

UCSF

UC San Francisco Previously Published Works

Title

Contemporary Trends in Low Risk Prostate Cancer: Risk Assessment and Treatment

Permalink

<https://escholarship.org/uc/item/79d1p1wd>

Journal

Investigative Urology, 178(3)

ISSN

0021-0005

Authors

Cooperberg, Matthew R
Broering, Jeannette M
Kantoff, Philip W
[et al.](#)

Publication Date

2007-09-01

DOI

10.1016/j.juro.2007.03.135

Peer reviewed



Published in final edited form as:

J Urol. 2007 September ; 178(3 Pt 2): S14–S19. doi:10.1016/j.juro.2007.03.135.

Contemporary Trends in Low-Risk Prostate Cancer: Risk Assessment and Treatment

Matthew R. Cooperberg¹, Jeannette M. Broering¹, Philip W. Kantoff², and Peter R. Carroll^{1,†}

¹Dept. of Urology, Program in Urologic Oncology, Urologic Outcomes Research Group, UCSF Comprehensive Cancer Center, University of California, San Francisco, CA

²Department of Medical Oncology, Dana Farber Cancer Institute, Harvard Medical School

Abstract

Purpose—To update national risk trends in prostate cancer with a focus on low-risk tumors, to re-examine trends in primary treatment for low-risk tumors, and to attempt to substratify low-risk patients based on pretreatment clinical data.

Materials and Methods—Data were abstracted from the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) registry. 10,385 men were diagnosed between 1990 and 2006 with localized disease. Low risk was defined as a prostate-specific antigen (PSA) level ≤ 10 ng/mL, a Gleason score ≤ 6 , and a clinical T stage $\leq 2a$. Temporal trends were assessed for patient distribution among risk groups and within the low-risk group for individual risk factors, Kattan nomogram prediction, Cancer of the Prostate Risk Assessment (CAPRA) score, and primary treatment. The ability of the CAPRA score to substratify low-risk prostatectomy patients was evaluated with survival analysis.

Results—The proportion of low-risk tumors in CaPSURE nearly doubled from 27.5% in 1990-1994 to 46.4% in 2000-2001, but has been relatively constant since. A growing proportion of low-risk tumors are cT1c, and virtually all are Gleason score 6. PSA and the percentage of positive biopsies have decreased throughout the study period, as did the mean CAPRA score. The use of active surveillance increased from a nadir of 6.2% in 2000-2001 to 10.2% in 2004-2006. The use of prostatectomy has also increased, whereas use of androgen deprivation and radiation has declined. Likelihood of recurrence increases significantly with rising CAPRA score.

Conclusions—Low-risk patients can be further substratified to identify those at very low-risk based on clinical variables. The use of surveillance is increasing, but overtreatment remains a concern among these patients.

Keywords

Prostatic neoplasms; Risk factors; Prognosis; Treatment; CAPRA; CaPSURE

Introduction

With 218,890 new cases anticipated for 2007, prostate cancer accounts for nearly 30% of all male cancers. 27,050 men are expected to die from the disease this year, a mortality figure which is surpassed by only lung cancers, yet represents only a small fraction of the number of men who are diagnosed.¹ Curative therapy has been shown to reduce prostate cancer-specific

[†] To whom correspondence should be addressed, at UCSF/Mt. Zion Cancer Center, 1600 Divisadero St, 3d Floor, San Francisco, CA 94115-1711. tel (415)353-7098, fax (415)353-7093, pcarroll@urol.ucsf.edu.

and overall mortality for selected men with the disease.² However, all available treatments exert a potentially significant negative impact on patient health-related quality of life.³ Furthermore, as more men are diagnosed at younger ages as having curable tumors, the time course of the disease is growing ever longer; men may expect to live many years after treatment, 4 or in some cases without treatment,⁵ and thus must consider seriously the long-term implications of their disease management decisions. Risk assessment at time of diagnosis based on available clinical data can help guide clinician-patient decision-making with respect to optimal treatment strategy; patients with a prostate-specific antigen (PSA) level <10 ng/mL, a biopsy Gleason score of ≤ 6 , and a clinical stage of $\leq T2a$ have typically been classified as low risk.⁶

A growing body of literature supports a role for a trial of active surveillance for carefully selected men with low-risk tumors.^{7, 8} We have previously found, however, that on a national level, use of active surveillance (watchful waiting) declined sharply among low-risk patients throughout the 1990s, even as low-risk tumors accounted for a steadily increasing proportion of diagnosed tumors.⁹ We conducted the present study with three goals: (1) to update our description of national trends in prostate cancer risk at presentation; (2) to examine whether any new trends in risk are associated with corresponding changes in treatment patterns; and (3) to assess our ability to substratify patients within the low-risk group using the recently validated University of California–San Francisco Cancer of the Prostate Risk Assessment (CAPRA) score.¹⁰

