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Platinum Priority – Prostate Cancer

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Careful Selection and Close Monitoring of Low-Risk Prostate Cancer Patients on Active Surveillance Minimizes the Need for Treatment

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Abstract

Background: With the advent of prostate-specific antigen (PSA) screening and the increase in the number of transrectal ultrasound-guided biopsy cores, there has been a dramatic rise in the incidence of low-risk prostate cancer (LRPC). Because >97% of men with LRPC are likely to die of something other than prostate cancer, it is critical that patients give thought to whether early curative treatment is the only option at diagnosis.

Objective: To identify a group of men with LRPC who may not require initial treatment and monitor them on our active surveillance (AS) protocol, to determine the percentage treated and the outcome and to analyze the quality-of-life data.

Design, setting, and participants: We defined patients eligible for AS as Gleason ≤ 6 , PSA ≤ 10 , and two or fewer biopsy cores with $\leq 20\%$ tumor in each core.

Measurements: Kaplan Meier analysis was used to predict the 5-year treatment free survival. Logistic regression determined the predictors of treatment. Data on sexual function, continence, and outcome were obtained and analyzed.

Results and limitations: The AS cohort consisted of 230 patients with a mean age of 63.4 yr; 86% remained on AS for a mean follow-up of 44 mo. Thirty-two of the 230 patients (14%) were treated for a mean follow-up of 33 mo. Twelve had a total prostatectomy (TP). The pathologic stage of these patients was similar to initially treated TP patients with LRPC. Fourteen underwent radiation therapy, and six underwent androgen-deprivation therapy. Fifty percent of patients had no tumor on the first rebiopsy, and only 5% of these patients were subsequently treated. PSA doubling time and clinical stage were not predictors of treatment. No patient progressed after treatment. Among the AS patients, 30% had incontinence, yet <15% were bothered by it. As measured by the Sexual Health Inventory for Men, 49% of patients had, at a minimum, moderate (≤ 16) erectile dysfunction.

Conclusions: If guidelines for AS are narrowly defined to include only patients with Gleason 6, tumor volume $\leq 20\%$ in one or two biopsy cores, and PSA levels ≤ 10 , few patients are likely to require treatment. Progression-free survival of those treated is likely to be equivalent to patients with similar clinical findings treated at diagnosis.

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1. Introduction

With the advent of prostate-specific antigen (PSA) screening and the increase in the number of transrectal ultrasound (TRUS)-guided biopsy cores, there has been a dramatic rise in the incidence of low-risk prostate cancer (LRPC; Gleason 6, T1c, low volume) [1,2]. Based on patients identified between 1996 and 2003, 91% of new cases of prostate cancer (PCa) were expected to be diagnosed with clinically localized disease and an anticipated 5-yr relative survival approaching 100% [3]. As many as 50% of PCa cases detected by screening may be “over-diagnosed,” with 5–12 yr of lead time before treatment becomes necessary [4]. Interestingly, treatment patterns have not reflected the downward stage and risk migration of these newly diagnosed LRPC patients [5,6]. Consequently, the dilemma regarding treatment decisions has become more challenging. Because >97% of men with LRPC are likely to die of something other than PCa [7], it is critical that patients give thought to whether early curative treatment—with a 50% likelihood of negative health-related quality of life (HRQoL) sequelae—is the only option at diagnosis.

The concept of active surveillance (AS) for LRPC has evolved since the 1990s. Initially, watchful waiting (WW) was advanced as a viable strategy for LRPC patients, delaying treatment and its associated comorbidities until clinical progression was observed [8,9]. Patients electing WW had localized disease but were older or had comorbidities that precluded them from having curative treatment. Often, those treated were prescribed palliative therapy, such as androgen-deprivation therapy. D’Amico et al created preliminary guidelines in 1998 to define LRPC and thus those patients eligible for AS: PSA levels ≤ 10 , Gleason score < 7 (no 4 or 5 in biopsy), and stage T1a–2a disease [10]. Over the past 10 yr, PSA velocity and density and cancer volume per core have contributed to refining the literature on AS [7,8].

The goal of this study was to investigate how best to follow LRPC patients who have made the decision to be carefully monitored on AS and to determine what percentage of AS patients were treated. In addition, if patients met the criteria for treatment while on AS, were they likely to be cured with treatment? We also analyzed the data on quality of life (QoL).

