THE IMPACT OF LOW FREE TESTOSTERONE ON PROSTATE CANCER: HIGH-RISK DISEASE, RECURRENCE AND TESTOSTERONE REPLACEMENT AFTER RADICAL PROSTATECTOMY

Linda My Huynh MSc, Maxwell Towe BS, Kaelyn See BS, Joshua Tran, Farouk M. El-Khatib MD, Huang Wei Su MSc, Faysal Yafi MD, Thomas Ahlering MD

UC Irvine Health; University of California – Irvine, Orange, CA USA

1. Introduction and Objectives

Historically, high serum testosterone was feared to exacerbate prostate cancer (PC); however, recent studies now link low testosterone to significant metabolic complication. Additionally, several groups have also suggested metabolic benefit to testosterone replacement therapy in prostate cancer patients. As such, the present study seeks to evaluate the impact of low free testosterone (FT) on PC risk and in prevention of disease recurrence following radical prostatectomy (RP).

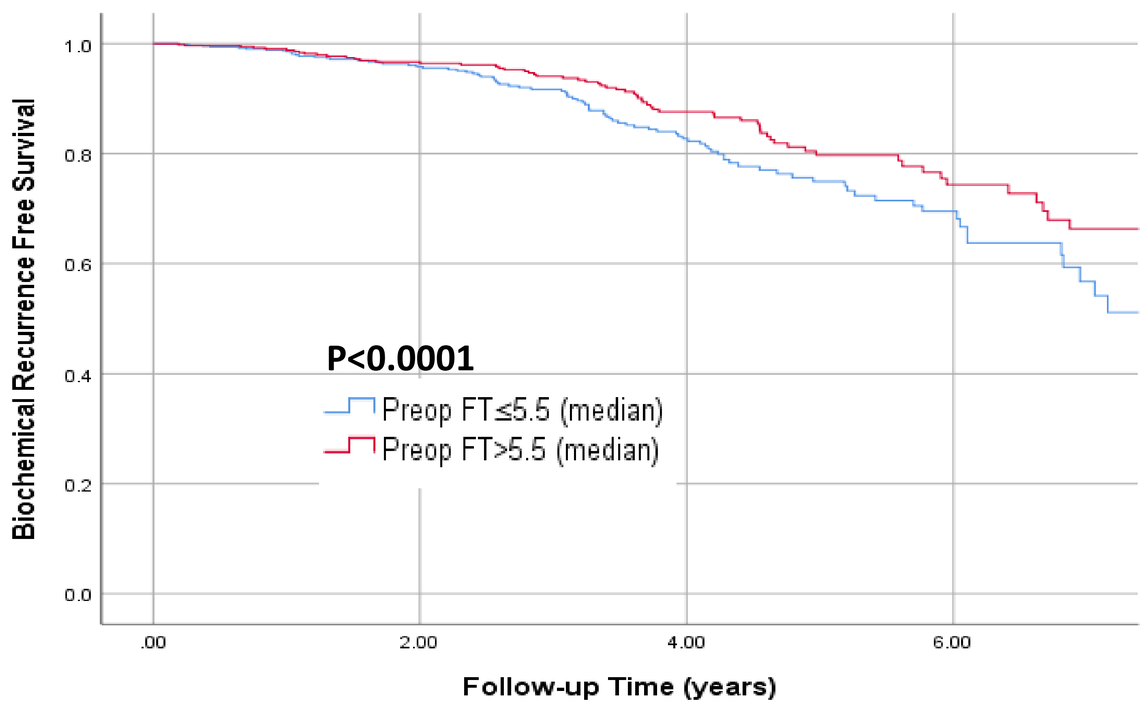
2. Materials and Methods

- 830 patients underwent RP, with prospectively-drawn total testosterone (TT), sex hormone binding globulin (SHBG) and calculated free testosterone (cFT).
- Logistic regression was used to assess impact of cFT on Gleason Grade Group (GGG), pathologic stage, and biochemical recurrence (BCR).
- A subset of 152 hypogonadal men with low-risk PC were placed on testosterone replacement therapy (TRT) after confirmation of undetectable PSAs and were proportionately matched to 419 controls never receiving TRT.
- Impact of TRT on BCR was assessed with stepwise multivariable analysis and time-to analysis.

3. Results – Effects of Endogenous cFT on Disease Characteristics and Biochemical Recurrence

Table 1. Logistic Regression of Factors predicting Post-RARP recurrence, including endogenous preoperative cFT.