Materials and Methods

Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE™) is a longitudinal, observational database of men with biopsy-proven prostate adenocarcinoma, actively recruited from 31 academic- and community-based urology practices across the United States. All prostate cancer patients are recruited consecutively by participating urologists, who report complete workup and treatment data. Data for patients diagnosed as having prostate cancer before 1995 but still followed by a urologist were initially entered into the database retrospectively; for those whose cancers were diagnosed since 1995, all data entry has been prospective. Completeness and accuracy of the data are ensured by random sample medical record review every 6 months. Additional details of the project methods and a description of the cohort's sociodemographic characteristics have been reported previously.¹¹

As of July 15, 2006, 13,124 men had registered and consented in the CaPSURE database. A total of 451 men whose cancer was diagnosed before 1990 were excluded, as were 501 with metastatic and/or locally advanced (clinical stage $\geq T3b$) disease. 1787 men (14.6%) with localized disease were missing PSA, clinical T stage (2002 system), and/or biopsy Gleason score data and were also excluded, leaving 10,385 for analysis. Low-risk patients were defined as above. Intermediate-risk patients were defined as those with a PSA level of 10.1 to 20 ng/mL, a Gleason score of 7, and/or a clinical stage of T2b. High-risk patients were those with a PSA level >20 ng/mL, a Gleason score of ≥ 8 , and/or a clinical stage of T2c-3a.⁶

Multivariable risk was further assessed with two well-validated instruments; the first is the original Kattan preoperative nomogram,¹² which predicts percent likelihood of biochemical recurrence-free survival at 5 years after surgery via a relatively complex mathematical weighting of Gleason score, clinical T stage, and a cubic spline transformation of PSA. The calculation of the score for large numbers of patients in CaPSURE was facilitated by prior collaboration with the nomogram's author.¹³ The second instrument, the CAPRA score, assigns points based on Gleason score (up to 3 points), categorized PSA level (up to 4 points), clinical T stage (up to 1 point), age (up to 1 point), and percentage of positive biopsy cores (PPB, up to 1 point). The CAPRA score is thus calculated from 0 to 10, with every 2 point increase in

CAPRA score representing roughly a doubling of risk of biochemical recurrence after prostatectomy.^{10, 14}

We analyzed temporal trends in patient distribution both among the three risk groups, with time periods defined to produce relatively even numbers of patients in each group, and to focus attention on the current decade. Within the low-risk group we further analyzed trends in individual risk factors (PSA, Gleason score, T stage, PPB), and in aggregate risk as assessed by the Kattan nomogram prediction and CAPRA scores. We also analyzed trends over time in primary treatment among low-risk patients. 494 patients in the analytic dataset (4.8%) were missing data on primary treatment. An additional 143 (1.4%) had primary treatment recorded as “other” or “none” (as opposed to active surveillance, coded in CaPSURE as “watchful waiting”) and were also excluded from treatment analyses. Use of neoadjuvant androgen deprivation therapy (NADT) over time was also examined among patients electing each form of local therapy. Because patients were unevenly distributed across the time periods, statistical significance of temporal trends in risk factors and diagnosis and in primary treatment patterns was assessed using the Cuzick nonparametric test for trend.

Finally, we performed survival analysis on low-risk radical prostatectomy patients to predict risk of recurrence (PSA level >0.2 on two occasions or any second treatment at least 6 months after surgery) stratified by CAPRA score. For this analysis, patients receiving any neoadjuvant (before surgery) or adjuvant (treatment within 6 months of surgery) treatment were excluded, as were those with <6 months of follow-up or fewer than two postoperative PSA values available. For this subset (N=1769), Kaplan-Meier plots were produced, and the log-rank test and Cox proportional hazards regression were used to identify significance of the CAPRA score as a predictor of biochemical recurrence. All analyses were performed using Stata for Macintosh, version 9.2 (Stata Corporation, College Station, TX).

Results

Among the 10,385 patients included in this analysis, 4232 (41.6%), 2761 (26.6%), and 3301 (31.8%) had low, intermediate, and high risk prostate cancer at diagnosis, respectively. Trends in the distribution of patients among the risk groups are presented in Figure 1. The proportion of low-risk patients nearly doubled from 1990-1994 (27.5%) to 2000-2001 (46.4%) and has remained relatively constant since. The greatest decline has been among high-risk patients: 46.0% in 1990-1994 to 29.9% in 2000-2001 and 25.1% in 2004-2006, whereas the proportion of intermediate-risk patients has been relatively constant.

