RECURRENCE RATES FOLLOWING TESTOSTERONE THERAPY IN A LARGE CLINICAL COHORT OF MEN WITH PROSTATE CANCER

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Intro: There is a limited body of evidence regarding the safety of testosterone (T) therapy (TTh) in men with a history of prostate cancer (PCa). This continues to be a controversial issue in clinical practice. We present here a large single-center experience of TTh in men after a variety of PCa treatments to help guide further clinical decision-making.

Methods: The electronic medical record database at a men's health center affiliated with an academic hospital was queried to identify men who received TTh for testosterone deficiency after diagnosis and/or treatment of PCa over the previous 5y.

Results: We identified 320 men with a diagnosis of both PCa and T deficiency. Of these, 222 men received TTh. Men with <3 mo follow-up during TTh were excluded from analysis (n=20). Mean age for the remaining 202 men was 68y (41-88), and mean follow-up was 47.0 months. Forms of PCa treatment were RP 92 men, radiotherapy 50 men, HIFU 3 men, and active surveillance 57 men. Seven men had advanced or metastatic PCa at time of TTh (results presented separately). BCR was observed in 6 men after RP (6.5%), in 1 man after XRT (2.0%), and in 2 after HIFU. Progression was noted in 2 men on AS (3.5%)

Conclusions: To our knowledge, this is the largest series to date of TTh in a group of men with PCa. Recurrence rates were consistent with published recurrence/progression rates for the various forms of PCa treatments and for AS. These results provide valuable and reassuring information for clinicians and patients considering TTh for symptomatic men with testosterone deficiency and a history of PCa.

Primary Objectives

The goal of this study was to review a large single-center experience of TTh in men after various PCa treatments, and to compare those recurrence or progression rates with other published results.

Background

- The use of TTh in men with PCa remains a controversial issue in clinical practice. A limited body of evidence exists regarding the safety of TTh in men with PCa
- The saturation model for T in the prostate has provided a rationale for the use of TTh in men with PCa [1]

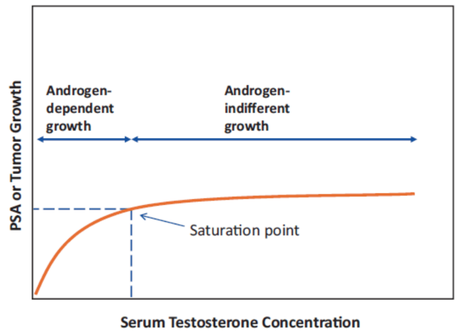

Figure 1: The saturation model suggests that T exerts its maximal effect on androgen receptors and PCa growth at very low concentrations, and plateaus at higher concentrations.

Methods

- EMR database was queried to identify men who received TTh for testosterone deficiency after diagnosis and/or treatment of PCa over the previous 5y.
- Testosterone was delivered via transdermal gels/liquids, short- and long-acting injections, and/or pellets.
- Biochemical recurrence (BCR) = PSA 0.3 ng/ml or higher after radical prostatectomy (RP), and PSA nadir plus 2 ng/ml after primary radiation treatment (external beam, brachytherapy).
- For men on active surveillance (AS) progression was defined as any biopsy showing higher Gleason score than initial diagnosis.
- Failure on HIFU was defined as any positive biopsy, or three successive elevations in PSA with a velocity ≥0.75 ng/mL/year

Results

Current study (grey) and historical comparisons

Treatment	N	Mean age ± SD	Mean follow-up (mo)	% BCR
RP + TTh	**86**	**66 ± 7.9**	**52 ± 36**	**11.7%**
RP + TTh (Ory et al., 2016)	22	75	48	0%
RP + TTh (Pastuzak et al., 2013)	103	61	27.5	3.1%
RP (Bolton et al., 2014)	2116	--	60	27%
RP (Pastuzak et al., 2013)	49	61	16.5	16%
RP (Caire et al., 2009)	4561	64.5	--	23.8%

Table 1: Percent biochemical recurrence (BCR) in prostate cancer patients treated with radical prostatectomy (RP) and testosterone (TTh)

Treatment	N	Mean age ± SD	Mean follow-up (mo)	% BCR
XRT + TTh	**49**	**73 ± 6.6**	**47 ± 37**	**3.9%**
XRT+ TTh (Ory et al., 2016)	50	75	40	6.0%
XRT (Zumsteg et al., 2015)	2694	69	83	22.6%

Table 2: Percent biochemical recurrence (BCR) in prostate cancer patients treated with radiotherapy (XRT) and testosterone (TTh). Bolded values indicate data collected from the current study.

Treatment	N = 222	Mean age ± SD	Mean follow-up in (mo)	% Progression
AS + TTh	**47**	**66.9 ± 8.7**	**51 ± 35**	**10.4%**
AS + TTh (Kacker et al., 2015)	28	59	38.9	10.7%
AS +TTh (Ory et al., 2016)	8	75	32	0%
AS (Cary et al., 2014)	238	61.7	51	11.8%
AS (Tosoian et al., 2011)	769	66	32	13.8%

Table 3: Percent progression in prostate cancer patients on an active surveillance regimen and testosterone (TTh). Bolded values indicate data collected from the current study.

Treatment	N	Mean age ± SD	Mean follow-up (mo)	% BCR
RP + salvage XRT +TTh	**5**	**70 ± 10**	**26 ± 31**	**0%**
RP + salvage XRT (Boorjian et al., 2012)	134	66	156	31.5%
RP + salvage XRT (Stish et al., 2016)	1427	66.7	108	54%
HIFU + TTh	**3**	**66 ± 2.0**	**21**	**66%**
HIFU (Poissonnier et al., 2007)	227	68.8	27.5	34%

Table 4: Percent biochemical recurrence in prostate cancer patients treated with either radical prostatectomy and salvage XRT or high intensity focal ultrasound (HIFU). Bolded values indicate data collected from the current study.

Conclusions

- This study appears to be the largest series to date providing observational data on men with PCa treated with T therapy.
- PCa recurrence/ progression rates in men who received T therapy appear to be no greater than expected rates for men who did not receive TTh
- This low recurrence/progression rate is similar to other published of TTh in men with PCa
- Of note are data from two key groups for which there has been minimal reported results:
  - Progression rate (higher Gleason score) of 10.4% in 47 men on active surveillance with >4y mean followup
  - 0% recurrence rate in 5 men treated with radical prostatectomy followed by salvage radiaton, with mean follow up of >2y.
- Taken together, these reassuring results provide justification for liberalizing the use of TTh in men with prostate cancer.

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