2. Methods

Since February 1992, men with LRPC have been identified and offered a surveillance regimen. Guidelines were initiated to define eligibility for AS: Gleason score ≤ 6 , PSA levels ≤ 10 , and two or fewer biopsy cores with $\leq 20\%$ tumor present in each core. All patients had T1a–T2 disease. Frequently, patients came to our center with a diagnosis of PCa: Their diagnostic biopsy usually consisted of a minimum of 10 cores. Curative treatment (total prostatectomy [TP] or radiation therapy [RT]) was urged on increase in tumor volume, Gleason grade > 3 , or more than two positive cores on rebiopsy. (We find the term *total prostatectomy* to be more appropriate than *radical prostatectomy* [11].)

Patient data were recorded in a retrospective database, approved by the institutional review board and designed to analyze clinical and pathologic information. The data were abstracted from the patient chart following patient visit and entered into the database.

All patients had to satisfy the requirements of the AS guidelines. Patients who had < 12 -mo follow-up and/or were ≥ 80 yr of age were excluded from the cohort. Patients 75–79 yr of age who at the time of diagnosis were healthy enough for curative treatment were offered AS.

Beginning in January 2007, data were obtained at each visit using the Sexual Health Inventory for Men (SHIM) [12] and the International Conference on Incontinence Short Form (ICI-SF) [13]. These questionnaires replaced the verbal data initially collected as part of the history and the physical.

Each AS patient was followed every 3–4 mo with a PSA and rectal exam (RE) for the first 2 yr, then every 6 mo. In addition, after 2000, a laterally directed and peripherally targeted TRUS biopsy of 10–12 cores was performed 9–12 mo after the initial visit (the first rebiopsy), and then every year or earlier if there was a dramatic rise in PSA or a change on RE. Patients were asked to sign a document that emphasized the guidelines for AS and the need for vigorous monitoring. The decision to discontinue AS was based on (1) Gleason grade > 3 on rebiopsy, (2) increase in tumor volume measured by percentage of tumor in each core, (3) increase in the number of positive cores, or (4) personal preference.

We identified patients from our TP database who met the criteria for AS but who elected TP at diagnosis. We compared their outcome with patients who underwent TP after being followed on AS. Statistical analysis was completed using SPSS v.17 (SPSS, Chicago, IL, USA). Descriptive data spanning time from diagnosis through follow-up were analyzed. Kaplan-Meier analysis was used to characterize the 5-yr probability of treatment-free survival as well as the 5-yr probability of treatment-free survival as determined by rebiopsy findings. Logistic regression analysis was performed to determine the best predictors for no treatment. A p value ≤ 0.05 was considered statistically significant.

3. Results

Two hundred thirty out of 250 patients met the criteria for AS (20 patients had not been followed for 12 mo). The mean age of the AS patients at diagnosis was 63.4 yr of age (median: 64; range: 42–79), with a mean PSA value of 5.07 ng/ml (median: 4.76). The mean follow-up for the cohort was 44 mo (median: 32; range: 12–208; Table 1).

Fifty percent of patients had no tumor on the first rebiopsy; 46% continued to have small-volume Gleason

Table 1 – Demographics of the active surveillance (AS) cohort versus treated AS patients

| | AS cohort | Treated AS patients |
|-------------------------|--|--|
| No. of patients | 230 | 32 |
| Age at diagnosis, yr | Mean: 63.4 Median: 64 Range: 42–79 | Mean: 65.3 Median: 68 |
| PSA at diagnosis, ng/ml | Mean: 5.07 Median: 4.80 | Mean: 5.66 Median: 5.14 |
| Length of follow-up, mo | Mean: 44 Median: 35 Range: 12–208 | Mean: 33 Median: 31 Range: 12–92 |
| Age at Tx, yr | N/A | Mean: 68.5 Median: 70 Range: 44–84 |
| First SHIM score | Mean: 14.2 Median: 17.5 | Mean: 16.9 Median: 21.5 |
| Last SHIM score | Mean: 11.8 Median: 13 | Mean: 14.23 (before Tx) Median: 20 |

AS = active surveillance; PSA = prostate-specific antigen; Tx = treatment; N/A = not available; SHIM = Sexual Health Inventory for Men.