Trends in each risk characteristic among the 4323 low-risk patients are illustrated in Figure 2. The proportion of low-risk patients with clinical stage T1c disease has risen dramatically and continues to rise, from 29.9% in 1990-1994 to 78.3% in 2004-2006. cT2a tumors are less prevalent, and cT1a and T1b tumors combined account for approximately 1% of tumors diagnosed between 2002 and 2006. In terms of biopsy Gleason grading, the number of low-risk tumors scored under 6 (i.e., with primary or secondary pattern 1 or 2) continues to decrease, from 67.1% of tumors in the early 1990s to 3.0% in recent years. The proportion of tumors diagnosed with a PSA value under 2 has remained essentially constant during the past 10 years, but low-risk tumors are increasingly likely to be associated with PSA values of 2 to 6 rather than 6 to 10; the mean PSA value has also declined steadily during the past decade, from 5.9 in 1995-1999 to 5.1 in 2004-2006. Finally, PPB has also declined, from a mean of 41% in 1990-1994 to 23% in 2004-2006. Although the mean has not changed since 2000, the frequency of tumors with $\leq 10\%$ of positive biopsy cores continues to rise, to more than a third of low-risk tumors in 2004-2006.

To assess possible changes in risk within the low-risk group we applied two multivariable instruments, the Kattan nomogram and the CAPRA score (Table 1). The mean CAPRA score among low-risk patients decreased from 2.0 to 1.4 over the study period ($P<0.001$). CAPRA scores 0 and 1 have become more common, whereas scores 2 and 3 have declined within this group ($P<0.001$). The mean Kattan predicted likelihood of 5-year biochemical recurrence-free survival also rose slightly, from 90.2% to 90.8% ($P<0.001$) during the study period.

Table 2 illustrates trends in primary treatment selection among low-risk patients. The use of radical prostatectomy (RP) has increased in the 2000s to nearly 60% of low-risk patients. Use of brachytherapy appears to have peaked, increasing from 3.6% in the early 1990s to 19% in 2000-2001, then decreasing to 13% in 2004-2006. Use of external-beam radiotherapy (EBRT) and primary androgen deprivation therapy (ADT) monotherapy has decreased in recent years among low-risk patients, whereas active surveillance, having decreased from 14.8% in 1990-1994 to 6.2% in 2000-2001, has since risen to 10.2% in 2004-2006. There are no obvious trends in the use of multimodal local therapy (RP + EBRT or brachytherapy + EBRT), both of which remain uncommonly used among low-risk patients. Likewise, use of NADT in association with RP, cryotherapy, and radiation therapy has remained generally constant, declining slightly in the most recent years—roughly 5% of contemporary RP patients and 30% of cryotherapy and radiation patients receive NADT before primary treatment. The overall trend in primary treatment selection is statistically significant ($p<0.001$).

A total of 11.2% of the low-risk patients experienced disease recurrence; median follow-up was 35.6 months. The results of the survival analysis are presented in Figure 3. The log-rank test demonstrated statistically significant differences in survival by CAPRA score overall ($p<0.001$). Pairwise log-rank comparisons revealed significant differences between CAPRA scores 3 and 2 ($p=0.002$) and between scores 2 and 1 ($p=0.028$), but not between scores 1 and 0 ($p=0.584$). On Cox proportional hazards analysis (table 3), each increase in CAPRA score above 0 was associated with a 1.7-fold risk of recurrence (95% confidence interval, 1.39-2.06). The 5-year actuarial biochemical recurrence-free survival varied within the low-risk group from 93.7% for a CAPRA score of 0 to 63.3% for a CAPRA score of 3 and 33.6% for CAPRA scores of 4 to 6.

Discussion

We previously reported a sharp rise in the proportion of prostate tumors diagnosed with low-risk features during the CaPSURE project up to 2001.⁹ This trend has not continued during this decade to date; the distribution of tumors has remained relatively constant across the three risk strata since the prior analysis. On the other hand, within the low-risk group, there are significant, ongoing trends toward lower-risk characteristics. Nonpalpable, T1c tumors account for an ever-growing proportion of low-risk tumors, up to 78% from 30% across the study period. T1c tumors are associated with lower risk of recurrence than T2a tumors under the Kattan nomogram¹² but not under the CAPRA scoring system.¹⁰ T1a/b tumors detected by transurethral resection for presumed benign disease account for a negligible proportion of contemporary tumors.

Biopsy specimens assigned a Gleason score below 6 likewise account for only 3% of low-risk tumors in 2004-2006, consistent with a well-documented change in pathologists' practices.¹⁵ Of note, however, a few tumors were assigned a primary or secondary Gleason pattern of 2 even in 2006. The mean PSA value among low-risk tumors continues to decrease, with tumors increasingly likely to be diagnosed with PSA values of 2 to 6 ng/mL rather than 6 to 10 ng/mL. Those diagnosed with a PSA value <2 ng/mL represent a relatively constant fraction. A total of 68.8% of these were palpable T2a tumors diagnosed by abnormal digital rectal examination results and 9.9% were T1a/b. The remaining 21.3% were T1c; it is unclear what

prompted the biopsy among these patients—perhaps a strong family history, rapid PSA velocity, or abnormal digital rectal examination results on the contralateral side from the positive biopsy specimen, coded by the diagnosing urologist as T1c.

