How do I control (monitor) patients receiving TRT after prostate cancer treatment

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Greta and John Hansen Chair in Men’s Health Research
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University of Ottawa
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Eli Lilly Inc, Pfizer, Abbott, American Medical Systems, Coloplast, Actavis Specialty Pharmaceuticals
Hey TB,

I have 2 guys that I would appreciate if you could see as soon as you can. Both have been referred previously. I know you are wait list is long but open can help me out by squeezing these guys in.

The 1st is Mr. AS, [redacted]

I referred this man to you earlier this year. He is still awaiting an appointment. He is really struggling and is going through a major depression. In fact, to try to get him out of the depression I have given him testosterone in spite of the fact that he was on ADT, at his psychiatrist's suggestion. [suicidal ideation]

He was a successful and energetic businessman prior to his ADT. Part of his depression is related to loss of sexual activity from his radiation therapy and now ADT side effects. I saw him today and I told him I would ask you personally if you could see him soon. Let me know and we can re-fax the consultation. Otherwise it was sent on May 13, 2014.

Thanks very much,

Chris

[redacted]

Associate Professor of Surgery, University of Ottawa
Medical Director,
The Ottawa Hospital Prostate Cancer Assessment Centre
Whereas most clinicians are familiar with the ethical concept “Primum non nocere,” or “First, do no harm,” all medical treatments entail some degree of risk, as does withholding treatment. A lesser known, but arguably more appropriate dictum for medical care is “Salus aegroti suprema lex,” or “Do what is best for the patient,” a concept that incorporates clinical judgment amid uncertainty, and honors the wishes and goals of the patient.
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Testosterone Replacement Therapy Following the Diagnosis of Prostate Cancer: Outcomes and Utilization Trends

Alan L. Kaplan, MD,* Quoc-Dien Trinh, MD,† Maxine Sun, PhD,‡ Stacey C. Carter, MD,* Paul L. Nguyen, MD,§ Ya-Chen Tina Shih, PhD,‖ Leonard S. Marks, MD,* and Jim C. Hu, MD, MPH*

*Department of Urology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; †Center for Surgery and Public Health, Division of Urologic Surgery, Brigham and Women’s Hospital, Boston, MA, USA; ‡Cancer Prognostics Health Outcomes Unit, University of Montreal Health Centre, Montreal, QC, Canada; §Department of Radiation Oncology, Brigham and Women’s Hospital, Boston, MA, USA; ‖Section of Hospital Medicine, Department of Medicine Program in the Economics of Cancer, University of Chicago, Chicago, IL, USA

Methods. Using linked Surveillance, Epidemiology, and End Results-Medicare data, we identified 149,354 men diagnosed with prostate cancer from 1992 to 2007. Of those, 1,181 (0.79%) men received exogenous testosterone following their cancer diagnosis. We used propensity scoring analysis to examine the effect of testosterone replacement on the use of salvage hormone therapy and overall and prostate cancer-specific mortality.

Main Outcome Measures. We assessed overall mortality, cancer-specific mortality, and the use of salvage hormone therapy.

Results. Following prostate cancer diagnosis, testosterone replacement was directly related to income and educational status and inversely related to age (all $P < 0.001$). Men undergoing radical prostatectomy and men with well-differentiated tumors were more likely to receive testosterone (all $P < 0.001$). On adjusted analysis, testosterone replacement therapy was not associated with overall or cancer-specific mortality or with the use of salvage hormone therapy.

Conclusions. In this population-based observational study of testosterone replacement therapy in men with a history of prostate cancer, treatment was not associated with increased overall or cancer-specific mortality. These findings suggest testosterone replacement therapy may be considered in men with a history of prostate cancer, but confirmatory prospective studies are needed. Kaplan AL, Trinh QD, Sun M, Carter SC, Nguyen PL, Shih YCT, Marks LS, and Hu JC. Testosterone replacement therapy following the diagnosis of prostate cancer: Outcomes and utilization trends. J Sex Med 2014;11:1063–1070.
The relationship between total testosterone levels and prostate cancer: A review of the continuing controversy

Julia KLAP\(^1\), Marianne SCHMID\(^1\) and Kevin R. LOUGHLIN\(^1\)

\(^1\)Division of Urologic Surgery, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA

The risk of TRT for men with a history of PCa appears to be small, but appropriate regular monitoring of such patients is recommended.