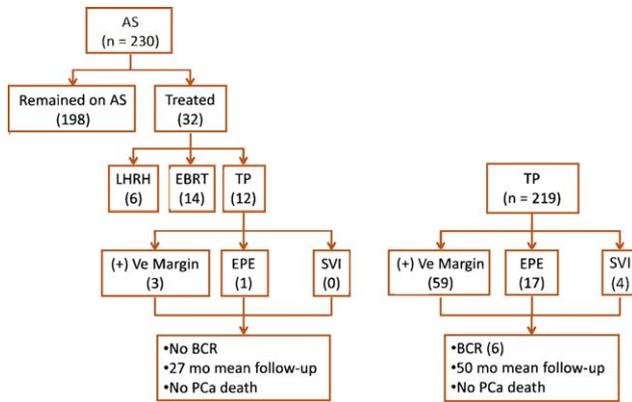


Fig. 1 – Outcome of treated active surveillance patients with total prostatectomy (TP) versus initially treated TP patients. AS = active surveillance; LHRH = luteinizing hormone-releasing hormone; EBRT = external-beam radiation therapy; TP = total prostatectomy; EPE = extraprostatic extension; SVI = seminal vesical invasion; BCR = biochemical recurrence; PCa = prostate cancer.

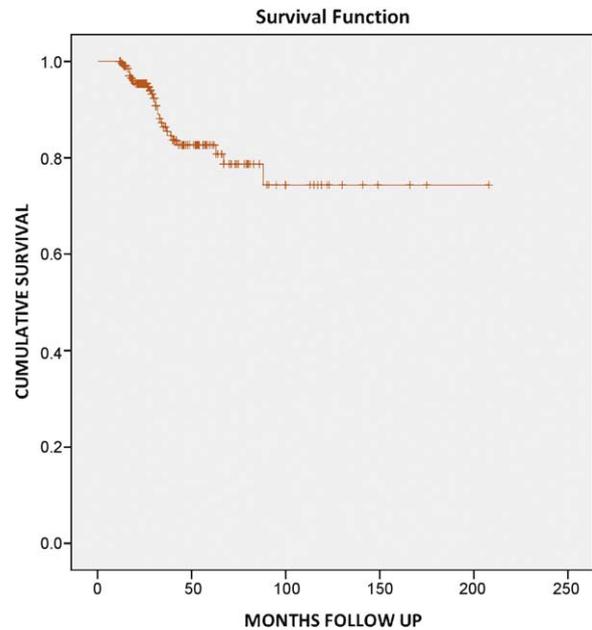


Fig. 2 – Kaplan-Meier treatment-free survival curve.

score 6 tumors. Six patients (2.5%) had Gleason grade 4, and three others had an increase in tumor volume. On the second rebiopsy, 15 patients had Gleason grade 4. On the third rebiopsy, three patients had Gleason grade 4. Five percent of patients who had no tumor in the first or second rebiopsy were treated, compared with 16.5% who had focal Gleason 6 on the first rebiopsy. There was no tumor in 49%, 52%, and 71% of the second, third, and fourth rebiopsies, respectively.

Of the 230 men in the AS cohort, 32 (14%) were treated over a mean follow-up of 33 mo (median: 31; range: 12–92). The mean age of the treated population at diagnosis was 65.3 yr of age; the mean PSA level (at diagnosis) was 5.66 ng/ml (Table 1). The mean age at time of treatment was 68.5 yr of age (range: 44–84).

Twelve of the 32 treated patients had TP, 14 had interstitial or external-beam RT (EBRT), and 6 underwent hormone therapy (HT; Fig. 1). Seven patients treated with TP had Gleason score 3 + 4 or 4 + 3 on the TP specimen; two had Gleason score 3 + 5 or 4 + 4 (Table 2). The mean follow-up post-surgery was 30 mo (median: 35). None of the TP patients have had biochemical recurrence (BCR). No patient has died of PCa.

A Kaplan-Meier analysis predicted that 85.7% of the entire AS cohort would be free from treatment at 5 yr (Fig. 2). Logistic regression was performed to determine which variables best predict those patients who would likely not undergo treatment. PSA doubling time (PSA DT) and clinical stage were not predictors for treatment. Any tumor at the first rebiopsy was a predictor for treatment ($p = 0.011$; coefficient of 1.517).

The SHIM and ICI-SF were completed by 172 of 230 patients. On the ICI-SF, 30% of AS patients demonstrated some degree of incontinence; few were bothered by it (bother score >0). The mean initial and final ICI scores were not significantly different 1.16 and 1.1 respectively.