The trends in stage and Gleason grade represent continuation of trends we previously reported,⁹ whereas the prior study did not document a decline in PSA levels between 1993 and 2001, perhaps due to different categorization of PSA values (0-4 vs 4-10 ng/mL); the mean PSA value was not assessed in the earlier study. The present analysis is the first to our knowledge to examine time trends in PPB rates. The mean PPB decreased by nearly 50% during the 1990s and has stabilized since the beginning of the new decade. However, there is an ongoing increase in the proportion of tumors diagnosed with $\leq 10\%$ of positive biopsy cores—i.e., a single core of at least a 10-core biopsy. These now represent more than one third of low-risk tumors, reflecting increased use of extended-template biopsy techniques.¹⁶

Multivariable risk analyses yield further insights. The low-risk group has been described as facing an 85% likelihood of biochemical recurrence-free survival after RP.⁶ The preoperative Kattan predicted likelihood of 5-year recurrence-free survival for this group varied from 70% to 96%; in this series the mean Kattan predictions were essentially constant at approximately 90%. Mean CAPRA scores, on other hand, decreased from 2.0 to 1.4, with tumors with CAPRA scores of 0 to 1—representing the lowest risk patients—increasing from 26% to 60% of low-risk tumors. We found that the CAPRA score was able to substratify RP patients well within the low-risk group; with increasing CAPRA score, the hazard ratios for recurrence progressed upward, and 5-year actuarial survival declined consistently.

A typical low-risk patient could be assigned a CAPRA score up to 3 for age older than 50 years, PSA value of 6 to 10 ng/mL, and/or a PPB of $>33\%$. A few patients in the low-risk group had CAPRA scores of 4 to 6 because the traditional low-risk group is defined by total Gleason score and thus includes rare patients with Gleason 2+4 or 4+2 biopsy specimens. The survival results in this analysis for patients with CAPRA scores of 4 to 6 should not be taken as typical for all RP patients with these scores, but illustrate the point that the presence of Gleason pattern 4 disease drives outcomes, and Gleason 2+4 or 4+2 tumors should not be included with low-risk patients in outcomes analyses.

With regard to treatment trends among low-risk patients, we previously reported a sharp decline in use of active surveillance, from 20.3% in 1993-1995 to 7.9% in 1999-2001, and raised the concern regarding possible overtreatment among low-risk patients.⁹ A recent analysis from the population-based Surveillance, Epidemiology, and End Results (SEER) registries reached similar conclusions regarding underutilization of surveillance among low-risk patients, estimating overtreatment rates of 10% of RP and 45% of radiation therapy patients whose cancer was diagnosed in 2000-2002. Two important limitations of this study are that it considered “lower-risk” patients to be those with Gleason scores of 2 to 4 or those older than 70 years with Gleason scores of 5 to 7, an outdated classification of Gleason grading, and that it included primary ADT with “expectant management,” which may not be valid in terms of cost, quality-of-life, or outcomes.¹⁷

With increasing appreciation of the role of active surveillance for selected patients with low-risk tumors, we now find a reversal of the trend, with active surveillance rising from 6.2% of patients in 2000-2001 to 10.2% in 2005-2006. Use of brachytherapy has fallen from a peak of 19.4% in 2000-2001 to 13.0% in 2005-2006, whereas use of RP has risen to nearly 60% of low-risk patients. Use of both primary ADT and NADT has decreased from peaks, respectively, of 10.6% and 15.2% in 2000-2001 to 6.6% and 11.6%, also marking a reversal of trends previously documented in both CaPSURE and SEER.^{9, 18}

This study has limitations. Data are submitted only by patients and urologists; therefore, any treatments by other practitioners that are not reported by patients either to their urologists or in their questionnaires may be missed. Quality assurance mechanisms, including medical record review of all hospital admissions, help to minimize this problem. An enrollment bias may persist which could artificially lower the proportion of observation patients: patients who are diagnosed as having prostate cancer but who elect not to undergo treatment may simply monitor their PSA levels with their primary care provider, or not at all. If diagnosed as having prostate cancer by a CaPSURE urologist and enrolled in the database, however, patients should have completed at least one treatment questionnaire.

