

Original Articles

PRETREATMENT TOTAL TESTOSTERONE LEVEL PREDICTS PATHOLOGICAL STAGE IN PATIENTS WITH LOCALIZED PROSTATE CANCER TREATED WITH RADICAL PROSTATECTOMY

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ABSTRACT

Purpose: In the last decade numerous groups have shown that low levels of pretreatment serum total testosterone consistently predict more aggressive disease, worse prognosis and worse treatment response in patients with metastatic prostate cancer. Prior studies have not demonstrated this same correlation in patients with known localized disease. We rigorously tested pretreatment total testosterone levels as a potential staging and prognostic marker in a large cohort of 879 patients with localized cancer treated with radical prostatectomy.

Materials and Methods: We retrospectively reviewed the clinical records of 879 patients treated with radical prostatectomy between January 1, 1986 and June 30, 2002 from 9 hospital sites. Nonparametric tests were used to compare the relationship of pretreatment testosterone to other variables. Multivariate logistic regression analysis was used to assess clinical predictors of extraprostatic disease. Kaplan-Meier survival methods and Cox regression analysis were used to assess predictors of biochemical recurrence.

Results: Patients with nonorgan confined prostate cancer (pT3–T4) showed significantly lower pretreatment total testosterone levels than those with organ confined cancer (pT1–T2) (nonparametric $p = 0.041$). In multivariate analysis pretreatment total testosterone emerged as a significant independent predictor of extraprostatic disease ($p = 0.046$). Total testosterone was not a significant predictor of biochemical (prostate specific antigen) recurrence ($p = 0.467$).

Conclusions: Pretreatment total testosterone was an independent predictor of extraprostatic disease in patients with localized prostate cancer. As testosterone decreases patients have an increased likelihood of nonorgan confined disease. Low testosterone was not predictive of biochemical recurrence, although trends observed dictate study in larger cohorts with mature followup.

KEY WORDS: testosterone, prostatic neoplasms, prostatectomy, neoplasm staging, prognosis

Since the introduction of the prostate specific antigen

(PSA) screening test there has been marked stage migration to a preponderance of clinically localized disease.¹ More than two-thirds of men now have localized disease at initial diagnosis and are candidates for primary local therapy with curative intent.¹ In the new PSA era with increasing localized disease the use of radical prostatectomy increased dramatically between the mid 1980s and late 1990s.² However, urologists are still limited in their preoperative ability to predict pathological tumor stage in a reliable manner. To date clinical stage, tumor grade (biopsy Gleason score) and serum PSA are the established preoperative prognostic markers for pathological stage.³ Yet it has been documented that 30% to 40% of men who undergo radical prostatectomy for clinically organ confined localized carcinoma of the prostate will have extraprostatic disease or experience disease recurrence.⁴

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Thus, the need for additional preoperative prognostic markers for patients with clinically localized disease is evident.

In 1941 Huggins et al firmly established a clear association between androgens and prostate cancer.⁵ Laboratory studies revealed that androgens are important for the growth and maintenance of the prostate, stimulating proliferation of human prostate cancer *in vitro* and producing prostate cancer in rodents.⁶ Serum PSA production has also been shown to be androgen dependent at the cellular level.⁷ More than a decade ago a clinical report demonstrated rapid clinical progression of unsuspected cancer after testosterone administration.⁸ However, current clinical data on prostate cancer and serum testosterone remain clouded by conflicting studies.

Pretreatment total testosterone in patients with metastatic prostate disease (stage D2) has been investigated by numerous groups during the last 2 decades. Studies have consistently demonstrated more aggressive disease, worse prognosis and worse treatment response in patients with low serum total testosterone levels.^{9–12} Studies have shown that low pretreatment testosterone levels (less than 300 ng/dl.) are significantly associated with shorter progression-free survival rates.⁹ Ribeiro et al found that low pretreatment testosterone levels resulted in more aggressive disease and worse prognosis in advanced prostate cancer.¹⁰ Chen et al noted that low testosterone levels were poor prognostic factors for patients undergoing androgen ablation irrespective of tumor grade.¹¹

