TESTOSTERONE REPLACEMENT THERAPY PREVENTS DISEASE PROGRESSION IN MEN UNDERGOING RADICAL PROSTATECTOMY

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Introduction

The use of testosterone replacement therapy (TRT) is currently not recommended in patients with a history of prostate cancer. However, recent data has shown that higher levels of free testosterone (FT) are associated with lower grade cancers, and may be protective against early biochemical recurrence (BCR).

The present study evaluates and compares risk of prostate cancer biochemical recurrence (BCR) following radical prostatectomy (RP) in men receiving versus not receiving testosterone replacement therapy.

Methods

824 patients undergoing for primary treatment of prostate cancer were followed between December 2009 and June 2018. All patients had preoperative testosterone and sex hormone binding globulin (SHBG) levels draw and free testosterone (cFT) was calculated prospectively.

152 (18%) patients with low preoperative cFT were placed on TRT for post-op sexual function recovery. Patients in the TRT group remained on TRT up until date of last follow up or until date of BCR.

TRT patients were proportionately matched to 419 control patients by pathologic Gleason Grade Group (GGG) and stage. Univariate and multivariate comparisons were used to compare rates and time to BCR (defined as 2 consecutive PSA values of 0.2 ng/dL or greater). Cox regression was used to generate a survival function at the mean of covariates.

Results, Figure 1: Cox Regression of Patient on TRT versus Controls

Median follow up time after RARP was 3.1 years. Of 824 patients, 152 (18.4%) were treated with TRT. After matching for pathologic stage and grade, there were 419 controls (50.8%).

Figure 1 illustrates a Cox regression for BCR, stratifying patients by TRT use. In hazard proportionate model including pathologic grade, stage, PSA, and FT, not being on TRT was a significant predictor of recurrence. In other words, TRT reduced BCR by approximately 50%.

A secondary analysis looking at time to BCR, revealed the use of TRT to prolonging latency to BCR, specifically by a mean of 1.5 years (p= 0.005).

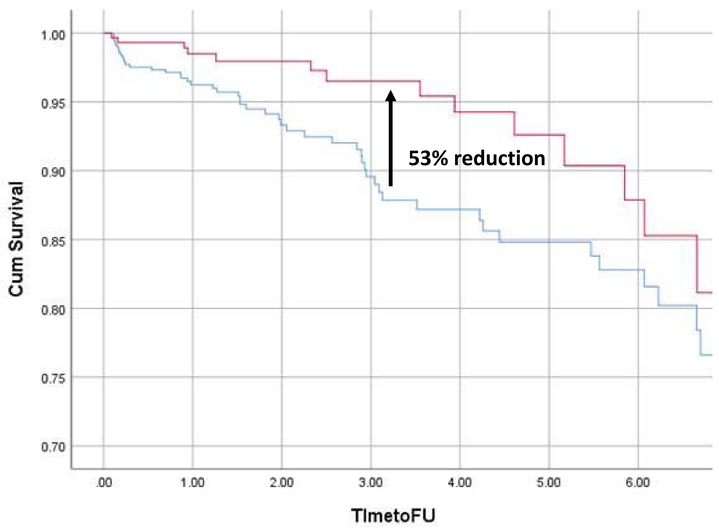

Table 1: Clinco-demographic profile of TRT patients and matched controls

	Control Mean	N=419 SD	TRT Mean	N=152 SD	P
Adjusted PSA (ng/dL)	6.9	5.1	7.2	5.9	0.575
Age (years)	62.0	7.2	61.4	7.9	0.402
BMI (kg/m^2)	27.0	3.4	28.1	4.3	**0.006**
Adjusted SHIM	20.1	6.4	19.8	6.3	0.540
Prostate Volume (mL)	55.9	20.6	56.8	20.3	0.655
Preop TT (ng/dL)	377.7	160.8	301.6	185.6	**<0.001**
Preop SHBG (nmol/L)	45.8	20.7	39.1	18.2	**0.001**
Preop FT (ng/dL)	6.4	3.4	5.5	4.1	**0.008**
	N	%	N	%	
GGG					0.982
1	124	29.5	43	28.3	
2	207	49.3	77	50.7	
3	64	15.2	23	15.1	
4	8	1.9	2	1.3	
5	17	4	7	4.6	
Pathologic Stage					0.944
pT2	361	86	131	86.2	
pT3	59	14	21	13.8	

Table 2: Multivariate analysis

Including pathological grade, stage, preoperative PSA, and FT as predictors of BCR, we found that TRT independently reduced absolute rate of BCR by 54% (OR: 0.54, p = 0.049).

	B	SE	Wald	Sig.	HR	95.0% CI for HR Lower	Upper
GGG (8-10 vs. <8 [ref])	1.664	0.311	28.673	<0.0001	5.28	2.872	9.708
Free Testosterone (cont.)	-0.14	0.063	4.911	0.027	0.869	0.768	0.984
pStage (T3 vs. T2 [ref])	1.407	0.268	27.638	<0.0001	4.084	2.417	6.901
Testosterone Replacement Therapy	-0.616	0.313	3.88	0.049	0.54	0.292	0.997
Preoperative PSA (cont.)	0.058	0.012	23.651	<0.0001	1.06	1.035	1.085

Conclusion

Although TRT has historically been contraindicated for PC patients for fear of disease acceleration, the present study demonstrated TRT significantly reduced both rate of and time-to BCR in post-RP patients. In all patients that experienced BCR, those that were on TRT had a 1.5 year longer latency of disease progression. These results suggest the need for a multi-center randomized control trial.

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