The CaPSURE practice sites have not been chosen at random and thus do not constitute a statistically valid sample of the United States patient population. However, they represent a broad range of geographic locales and a mix of academic and community sites, which we believe to be the best available sample for the analysis of temporal trends in “real-world” practice. It is possible that the results would have been different with different grouping of the years of diagnosis, but given the consistently strong trends and low p-values realized, this seems unlikely. The 1998 Kattan preoperative nomogram has recently been updated by Stephenson et al,¹⁹ and the 2006 version incorporates more detailed information on biopsy cores taken and positive. It is quite possible that the 2006 nomogram would better reflect a decline in risk within the low-risk group, and would be more relevant to contemporary patients. However, the newer nomogram has not yet been validated in the community setting, and cannot readily be calculated for large numbers of patients. The CAPRA score has to date been validated only for RP patients, and results of our survival analysis should not yet be extrapolated to patients undergoing other treatments.

Conclusions

The proportion of prostate cancer patients assigned to the low-risk group as defined by a PSA level of ≤ 10 ng/mL, a clinical stage $\leq T_a$, and a Gleason score of ≤ 6 has stabilized at just under half of patients with newly diagnosed prostate cancer in the first 6 years of the new millennium. However, within this group, there are significant and ongoing trends toward lower risk at presentation as assessed by PSA, PPB, and multivariable CAPRA score. The CAPRA score is able to substratify RP patients effectively within the low-risk group based on risk of biochemical recurrence and helps confirm that patients with Gleason scores of 2+4 or 4+2 should not be considered low risk despite a Gleason sum of 6. Rates of active surveillance have increased since the start of this decade, but especially given the ongoing downward trends in risk, a period of surveillance rather than immediate treatment is still likely under-used as a first management option for many eligible men with low-risk disease. Methods for selecting out those appropriate for active surveillance using clinical markers and molecular markers is greatly needed.

References

1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics, 2007. *CA Cancer J Clin* 2007;57:43. [PubMed: 17237035]
2. Bill-Axelson A, Holmberg L, Ruutu M, Haggman M, Andersson SO, Bratell S, et al. Radical prostatectomy versus watchful waiting in early prostate cancer. *N Engl J Med* 2005;352:1977. [PubMed: 15888698]
3. Wei JT, Dunn RL, Sandler HM, McLaughlin PW, Montie JE, Litwin MS, et al. Comprehensive comparison of health-related quality of life after contemporary therapies for localized prostate cancer. *J Clin Oncol* 2002;20:557. [PubMed: 11786586]

4. Roehl KA, Han M, Ramos CG, Antenor JA, Catalona WJ. Cancer progression and survival rates following anatomical radical retropubic prostatectomy in 3,478 consecutive patients: long-term results. *J Urol* 2004;172:910. [PubMed: 15310996]
5. Albertsen PC, Hanley JA, Fine J. 20-year outcomes following conservative management of clinically localized prostate cancer. *JAMA* 2005;293:2095. [PubMed: 15870412]
6. D'Amico, AV. Combined-modality staging in predicting prostate-specific antigen outcome after definitive local therapy for men with clinically localized prostate cancer. In: D'Amico, AV., editor. *Prostate cancer: principles & practice*. Philadelphia, PA: Lippincott Williams & Wilkins; 2002. p. 254-268.
7. Warlick C, Trock BJ, Landis P, Epstein JI, Carter HB. Delayed versus immediate surgical intervention and prostate cancer outcome. *J Natl Cancer Inst* 2006;98:355. [PubMed: 16507832]
8. Klotz L. Active surveillance with selective delayed intervention for favorable risk prostate cancer. *Urol Oncol* 2006;24:46. [PubMed: 16414494]
9. Cooperberg MR, Lubeck DP, Meng MV, Mehta SS, Carroll PR. The changing face of low-risk prostate cancer: trends in clinical presentation and primary management. *J Clin Oncol* 2004;22:2141. [PubMed: 15169800]
10. Cooperberg MR, Pasta DJ, Elkin EP, Litwin MS, Latini DM, DuChane J, et al. The University of California, San Francisco Cancer of the Prostate Risk Assessment score: a straightforward and reliable preoperative predictor of disease recurrence after radical prostatectomy. *J Urol* 2005;173:1938. [PubMed: 15879786]
11. Cooperberg MR, Broering JM, Litwin MS, Lubeck DP, Mehta SS, Henning JM, et al. The contemporary management of prostate cancer in the United States: lessons from the cancer of the prostate strategic urologic research endeavor (CaPSURE), a national disease registry. *J Urol* 2004;171:1393. [PubMed: 15017184]
12. Kattan MW, Eastham JA, Stapleton AM, Wheeler TM, Scardino PT. A preoperative nomogram for disease recurrence following radical prostatectomy for prostate cancer. *J Natl Cancer Inst* 1998;90:766. [PubMed: 9605647]
13. Greene KL, Meng MV, Elkin EP, Cooperberg MR, Pasta DJ, Kattan MW, et al. Validation of the Kattan preoperative nomogram for prostate cancer recurrence using a community based cohort: results from Cancer of the Prostate Strategic Urological Research Endeavor (CaPSURE). *J Urol* 2004;171:2255. [PubMed: 15126797]
14. Cooperberg MR, Freedland SJ, Pasta DJ, Elkin EP, Presti JC Jr, Amling CL, et al. Multiinstitutional validation of the UCSF cancer of the prostate risk assessment for prediction of recurrence after radical prostatectomy. *Cancer* 2006;107:2384. [PubMed: 17039503]
15. Smith EB, Frierson HF Jr, Mills SE, Boyd JC, Theodorescu D. Gleason scores of prostate biopsy and radical prostatectomy specimens over the past 10 years: is there evidence for systematic upgrading? *Cancer* 2002;94:2282. [PubMed: 12001128]
16. Terris MK. Prostate biopsy strategies: past, present, and future. *Urol Clin North Am* 2002;29
17. Miller DC, Gruber SB, Hollenbeck BK, Montie JE, Wei JT. Incidence of initial local therapy among men with lower-risk prostate cancer in the United States. *J Natl Cancer Inst* 2006;98:1134. [PubMed: 16912266]
18. Shahinian VB, Kuo YF, Freeman JL, Orihuela E, Goodwin JS. Increasing use of gonadotropin-releasing hormone agonists for the treatment of localized prostate carcinoma. *Cancer* 2005;103:1615. [PubMed: 15742331]
19. Stephenson AJ, Scardino PT, Eastham JA, Bianco FJ Jr, Dotan ZA, Fearn PA, et al. Preoperative nomogram predicting the 10-year probability of prostate cancer recurrence after radical prostatectomy. *J Natl Cancer Inst* 2006;98:715. [PubMed: 16705126]