Conversely in studies on patients with clinically localized prostate cancer total testosterone level has not been found to be predictive of stage. In addition, no correlation has been found with known clinicopathological features, such as PSA, tumor volume, prostatic weight, Gleason score or extraprostatic extension.^{13–15} In particular, 2 studies have investigated serum total testosterone in small cohorts of men with clinically localized disease treated with radical prostatectomy. Neither study was able to demonstrate significant association with total testosterone.^{13,14} Hoffman et al showed that patients with low free testosterone had more aggressive disease.¹⁴

To confound the situation further some studies on localized prostate cancer have demonstrated results opposite those in traditional metastatic disease literature. These studies revealed that high testosterone levels were associated with higher rates of metastatic relapse. Zagars et al found that higher pretreatment total testosterone, especially greater than 500 ng/dl., significantly correlated with metastatic relapse but not PSA recurrence.¹⁵ Gann et al suggested that high testosterone and low sex hormone binding globulin were associated with a higher risk of prostate cancer.¹⁶ Finally, Imamoto et al noted that pretreatment total testosterone levels in patients with clinically localized disease were significantly lower than those in patients with stage D2 disease.¹⁷

Thus, in an effort to clarify the incompletely understood association of testosterone with prostate cancer, we used the mature Department of Defense (DoD) Center for Prostate Disease Research (CPDR) Multicenter Research Database to analyze pretreatment testosterone levels in patients with clinically localized prostate cancer. We performed a retrospective analysis in a patient population with prostate disease that was predominantly clinically organ confined who were treated with radical prostatectomy and who had pretreatment testosterone data available. We rigorously tested pretreatment total testosterone levels as a potential staging and prognostic marker in this large cohort of 879 patients.

MATERIALS AND METHODS

In July 2002 we retrospectively evaluated all clinical and followup information on patients with prostate cancer

treated with radical prostatectomy in the DoD CPDR Tri-Service Multicenter Prostate Disease Research Database between January 1, 1986 and June 30, 2002. Our criteria required patients to have serum total testosterone levels determined at diagnosis or before treatment. Testosterone was not drawn at a specific time and was at the discretion of the treating physician, although testosterone value was a field on the CPDR staging form as an encouraged test in our clinical research. This query revealed 928 patients, of whom 49 were excluded from the study secondary to receiving neoadjuvant treatment before surgery. However, it was unknown if any patients were on testosterone replacement, which would have been rare.

Clinical information and followup were collected as part of the DoD CPDR Tri-Service Multicenter Prostate Disease Research Database. Prospective and retrospective comprehensive clinical data were collected on all consenting patients with prostate cancer. As of January 1, 1994 the data collection was prospective for all new patients with prostate cancer. Similar retrospective data were also collected on all those treated since 1970 through inpatient and outpatient record reviews and patient interviews. Standardized data collection forms for prostate biopsy, registration, staging, surgery, surgical pathology, radiation treatment, hormonal treatment, cryotherapy, followup and necropsy were developed for use. Data were collected and entered by physicians and data managers, then maintained in a relational data base. The CPDR Database has been approved by the Uniformed Services University Research Administration institutional review board as well as the institutional review boards of all participating military hospitals.

Pretreatment serum total testosterone levels were recorded in 2 different concentrations among the 9 hospitals using a commercially available radioimmunoassay. Results were recorded in ng/ml. and ng/dl. with the normal range quoted by the producer as 286 to 1,510 ng/dl. For this study all results were reported in ng/dl.

Radical prostatectomy pathology reports were retrospectively reviewed and histological analysis performed with standard processing for patients treated before May 1993. After May 1993 the prostates were prospectively evaluated by whole mount 2.25 mm. step sectioning at the Armed Forces Institute of Pathology. Organ confined prostate cancer (pT1–T2) was defined as a specimen that had no capsular penetration, positive surgical margins, or seminal vesicle or pelvic lymph node involvement. Extraprostatic disease (pT3–T4) was defined as cancer on any inked margin, any capsular penetration, or pelvic lymph node or seminal vesicle involvement.

