. The Journal of Urology, 19(2), 639-644.

Retrospective study of prostate cancer survivors treated with prostatectomy: 103 were hypogonadal, meaning either symptomatic of hypogonadism or having serum testosterone levels below 300 ng/dl, and treated with transdermal TRT following prostatectomy and 49 were eugonadal, without symptoms and with testosterone levels above 300 ng/dl. While PSA increased in the treatment group, only 4 cases of cancer recurrence were observed, while 8 were reported in the reference group. This study concluded that TRT does not appear to increase risk of prostate cancer recurrence.

3. The effect of testosterone replacement therapy on prostate cancer: a systematic review and meta-analysis. Cui Y, Zong H, Yan H, Zhang Y (2014 Jun). Prostate Cancer Prostatic Dis, 17(2), 132-43. doi: 10.1038/pcan.2013.60

This meta analysis of 22 RCTs totaling 2351 patients, half of which were greater than 12 months in duration, compared risk of prostate cancer related to route of administration of TRT. Despite differences in risk per route of administration, the risk was never statistically significant and the researchers concluded that TRT does not promote the development or progression of prostate cancer.

4. Is there a protective role of testosterone against high-grade prostate cancer? Incidence and severity of prostate cancer in 553 patients who underwent prostate biopsy: a prospective data register. Yassin A, Salman M, Talib RA, and Yassin D-J (2017). The Aging Male, 20(2), 125-133. DOI: 10.1080/13685538.2017.1298584

The results of this case study suggest that TRT may protect against high-grade prostate cancer. 42 hypogonadal men treated with TRT and 162 untreated along with 349 eugonadal men underwent prostate biopsies. Positive biopsies occurred in 51.9% of untreated hypogonadal men, 37.8% of eugonadal men and only 16.7% of the treated group. Gleason scores were above 6 in 59.5% of untreated hypogonadal men, 57.6% of the eugonadal men, and only 28.6% of treated hypogonadal men. Staging and grading was significantly lower in the TRT-treated men.

5. Testosterone Replacement Therapy and Risk of Favorable and Aggressive Prostate Cancer. Loeb S, Folkvaljon Y, Damber J-E, Alukai J, Lambe M, and Stattin P (2017 Mar). Journal of Clinical Oncology, 35(13), 1430-1436. DOI: 10.1200/JCO.2016.69.5304

This case control study involving 38,570 Swedish men with prostate cancer and 192,838 age-matched men without prostate cancer investigated whether any association exists between testosterone replacement therapy (TRT) and prostate cancer risk. One percent of the subjects received TRT. While no association was found between TRT and

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overall prostate cancer risk, TRT was significantly associated with lower risk of aggressive prostate cancer. More favorable-risk prostate cancer was found in the TRT group, but this may reflect increased screening by physicians prescribing TRT.

6. Testosterone and Prostate Safety. Morgentaler A and Schulman C (2009). Front Horm Res, 37, 197-203.

A study out of the Division of Urology at Harvard Medical School indicates that the lack of prostate risk despite increased serum testosterone levels can be explained by data showing that exogenous testosterone does not raise intraprostatic concentrations of testosterone or dihydrotestosterone, suggesting a saturation model. This paper concludes that in light of the available evidence testosterone therapy is safe for the prostate. However, as the population at risk for testosterone deficiency overlaps with that at risk for prostate cancer, it is important to screen patients receiving testosterone therapy for prostate cancer.

7. Does Testosterone Therapy Increase the Risk of Prostate Cancer? Dobs AS and Morgentaler A (2008 Oct). Endocr Pract, 14(7), 904-11.

A review article that summarizes trials of up to 36 months in length that found no evidence of an associated relationship between exogenous testosterone therapy and prostate cancer. Additionally, this review indicates that low endogenous testosterone may present an increased risk of prostate cancer.

8. Testosterone Replacement Therapy and Prostate Risks: Where's the Beef? Morgentaler A (2006). The Canadian Journal of Urology, 13 (Supplement 1), 40-43.

A review article on the risks of testosterone replacement therapy (TRT) and prostate cancer. The author notes men with endogenously higher testosterone levels have no
associated increased risk of prostate cancer. He also notes that clinical trials with exogenous testosterone supplementation demonstrate no increased risk of
prostate cancer. Interestingly, the author found that hypogonadal men with low testosterone levels and low prostate-specific antigen (PSA) values have a cancer rate
over double the normal population concluding that low testosterone levels are not protective against prostate cancer but in fact may associated with high grade cancers.

9. Testosterone Replacement Therapy in Hypogonadal Men at High Risk for Prostate Cancer: Results of 1 Year of Treatment in Men with Prostatic Intraepithelial Neoplasia. Rhoden E L and Morgentaler A (2003 Dec). J Urol, 170, 2348-2351.

A study evaluating prostatic changes in hypogonadal men treated with testosterone replacement therapy (TRT) for 1 year. The men were divided into 2 groups: Prostatic
intraepithelial neoplasia (PIN) negative and positive men. The conclusion after 1 year showed that testosterone replacement therapy (TRT) does not increase the risk of
prostate cancer in either PIN+ or PIN- males, demonstrating that TRT is not contraindicated in men with a history of PIN.

10. Testosterone Therapy in the Aging Male: What About the Prostate? Schultheiss D, Machtens S and Jonas U (2004). Andrologia, 36, 355-365

A good review article on the prostate, the history of treatment therapies for prostate enlargement and hormones that affect the prostate health. Studies show that after the fourth decade of life the prostate growth is independent

of hormone status and in fact as testosterone levels fall in later decades of life the prostate volume increases. More importantly the growth of the prostate in healthy aging men is caused by a shift of hormonal ratios i.e. the androgen/estrogen ratio decreases. It may be the relative increase in estrogen that increases cellular proliferation of the prostate and reduces normal apoptosis leading to benign prostatic hyperplasia (BPH). It is most likely estrogen signaling that is involved in the mechanism of prostate carcinogenesis, not testosterone.

As in the article above, the authors note that higher serum testosterone levels appear to demonstrate no increased risk of prostate cancer development. As well, testosterone replacement therapy (TRT) in a male with undetected prostate cancer does not appear to accelerate the growth of the cancer.

12. Testosterone Replacement Therapy in Hypogonadal Men and Prostate Cancer Risk. Kirby R and Gould D (2005). BJU International 96, 471 – 476.

Commentary on testosterone replacement therapy (TRT) and prostate cancer. Several studies using TRT over a period of 6-36 months have shown no increased risk of prostate cancer. There appears to be no compelling evidence that testosterone has a causative role in prostate cancer or in stimulating latent foci. In fact, prostate cancer becomes more prevalent at the age when testosterone levels decline. However, once malignant transformation is established testosterone plays a role in stimulating malignant cell activity.

13. Re: Prostate Cancer in Men Using Testosterone Supplementation. Morgentaler A and Rhoden EL (2006 Apr). J Urol, 175(4), 1572-1574.

The authors comment on the research paper which suggested that testosterone replacement therapy increases the risk of prostate cancer. The authors suggest a different interpretation of the data showing that the original study had serious flaws including missed baseline information regarding prostate-specific antigens (PSA) and delays of more than 2 years for cancer diagnosis "If testosterone replacement therapy (TRT) really acted as a switch that caused cancer to grow, would not one expect to see a worrisome increase in PSA or a change in the digital rectal examination within the first year of hormonal stimulation?" There is a substantial body of literature indicating that higher testosterone levels are not related to prostate cancer risk. There is no evidence that TRT, or high endogenous testosterone, increases the risk of prostate cancer.