Abbreviations

ADT	androgen deprivation therapy
CAPRA	Cancer of the Prostate Risk Assessment
CaPSURE	Cancer of the Prostate Strategic Urologic Research Endeavor

EBRT	external-beam radiation therapy
NADT	neoadjuvant androgen deprivation therapy
PPB	percentage of positive biopsy cores
PSA	prostate-specific antigen
RP	radical prostatectomy
SEER	Surveillance, Epidemiology, and End Results

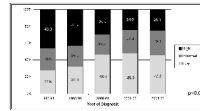
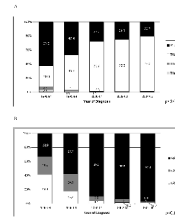
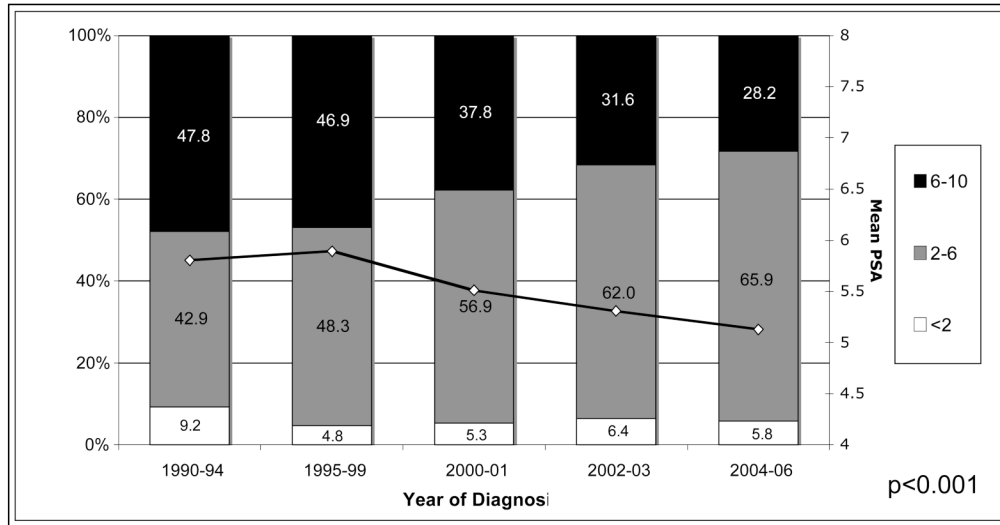


Figure 1.

Trends in patient clinical risk stratification at time of diagnosis. Percentage of men stratified to low-, intermediate-, and high-risk groups in each year group. Numbers indicate aggregate totals for each group in each time period: 1990-1994, 1995-1999, 2000-2001, 2002-2003, and 2004-2006. The trend toward more low- and less high-risk disease at diagnosis was significant ($P < 0.001$).