Histopathological grading was done according to the WHO method of glandular differentiation. The value of grade used in this study was a combination of WHO and Gleason systems. Gleason grades 2 to 4 or WHO grade well was considered grade well, Gleason grades 5 to 7 or WHO grade moderate was considered grade moderate and Gleason grades 8 to 10 or WHO grade poor was considered grade poor. Staging was based on the modified Whitmore-Jewett system and 1992 TNM classification. Biochemical recurrence of prostate cancer was defined as 2 successive PSA measurements greater than 0.2 ng/ml.

Nonparametric tests were used to study the relationship of pretreatment testosterone and pathological stage to other variables in univariate analysis. Multivariate logistic regression analysis assessed the clinical usefulness of pretreatment testosterone and 8 other covariates as predictors of pathological stage. In all analyses $p < 0.05$ was considered statistically significant. Pathological stage was a dichotomous categorical variable with 2 levels (pT1–T2 versus pT3–T4), as were race (black versus not black) and adjuvant treatment (yes versus no). The biopsy and pathological Gleason (WHO) grade were categorical variables with 4 levels (2 to 4, well, 5

to 6, moderately, 7, moderate, 8 to 10, poor). Clinical stage was a categorical variable with 3 levels (cT1 versus cT2 versus cT3–T4). Pretreatment total testosterone, creatinine, age, prostatic acid phosphatase (PAP), alkaline phosphatase and log transformed PSA entered the model as continuous variables. Kaplan-Meier survival curves and Cox regression analyses were used to study the relationship of several of these variables to PSA recurrence.

RESULTS

Relationship of total testosterone and other variables to pathological stage. Table 1 shows the distribution of the 879 patients with localized prostate cancer treated with radical prostatectomy who had pretreatment testosterone data available for analysis from 9 hospital sites. Table 2 summarizes demographic data, pretreatment serum levels of selected tests, clinical stage and biopsy Gleason (WHO) score. Selected surgical factors, pathological Gleason (WHO) score and pathological stage of the patient cohort are shown in table 3.

Table 4 shows the mean, median and range of total testosterone (entered as a continuous variable) in a univariate analysis with each of the stratified covariate groups. Most noteworthy in this table, and shown in figure 1, is the relationship of pretreatment total testosterone level to pathological stage. Patients with nonorgan confined pathological stage disease had significantly lower serum total testosterone than those with organ confined cancer (nonparametric $p = 0.041$). Increasing pretreatment PAP was associated with statistically significant increases in serum total testosterone ($p = 0.044$). There was a trend toward decreasing testosterone values with increasing age, but these values were not significantly different ($p = 0.103$). Pretreatment total testosterone values did not differ significantly compared to race, pretreatment alkaline phosphatase, pretreatment creatinine, pretreatment PSA, clinical stage, biopsy Gleason (WHO) score and pathological Gleason (WHO) score. Although not significant, another interesting trend was as serum PSA increased, mean total testosterone levels decreased ($p = 0.269$).

Table 5 shows a multivariate logistic regression model with testosterone and 8 other covariates and 4 factors entered as statistically significant independent predictors of extraprostatic disease. Pretreatment total testosterone level was an independent significant predictor of pathological stage ($p = 0.046$). The other predictors were log value of pretreatment PSA levels ($p < 0.0001$), biopsy Gleason (WHO) score ($p = 0.0160$) and pretreatment prostatic acid phosphatase levels ($p = 0.0287$). Age, race, clinical stage, alkaline phosphatase and creatinine were not statistically significant predictors of pathological stage (not shown).

Relationship of total testosterone and other variables to biochemical recurrence. At the time of this analysis mean followup for the 879 patients was 37.7 months and 12 men died during followup with no PSA or clinical recurrence. End point events observed during followup were 129 (14.7%) patients with PSA recurrence, 22 (2.5%) with distant meta-