	B	S.E.	Wald	Sig.	OR	95% C.I.	
						Low	High
Age, cont.	0.02	0.016	1.534	0.216	1.02	0.989	1.052
Preoperative PSA, cont.	0.101	0.018	31.526	**<0.001**	1.106	1.068	1.146
GGG [<4+5 (ref) vs. 9-10]	1.734	0.244	50.583	**<0.001**	5.661	3.511	9.128
p-stage [pT2 (ref) vs. pT3/T4]	1.531	0.237	41.655	**<0.001**	4.625	2.905	7.364
Preoperative FT, cont.	-0.449	0.235	3.639	**0.046**	0.638	0.402	0.999

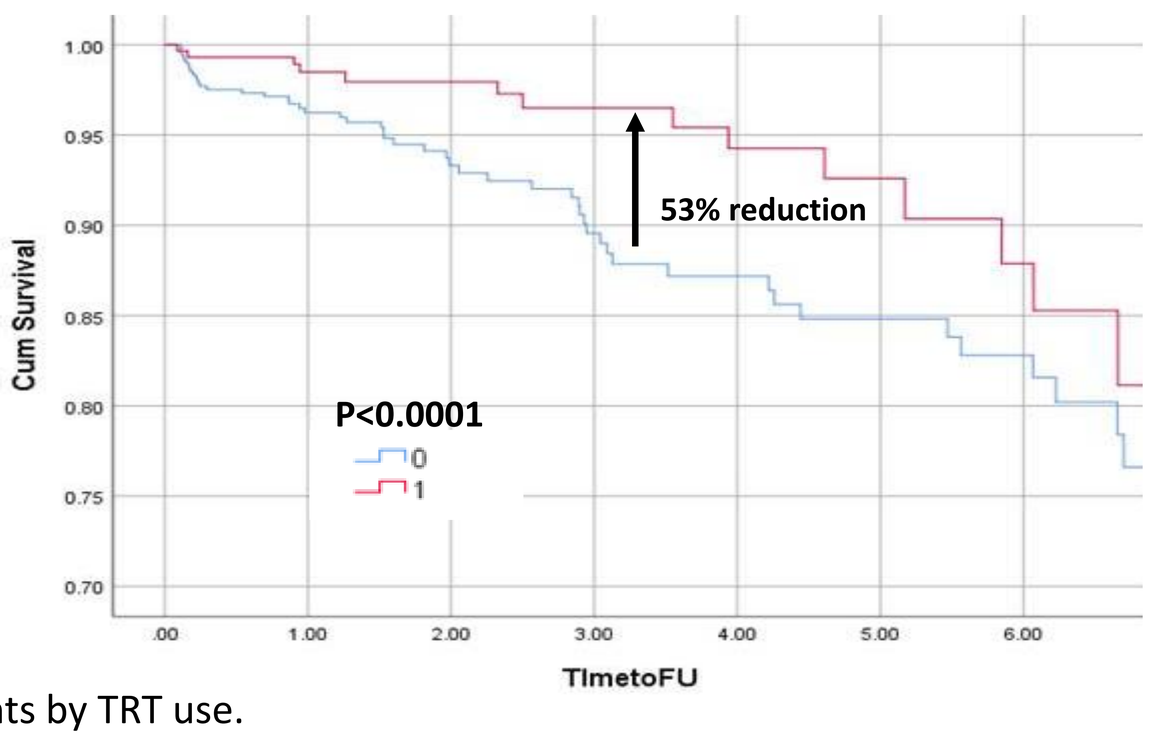


- Figure 1 illustrates a cox regression for BCR-free survival, stratifying patients by preoperative cFT. 415 patients had a preoperative cFT≤5.5 that was compared to 415 patients with preoperative FT >5.5.
- After adjusting for preoperative PSA, BMI, and age, low cFT was significantly associated with increased likelihood of GGG 9-10 (P=0.036), stage pT3/T4 (P=0.047), and BCR within 3-years post-RP (P<0.0001).

4. Results – Impact of Testosterone Replacement Therapy in Hypogonadal Patients Post-RARP

Table 2. Logistic Regression of Factors predicting Post-RARP recurrence, including testosterone replacement therapy.

	B	S.E.	Wald	Sig.	OR	95% C.I.	
						Low	High
TRT [TRT (ref) vs. control]	-0.616	0.313	3.88	**0.049**	0.54	0.292	0.997
Preoperative PSA, cont.	0.058	0.012	23.651	**<0.001**	1.06	1.035	1.085
GGG [<4+5 (ref) vs. 9-10]	1.664	0.311	28.673	**<0.001**	5.28	2.872	9.708
p-stage [pT2 (ref) vs. pT3/T4]	1.407	0.268	27.638	**<0.001**	4.084	2.417	6.901
Preoperative FT, cont.	-0.14	0.063	4.911	**0.027**	0.869	0.768	0.984



- Figure 2 illustrates a cox regression for BCR-free survival, stratifying patients by TRT use.
- 152 patients on TRT were matched by GGG and p-stage to 472 controls. P-stage, PSA, and FT, not being on TRT were significant predictors of recurrence; TRT reduced BCR by approximately 53%.
- A secondary analysis looking at time to BCR, revealed the use of TRT to prolonging latency to BCR, by an average of 1.5 years (p<0.0001).

5. Conclusion

Low cFT contributes to high-risk PC via independently increasing GGG, pathologic stage, and likelihood of biochemical recurrence post-RARP. Men with biochemically low cFT benefit may benefit oncologically with normalization of cFT via TRT – both via a 53% reduction in rate of BCR and a 1.5-year delay in time to BCR.

These results argue against previous notions that high testosterone exacerbates prostate cancer progression and suggests the need for well-designed, prospective studies assessing the potential benefit of TRT in PC patients.

UC Irvine Health
Department of Urology