C



D

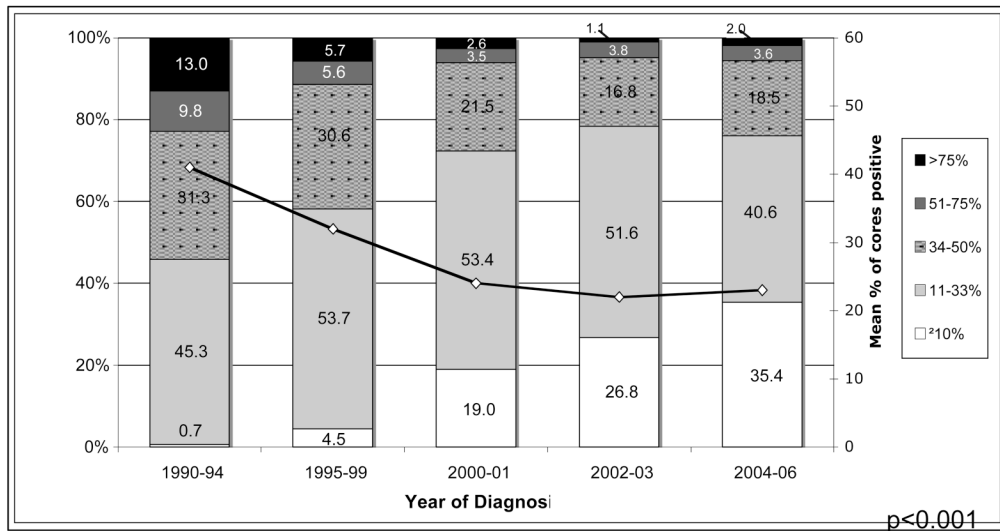


Figure 2. Time trends in individual risk characteristics among low-risk patients. Distribution over time of clinical T stages (A), Gleason scores (B), serum prostate-specific antigen (PSA) levels (C),

and percentage of positive biopsy cores (PPB) (D). Trends in distribution of each risk characteristic were statistically significant at $P < 0.001$. On panels C and D, the mean PSA and PPB, respectively, are plotted on the secondary y-axis for each time period.

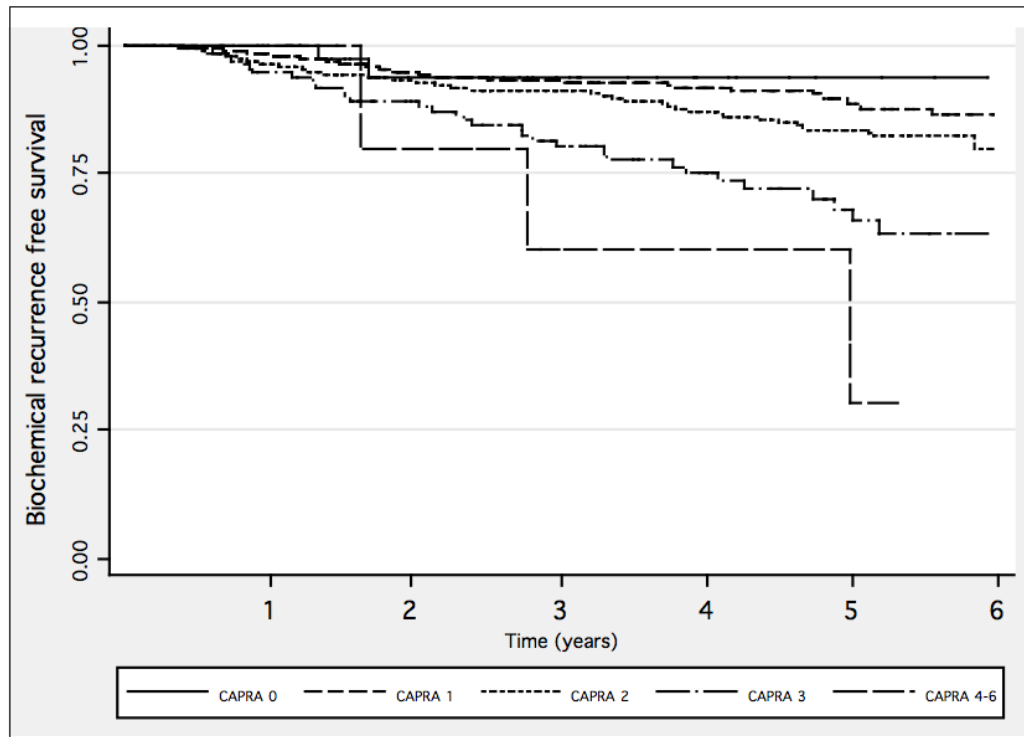


Figure 3. Biochemical survival among radical prostatectomy patients with low-risk prostate cancer. Kaplan-Meier curves for biochemical recurrence-free survival among patients with low-risk prostate cancer undergoing radical prostatectomy, stratified by Cancer of the Prostate Risk Assessment (CAPRA) score.