TABLE 2. Overall pretreatment characteristics of 879 patients

Variable	No. Pts. (%)
Total testosterone (ng./dl.):	
Less than 200	110 (12.5)
200–299	203 (23.1)
300–399	262 (29.8)
400–499	174 (19.8)
Greater than 500	130 (14.8)
Mean/median	362.4/348.0
Race:	
Not black	655 (74.6)
Black	207 (23.5)
Unknown	17 (1.9)
Age:	
Younger than 55	129 (14.7)
55–59	162 (18.4)
60–64	259 (29.5)
65–70	241 (27.4)
Older than 70	88 (10.0)
Mean/median	62.3/63.3
Diagnosis PSA (ng./ml.):	
0–4	157 (17.9)
4.1–10	532 (60.5)
10.1–20	114 (13.0)
Greater than 20.1	32 (3.6)
Unknown	44 (5.0)
Mean/median	7.4/5.7
Alkaline phosphatase (U./l.):	
Less than 5	411 (46.8)
75–99	295 (33.6)
Greater than 100	99 (11.3)
Unknown	74 (8.4)
Mean/median	77.6/75.0
PAP (ng./ml.):	
Less than 1.00	185 (21.1)
1.00–1.99	355 (40.4)
2.00–2.99	104 (11.8)
Greater than 3.00	76 (8.6)
Unknown	159 (18.1)
Mean/median	1.7/1.4
Biopsy Gleason (WHO) score:	
4 or Less	90 (10.2)
5–6	497 (56.5)
7	162 (18.4)
8–10	39 (4.4)
Unknown	91 (10.3)
Serum creatinine (mg./dl.):	
1.0 or Less	455 (51.8)
1.1–1.3	343 (39.0)
Greater than 1.3	63 (7.2)
Unknown	18 (2.0)
Mean/median	1.1/1.0
Clinical stage:	
cT1 or lower	485 (55.2)
cT2a	229 (26.1)
cT2b	97 (11.0)
cT2c	54 (6.1)
cT3–T4	4 (0.5)
Unknown	10 (1.1)
Treatment of benign prostatic hyperplasia:	
Yes	183 (20.8)
No	696 (79.2)

TABLE 1. Radical prostatectomy sites and cases

CPDR Site	No. Cases (%)
Brooke Army Medical Center	124 (14.1)
Eisenhower Army Medical Center	19 (2.2)
Madigan Army Medical Center	19 (2.2)
Malcolm Grow Medical Center	34 (3.9)
Naval Medical Center Portsmouth	9 (1.0)
Naval Medical Center San Diego	77 (8.7)
National Naval Medical Center	7 (0.8)
Wilford Hall Medical Center	200 (22.8)
Walter Reed Army Medical Center	390 (44.3)
Total	879 (100.0)

static relapse (D2 disease) and 4 (0.5%) dead of prostate cancer. Table 6 shows univariate analysis data from selected factors using Kaplan-Meier survival methods to predict biochemical recurrence-free survival. The 5 groups of pretreatment serum total testosterone levels did not show significant differences in PSA recurrence rates ($p = 0.467$). Pretreatment PSA, pretreatment PAP, race, pathological Gleason (WHO) score and pathological stage were all significant predictors of PSA recurrence, and all other covariates were statistically insignificant.

Based on evidence in the literature, we also performed a survival analysis on 2 groups of testosterone using the clinical cutoff point of 300 ng./dl. Figure 2 demonstrates that this value was not a significant predictor of PSA recurrence ($p = 0.347$). In multivariate Cox regression analysis (not shown) treatment age, pathological stage and race were independent predictors of PSA recurrence. Pretreatment testosterone was not a significant predictor of PSA recurrence ($p = 0.119$).

TABLE 3. *Surgical factors in 879 patients radical*

Variable	No. Pts. (%)
Treatment modality:	
Primary radical prostatectomy only	827 (94.1)
Radical prostatectomy + adjuvant*	52 (5.9)
Pathological Gleason (WHO) score:	
4 or Less	16 (1.8)
5-6	438 (49.8)
7	320 (36.4)
8-10	78 (8.9)
Unknown	27 (3.1)
Pathological stage:	
pT2 or lower	514 (58.5)
pT3a	219 (24.9)
pT3b	56 (6.4)
pT3c	54 (6.1)
pT4	8 (0.9)
Unknown	28 (3.2)
Nerve sparing:	
Unilat.	136 (15.5)
Bilat.	278 (31.6)
Not done	465 (52.9)
Margin status:	
Pos.	275 (31.3)
Neg.	604 (68.7)
Capsule status:	
Pos.	279 (31.7)
Neg.	600 (68.3)
Seminal vesicle status:	
Pos.	64 (7.3)
Neg.	815 (92.7)
Node status:	
Pos.	15 (1.7)
Neg.	864 (98.3)

* Adjuvant treatment consisted of androgen ablation or external beam radiation.

