PE29 The impact of low free testosterone on prostate cancer: High-risk disease, biochemical recurrence, and testosterone replacement after radical prostatectomy

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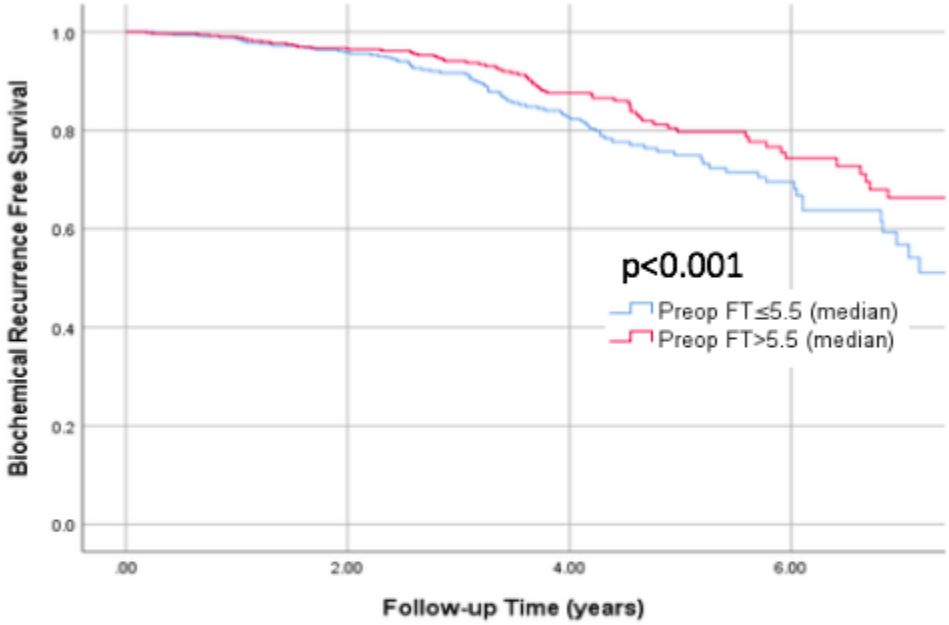
Introduction & Objectives: Historically, high serum testosterone was feared to exacerbate prostate cancer (PC); however, recent studies now link low testosterone to significant metabolic complication. The present study seeks to evaluate the impact of low free testosterone (FT) on PC risk and recurrence following radical prostatectomy (RP).

Materials & Methods: 830 patients underwent RP, with prospectively-drawn total testosterone (TT), sex hormone binding globulin (SHBG) and calculated FT. Logistic regression was used to assess impact of FT on Gleason Grade Group (GGG), stage, and biochemical recurrence (BCR). A subset of 152 hypogonadal men with low-risk PC were placed on testosterone replacement therapy (TRT) and were proportionately matched to 419 controls. Impact of TRT on BCR was assessed with stepwise multivariable analysis.

Results: After adjusting for preoperative PSA, BMI, and age, low FT 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 ($p<0.0001$) [Figure 1]. Further, hypogonadal patients on TRT were 53% less likely to experience a BCR, after accounting for GGG, stage, preoperative TT, cFT, and PSA. In patients destined to recur, TRT increased time to BCR by an average of 1.5 years ($p<0.0001$) [Figure 2].

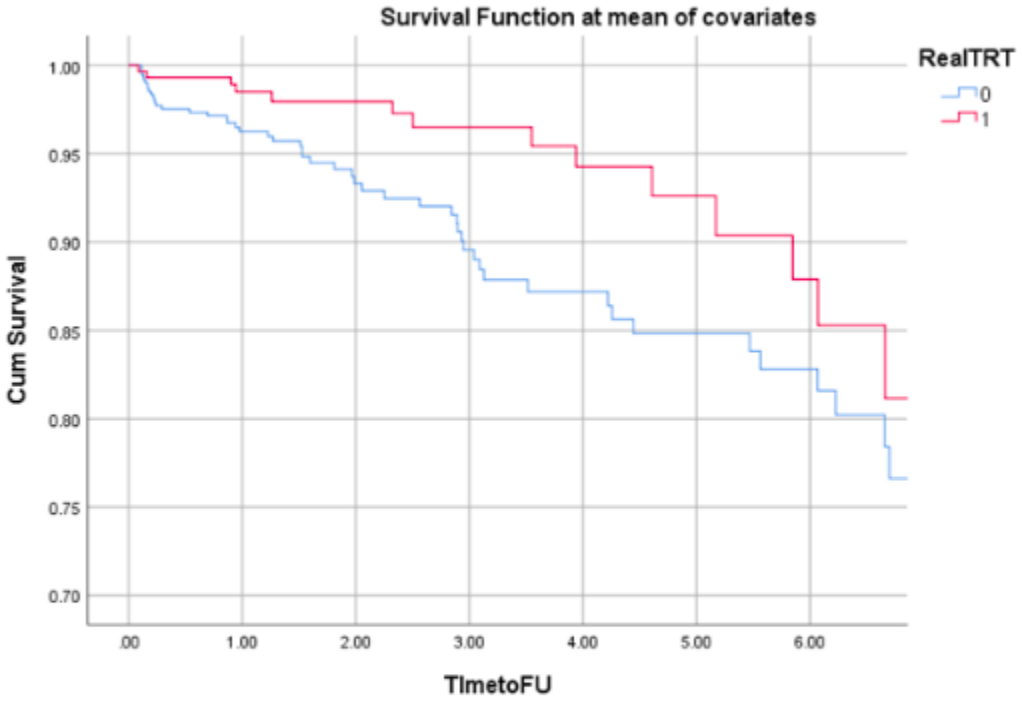
Conclusions: Low FT contributes to high-risk PC via increased GGG, stage, and likelihood of recurrence. Men with biochemically low FT benefit oncologically with normalization via TRT – both via a 53% reduction in rate of BCR and a 1.5-year delay in time to BCR. These results argue against previous notions that high testosterone furthers PC progression and suggests the need for prospective studies assessing benefit of TRT in PC patients.

Figure 1: Cox Regression of BCR-free survival, stratified by preoperative FT (N=415 patients with preoperative FT≤5.5 versus N=415 patients with preoperative FT<5.5)



	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 2: Cox Regression of BCR-free survival, stratified by testosterone replacement therapy (N=152 TRT patients matched by GGG and p-stage to N=472 control patients)



	B	S.E.	Wald	Sig.	OR	95% C.I.	
						Low	High
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
TRT [TRT (ref) vs. control]	-0.616	0.313	3.88	**0.049**	0.54	0.292	0.997