Table 1

Trends in CAPRA and Kattan scores among low-risk patients*

Scores	Year of diagnosis							Total
	1990-1994	1995-1999	2000-2001	2002-2003	2004-2006			
CAPRA								
0	2 (0.7)	7 (1.2)	18 (1.8)	22 (2.1)	22 (2.7)	71 (1.9)		
1	73 (25.4)	218 (36.3)	492 (48.1)	594 (55.9)	461 (57.4)	1838 (48.7)		
2	136 (47.4)	288 (48.0)	441 (43.1)	380 (35.8)	278 (34.6)	1523 (40.3)		
3	73 (25.4)	86 (14.3)	72 (7.0)	66 (6.2)	42 (5.2)	339 (9.0)		
4	2 (0.7)	1 (0.2)	1 (0.1)	0 (0.0)	0 (0.0)	4 (0.1)		
5	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)		
6	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.0)		
Total	287	600	1,024	1,063	803	3,777		
Mean CAPRA score	2.01	1.76	1.56	1.47	1.42	1.56		
Mean Kattan score	90.24	90.07	90.41	90.57	90.80	90.40		

* Data are number (percentage) of patients unless otherwise indicated. CAPRA = Cancer of the Prostate Risk Assessment.

Table 2

Trends in primary treatment among low-risk patients*

Primary treatment	Year of diagnosis						Total
	1990-1994	1995-1999	2000-2001	2002-2003	2004-2006		
RP	211 (53.7)	377 (54.1)	560 (52.5)	637 (58.6)	437 (59.6)	2222 (55.9)	
(NADT)	(2.4)	(6.1)	(3.0)	(4.6)	(5.7)	(4.5)	
RP + EBRT	11 (2.8)	14 (2.0)	6 (0.6)	5 (0.5)	3 (0.4)	39 (1.0)	
(NADT)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	
Cryotherapy	26 (6.6)	15 (2.2)	21 (2.0)	28 (2.6)	32 (4.4)	122 (3.1)	
(NADT)	(15.4)	(33.3)	(38.1)	(46.4)	(25.0)	(31.1)	
Brachytherapy	14 (3.6)	97 (13.9)	207 (19.4)	183 (16.8)	95 (13.0)	596 (15.0)	
(NADT)	(14.3)	(28.9)	(32.4)	(35.5)	(29.5)	(31.9)	
Brachytherapy + EBRT	1 (0.3)	8 (1.2)	9 (0.8)	10 (0.9)	4 (0.6)	32 (0.8)	
(NADT)	(0.0)	(62.5)	(55.6)	(40.0)	(25.0)	(46.9)	
EBRT	51 (13.0)	66 (9.5)	84 (7.9)	45 (4.1)	39 (5.3)	285 (7.2)	
(NADT)	(11.8)	(27.3)	(45.2)	(26.7)	(23.1)	(29.1)	
ADT	21 (5.3)	47 (6.7)	113 (10.6)	85 (7.8)	48 (6.6)	314 (7.9)	
Active surveillance	58 (14.8)	73 (10.5)	66 (6.2)	94 (8.7)	75 (10.2)	366 (9.2)	
Total	393	697	1066	1087	733	3976	
(NADT)	(5.4)	(13.7)	(15.2)	(13.6)	(11.6)	(12.9)	

* Data are presented as number (percentage) of patients. For each local treatment (excluding WW and ADT), the second line in each cell indicates the percentage of patients also receiving NADT. ADT, androgen deprivation therapy; EBRT, external-beam radiation therapy; NADT, neoadjuvant androgen deprivation therapy; RP, radical prostatectomy.

Table 3

Survival analysis among low-risk patients by CAPRA score*

CAPRA score	HR (95% CI)	P value	5-Year recurrence-free survival (95% CI)
Continuous	1.70 (1.39–2.06)	<0.001	
0	Referent		93.7 (98.4-74.8)
1	1.51 (0.37-6.18)	0.570	88.0 (90.5-84.9)
2	2.26 (0.55-9.22)	0.256	82.4 (85.2-79.0)
3	4.31 (1.03-18.01)	0.045	63.3 (68.5-57.3)
4-6	9.76 (1.63-58.46)	0.013	33.6 (40.2-26.3)

* Hazard ratios (HRs) with 95% confidence intervals (CIs) given for Cancer of the Prostate Risk Assessment (CAPRA) as a continuous variable (4-6 treated as equal to 4) and at each level compared with a CAPRA score of 0 as a referent. Five-year actuarial biochemical recurrence-free survival calculated via Kaplan-Meier analysis.