DISCUSSION

Total testosterone predicts pathological stage. The major finding of our study is that patients with clinically localized prostate cancer treated with radical prostatectomy have a statistically significant correlation between pretreatment total testosterone levels and pathological stage. This correlation held up in multivariate analysis when pretreatment total testosterone emerged as an independent predictor of extraprostatic disease. As serum testosterone decreases patients have an increased likelihood of nonorgan confined disease (pT3-T4). These results indicate that low pretreatment total testosterone may be a marker for more aggressive disease in clinically localized prostate cancer. However, confounding variables of circadian rhythm of secretion, influence of body mass index and interassay variability for serum testosterone herald caution to these retrospective results. A controlled prospective study would seem to be indicated based on our results.

Patients with metastatic prostate cancer and testosterone levels less than 300 ng./dl. have been shown to have more aggressive disease, worse prognosis and worse treatment response than those with normal or increased serum total testosterone.⁹⁻¹² To our knowledge, before our study no group had shown the same association between total testosterone and clinically localized prostate cancer. In 1995 Monda et al performed a study similar to ours, and found that total testosterone had no clinical value in predicting pathological stage. Their cohort consisted of only 90 patients treated with radical prostatectomy.¹³ In 2000 Hoffman et al

TABLE 4. *Nonparametric univariate analysis of relationship of pretreatment testosterone to patient demographics and surgical pathology*

Variable	Testosterone (ng./dl.)			p Value
	Mean	Median	Range	
Pathological stage:				0.041
pT1-T2	373.2	356.4	19-1,490	
pT3-T4	348.9	340.0	30-846	
Race:				0.363
Not black	361.0	343.0	30-1,490	
Black	369.6	362.8	33-846	
Age:				0.103
Younger than 55	383.3	370.0	92-846	
55-59	347.9	330.0	19-704	
60-64	375.5	360.0	91-917	
65-70	350.2	348.0	30-901	
Older than 70	353.4	323.0	40-1,490	
Pretreatment/diagnosis PSA (ng./ml.):				0.269
0-4	365.4	350.0	103-1,490	
4.1-10	364.4	356.2	19-901	
10.1-20	351.6	339.0	34-700	
Greater than 20	329.6	301.5	100-810	
Pretreatment alkaline phosphatase (U./l.):				0.523
Less than 75	355.2	342.0	19-901	
75-99	369.0	348.0	34-1,490	
Greater than 100	358.8	348.0	110-917	
Pretreatment PAP (ng./ml.):				0.044
Less than 1.00	355.1	340.0	19-917	
1.00-1.99	353.5	339.0	40-1,490	
2.00-2.99	341.9	343.5	30-880	
Greater than 3.00	395.4	390.0	110-846	
Biopsy Gleason (WHO) score:				0.834
4 or Less	359.1	354.5	30-880	
5-6	367.3	352.0	19-1,490	
7	360.1	336.3	34-901	
8-10	343.7	349.7	110-665	
Pretreatment serum creatinine (mg./dl.):				0.860
1.0 or Less	362.6	346.0	19-917	
1.1-1.3	359.1	350.0	40-1,490	
Greater than 1.3	356.5	320.0	33-901	
Clinical stage:				0.784
cT1	357.2	342.0	33-917	
cT2	370.1	355.5	19-1,490	
cT3-T4	344.2	365.0	157-490	
Pathological Gleason (WHO) score:				0.381
4 or Less	311.1	307.5	170-470	
5-6	367.0	350.5	33-1,490	
7	365.1	344.5	91-901	
8-10	343.2	348.9	30-665	