The preponderance of studies examining the safety of exogenous testosterone administration in men with a history of PCa would suggest that there is little, if any risk, in such a circumstance. However, the risk has not been proven to be zero, so the most prudent course is to follow such men with regular PSAs and digital rectal exams.
POST-RADICAL PROSTATECTOMY TREATMENT WITH TESTOSTERONE
Testosterone Replacement Therapy in Patients with Prostate Cancer After Radical Prostatectomy

Alexander W. Pastuszak,* Amy M. Pearlman,* Win Shun Lai,* Guilherme Godoy,* Kumaran Sathyamoorthy,* Joceline S. Liu,* Brian J. Miles,* Larry I. Lipshultz† and Mohit Khera‡,§

From the Scott Department of Urology (AWP, GG, KS, LIL, MK), Baylor College of Medicine (WSL), and Methodist Urology Associates, The Methodist Hospital (BJM), Houston, Texas; Department of Urology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania (AMP); and Department of Urology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois (JSL)

While the accepted lower limit of normal serum T is 300 to 375 ng/ml, our clinical experience indicates that men with hypogonadal symptoms, even with serum T levels greater than the lower limit of normal, benefit from TRT. Thus, men with hypogonadal symptoms and serum T levels greater than 300 ng/dl were also treated. Baseline serum hormone, PSA, Hgb and Hct levels were assessed within 3 months of RP, and sequentially every 3 to 6 months after TRT initiation.
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The Laboratory Diagnosis of Testosterone Deficiency

DARIUS A. PADUCH, MD, PHD, ROBERT E. BRANNIGAN, MD, EUGENE F. FUCHS, MD, EDWARD D. KIM, MD, JOEL L. MARMAR, MD, AND JAY I. SANDBLOW, MD

measurements in the clinical laboratory setting. There is no universally accepted threshold of T concentration that distinguishes eugonadal from hypogonadal men, thus laboratory results have to be interpreted in the appropriate clinical setting. This review focuses on clinical, biological and technological challenges that affect serum T measurements to educate clinicians regarding technological advances and limitations of currently available laboratory methods to diagnose hypogonadism. A
Considering that serum T level is used as a surrogate of target organ concentration of T and based on a review of the published literature and the best clinical judgment of the authors of this manuscript, this panel emphasizes that signs and symptoms suggestive of hypogonadism and laboratory measured T level are equally important indicators of hypogonadism and indicators for treatment until more research is done. We believe that rigid use of T cut-off (300 ng/dL) may lead to unnecessary treatment of asymptomatic men as well as under-treatment of men with persistent signs and symptoms.
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serum hormone, PSA, Hgb and Hct levels were assessed within 3 months of RP, and sequentially every 3 to 6 months after TRT initiation.
• PSA velocity (PSAV) was calculated using linear regression of three of more measured serum PSA levels obtained during at least a 12 month period
While a statistically significant increase in PSA was observed in the high risk and nonhigh risk treatment groups, this increase was not supportive of CaP recurrence, with PSAV being lower than an expected PSAV of 0.30 to 0.43 ng/ml per year in hypogonadal men without prostate cancer on TRT, and lower than in men after RP with BCR, in whom PSAV may be between 0.11 and 0.25 ng/ml per month.\textsuperscript{17,23,24}
CONCLUSIONS

In hypogonadal men with a history of prostate cancer after RP, TRT results in increases in serum T levels, with a small but significant rise in PSA and a lower BCR rate in treated men compared with age matched reference men without symptomatic evidence of hypogonadism, even in men with a history of CaP bearing high risk features. However, given the retrospective nature of this and prior studies, TRT in men with a history of CaP should be performed with a vigorous surveillance protocol. Furthermore, the global experience with TRT in the setting of CaP remains limited, with fewer than 600 patients evaluated and treated in disparate ways.
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Current state of practice regarding testosterone supplementation therapy in men with prostate cancer

Jason R. Kovac*, Michael M. Pan, Larry I. Lipshultz, Dolores J. Lamb

Scott Department of Urology, The Center for Reproductive Medicine and the Department of Molecular and Cellular Biology, Baylor College of Medicine, Houston, TX, United States