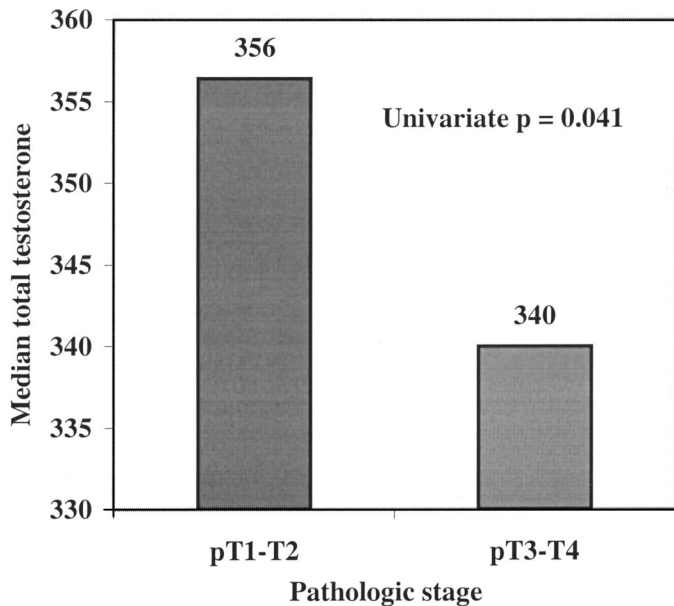


FIG. 1. Low pretreatment total testosterone levels predict extraprostatic disease in patients treated with radical prostatectomy.

also performed a similar study, and found that lower levels of pretreatment free testosterone were associated with more aggressive disease.¹⁴ However, they did not find an association with total testosterone levels, and their prostatectomy cohort consisted of only 57 patients. In our study total testosterone was a predictor of extraprostatic disease in univariate and multivariate analyses. Our findings, when compared to the previous 2 studies with similar cohorts, were discovered secondary to the power of our large cohort of patients available for analysis compared to the other relatively small cohorts of patients.

Our study revealed results opposite to those of several recent studies that proposed that high levels of testosterone were associated with worse disease.¹⁵⁻¹⁷ These studies relied on clinical staging, and the primary treatment was radiation and/or hormonal therapy. The actual status of disease in their patients was not confirmed by pathological assessment of radical prostatectomy. Thus, the conclusions about pathological stage and biochemical recurrence were not possible or as reliable.

While we showed that low testosterone was an independent predictor of pathological stage, there are a number of limitations to our study. As previously noted testosterone has a circadian rhythm of secretion and we did not control the time of the assay. Other factors such as body mass index influence testosterone levels for which we were unable to control. We did not know the status of men regarding androgen replacement therapy although this was likely a rare event in our cohort. Despite these limitations, the results are provocative and should prompt more controlled study.

TABLE 5. Multivariate logistic regression analysis of significant independent predictors of extraprostatic disease (pT1-T2 versus pT3-T4)

Variable	Odds Ratio	95% CI	p Value
Log PSA	1.814	1.347-2.443	<0.0001
Biopsy Gleason (WHO) score:			0.0160
2-4 vs. 5-6	1.765	1.023-3.047	
2-4 vs. 7	2.624	1.402-4.912	
2-4 vs. 8-10	2.782	1.100-7.034	
PAP (ng./ml.)	1.196	1.019-1.404	0.0287
Total testosterone	0.999	0.998-1.000	0.0464

Only significant predictors shown.

TABLE 6. Univariate analysis of selected factors and their correlation with biochemical recurrence

Factor	No. Pts.	% 3-Yr. Biochemical Recurrence Rate	% 5-Yr. Biochemical Recurrence Rate	p Value
Race:				
Not black	571	15	25	0.0002
Black	176	30	39	
PSA (ng./ml.):				
0-4	137	9	25	<0.0001
4.1-10	463	16	23	
10.1-20	103	28	45	
Greater than 20	25	50	55	
PAP (ng./ml.):				
Less than 1.00	161	13	22	0.0027
1.00-1.99	305	19	27	
2.00-2.99	92	17	37	
Greater than 3.00	66	30	41	
Pathological Gleason (WHO) score:				
4 or Less	15	22	22	<0.0001
5-6	378	9	17	
7	271	23	36	
8-10	71	45	58	
Pathological stage:				
pT1-T2	415	10	16	<0.0001
pT3-T4	343	28	42	
Testosterone (ng./dl.):				
Less than 200	97	24	32	0.467
200-299	179	17	33	
300-399	220	21	26	
400-499	149	15	35	
Greater than 500	113	13	16	
Testosterone (ng./dl.):				
300 or Less	276	20	32	0.347
Greater than 300	482	17	26	

The mechanism for this testosterone effect remains unclear. Some groups have speculated that low testosterone levels are secondary to chronic disease status and are the consequence of advanced disease rather than a causative factor.¹² Most recently Zhang et al studied total and free testosterone before and after radical prostatectomy in 164 patients, and found that low testosterone was associated with high grade disease.¹⁸ Furthermore, levels were higher after prostate removal suggesting that prostate cancer itself inhibited androgen levels. Other groups have speculated low serum testosterone results in the growth of more androgen

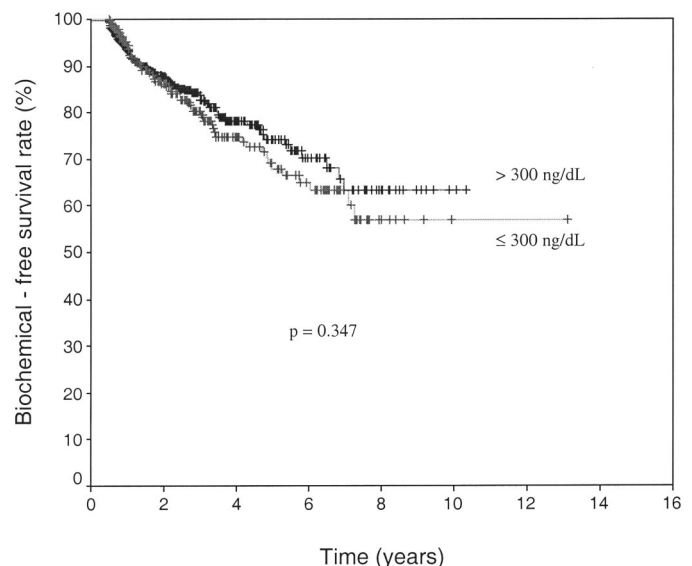


FIG. 2. Low pretreatment total testosterone does not significantly predict PSA recurrence after radical prostatectomy (mean followup 37.7 months).

independent carcinoma cells.¹⁰ Still others have proposed that a central mechanism may be involved.

Miller et al noted increased testosterone levels as well as other serum hormone levels after radical prostatectomy.¹⁹ It has been suggested that this increase occurs because the prostate and/or prostate cancer cells may produce inhibin or some other substance that has a centrally acting inhibitory role (negative feedback) on the hypothalamic pituitary axis.^{7,20} When the prostate and/or the cancer is removed this inhibitory substance is also removed allowing testosterone levels to increase.²¹ Low testosterone association with pathological stage may be related to the biology of the disease, or possibly be circumstantial or coincidental. Although we did not see an association between total testosterone and age, race and clinical stage, it is possible that low testosterone was a surrogate of other factors that relate to pathological stage.

Clearly combining PSA, clinical stage, and preoperative biopsy grade and quantitative biopsy histology increases the preoperative ability to predict pathological stage.³ Pretreatment total testosterone levels might be used by clinicians in the future assessment and management of localized prostate cancer. Perhaps future risk assessment models and nomograms should incorporate total testosterone levels, particularly those models using neural network analysis considering a multitude of prognostic factors.

Total testosterone does not predict biochemical recurrence. It is generally accepted that worse tumor grade, extraprostatic disease and PSA are significant predictors of biochemical recurrence of prostate cancer in patients treated with radical prostatectomy. The data from our 879 patient cohort demonstrated these same covariates to be statistically significant independent predictors of PSA recurrence. Although not significant, low total testosterone, especially less than 300 ng/dl., showed a trend as a predictor of PSA recurrence (table 6 and fig. 2). Large clinical trials are likely needed to ascertain the prognostic value of testosterone level in relation to biochemical or clinical recurrence. This area awaits further study and, as suggested by our data, might be promising.

CONCLUSIONS

Patients with localized prostate cancer treated with radical prostatectomy have a statistically significant correlation between pretreatment total testosterone levels and pathological stage. In multivariate analysis total testosterone emerged as an independent predictor of extraprostatic disease. As serum testosterone decreases patients have a higher likelihood of nonorgan confined disease (pT3–T4). Low total testosterone level was not predictive of biochemical recurrence, although trends observed dictate study in larger cohorts with mature followup.

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