Monitoring with digital rectal examination and PSA every 3 months is the current standard in our center. The patient must be willing to provide informed consent, especially given the lack of randomized, prospective trials. Furthermore, no other medical contraindication for TST (i.e. erythrocytosis, sleep apnea) should exist and no TST should be used in men currently on ADT. The optimal timing for the commencement of TST in men with PCa is currently unknown; however, at the Baylor College of Medicine, we begin testing serum hormone levels 3 months following surgery.
BRACHYTHERAPY AND TREATMENT WITH TESTOSTERONE
Serum PSA and testosterone concentrations were recorded monthly for 3 months, then every 3 months for the first year, every 6 months for the second year, and annually then after.
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CONCLUSIONS:
With a median of 31-months follow-up, long-acting testosterone injections in men with prostate cancer treated with brachytherapy produced significant clinical benefits. There were no cases of rising serum PSA, prostate cancer progression or recurrence.
ACTIVE SURVEILLANCE AND TREATMENT WITH TESTOSTERONE
Testosterone Therapy in Men With Untreated Prostate Cancer

Abraham Morgentaler,* † Larry I. Lipshultz,‡ Richard Bennett,§ Michael Sweeney,§ Desiderio Avila, Jr.§ and Mohit Khera||

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From Men’s Health Boston, Division of Urology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts (AM, MS), and the Department of Urology, Baylor Medical College, Houston, Texas (LL, RB, DA, MK)

Surveillance consisted of PSA and digital rectal examination of the prostate at 3-month intervals, and followup prostate biopsy at yearly intervals. Biopsy results were based on reports generated by the Pathology staff at Beth Israel Deaconess Medical Center in Boston, Massachusetts, and at Baylor Medical College in Houston, Texas.
CONCLUSIONS
had transrectal ultrasound-guided prostate biopsy performed on April 3, 2014 and returns today accompanied by his spouse to discuss the results. He had no problems with the biopsy and no complications.

The ultrasound showed a 21 cc prostate with a PSA density in the low range of 0.09. The pathology showed no significant changes here. The right mid medial core showed less than 5% involvement with Gleason 6 prostate cancer. The rest of the cores were negative.

I have explained that this gives us further support for the active surveillance approach. He is strongly in support of this strategy. I have outlined our current active surveillance protocol to him. I will be seeing him back in a 6 monthly basis and we will start with the 1st visit in 6 months with a repeat PSA.
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• Symptomatic hypogonadism......treat.
• How to follow if decide to treat?
• There is no consensus on “careful monitoring” of our patients

• There are no specific differentiators for “vigorous surveillance protocol”

• We use 1,1,1 then 3,3 then 6 month intervals including PSA, measure of T levels, and HCT/HGb
The testosterone supplementation therapy has brought his total testosterone from 4.4, which is hypogonadal to 19.2. This is in a safe therapeutic range, within normal limits. He is seeing symptomatic improvement.

PSA was 1.88 in January 2014. It is now 1.50.

We will continue to monitor appropriately, this patient who is on active surveillance for his prostate cancer under Dr. [REDACTED], and under my care for his hypogonadism.

Dictated using voice recognition Civic Campus The Ottawa Hospitals.

Dr Anthony J Bella MD FRCSC
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We have successfully targeted a normal range for testosterone supplementation levels, which are currently at total testosterone 23.6. We are using 150 mg q.2 weeks testosterone enanthate.

Hemoglobin is 131. Hematocrit 0.392.

The PSA was 0.02 in April of this year, then 0.15 on September 3 which was the initial date of consultation. Subsequent to the testosterone supplementation therapy, the value is now 0.19. Dr. will be reevaluating from an oncologic standpoint, and I will discuss his directly with Dr. given the increase in PSA value.

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Dr Anthony J Bella MD FRCSC
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CONCLUSIONS – POST RP

- We use 1,1,1 then 3,3 then 6 month intervals including PSA, measure of T levels, and HCT/HGb

- Post-RP pts receive TST/TRT if organ confined disease (negative margins, no SV invasion, Gleason less than 8) and undetectable PSA (<0.04)

- PSA rise to over 0.2 triggers oncologic assessment
CONCLUSIONS – ACTIVE SURVEILLANCE

• For active surveillance, biopsy at 6-12 months includes anterior directed cores (CCO-PEBC Guidelines first authored by my colleague Prof. Chris Morash)

• If continues on AS, biopsy q3-5 yrs until age 80

• If young age, more than 2 cores, more than 50% any core – q2 yr biopsy

• Multiparametric MRI for discordant findings (PSA increase with no Gleason change or volume on bx) used for “fusion” targeted biopsy

• To come off TST/TRT – increase in Gleason score or concerning rise in PSA (no clear guide here)
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