Forty-nine percent of patients had at least moderate erectile dysfunction (ED), as measured by the SHIM. The mean scores (initial mean score: 14.2 [median: 17.50]; final mean score: 11.8 [median: 13]) also indicated moderate ED in the cohort at large. A paired-sample student *t* test

Table 2 – Results following total prostatectomy of treated active surveillance patients

| Gleason score at Tx | Volume, % | EPE | SVI | Margin | BCR | Follow-up, mo |
|---------------------|-----------|-----|-----|--------|-----|---------------|
| 3 + 4 | 15 | – | – | + | – | 37 |
| 3 + 4 | 16 | – | – | – | – | 24 |
| 3 + 3 | 1.5 | – | – | + | – | 37 |
| 3 + 3 | 6 | – | – | – | – | 37 |
| 3 + 4 | 3 | – | – | – | – | 32 |
| 3 + 3 | 2.5 | – | – | – | – | 47 |
| 4 + 3 | 6+ | – | – | – | – | 32 |
| 3 + 4 | 20 | + | – | – | – | 16 |
| 3 + 4 | 10 | – | – | – | – | 29 |
| 4 + 4 | 1 | – | – | – | – | 20 |
| 3 + 5 | 15 | – | – | – | – | 2 |
| 3 + 4 | – | – | – | + | – | 2 |

Tx = treatment; EPE = extraprostatic extension; SVI = seminal vesical invasion; BCR = biochemical recurrence.

Table 3 – Decline in erectile function in different age groups

| Age group, yr | No. | p value (first SHIM/ last SHIM) | Follow-up, mo |
|------------------|-----|------------------------------------|-----------------------------|
| Group I: 40–49 | 12 | $p \leq 0.019$ (20/11.2) | Mean: 36 Median: 27 |
| Group II: 50–59 | 41 | $p = 0.376$ (18.1/17) | Mean: 42 Median: 30.5 |
| Group III: 60–69 | 65 | $p \leq 0.10$ (13.5/10.7) | Mean: 40.6 Median: 31.50 |
| Group IV: 70–79 | 19 | $p \leq 0.032$ (12.2/9.2) | Mean: 47 Median: 38.05 |

SHIM = Sexual Health Inventory for Men.

analyzing the initial/last SHIM scores revealed that the last scores were significantly lower ($p < 0.001$). The significant increase in ED was seen in three of four age groups (40–49; 50–59; 60–69; 70–79; Table 3). There was no significant difference in the mean age between patients with ED and patients with normal erectile function ($p = 0.75$).

AS patients with SHIM scores ≥ 21 (30%) and normal erectile function at diagnosis were studied to determine whether multiple TRUS biopsies had an effect on potency. The group's mean age was 58.57 yr of age (median: 58.50). Interestingly, over a mean follow-up of 35 mo (median: 28), there was a significant increase ($p \leq 0.001$) in ED (mean: 23.65 to mean: 17.98) from the initial SHIM.

Our AS guidelines were met by 219 out of 2100 patients who initially had TP rather than selecting AS. Only 22% of these patients contained Gleason grade 4 or 5 in the surgical specimen. In the 219 patients, 59 (27%) had a positive margin, 17 (7.5%) had extraprostatic extension (EPE), and 4 (2%) had seminal vesicle invasion (SVI; Fig. 1). There was no significant difference in the positive margin rate between initially treated patients and patients treated following AS ($p = 0.52$), EPE ($p = 0.73$), or SVI ($p = 0.79$).

4. Discussion

Today, clinicians recognize that a growing number of cancers detected by PSA screening are likely to be LRPC and may never be life-threatening during the patient's lifetime. Nevertheless, LRPC patients are often subjected to treatment and its HRQoL consequences without bettering their chances for progression-free survival (PFS) [14].

Although the percentage of patients who have treatment for LRPC after initial AS ranges from 17% to 33%, no markers accurately define which tumors "progress" [15]. There is concern among urologists that tumors, while being monitored, may progress beyond the opportunity for cure. Ploussard et al suggested that PCa patients initially diagnosed by a 21-core biopsy who then select AS had a higher likelihood of more favorable disease on TP [16]. Others have argued, though, that men diagnosed based on a more limited initial biopsy have also demonstrated favorable outcomes at treatment following AS [17].

Several critical factors should have influenced support of AS. Change in the technique of prostate biopsies and increased numbers of cores obtained have moderated grade migration on the surgical specimen. Over the past 15 yr, we

found 20% fewer (from 47% to 27%) "under-graded" tumors than previously observed [18].

By carefully selecting the AS cohort to include only those patients who have been compliant with the guidelines of close surveillance and who have low-volume disease ($\leq 20\%$ of tumor in two or fewer cores), a relatively small percentage (14% in this cohort) have required treatment. Among those eventually treated with surgery or RT, no patient has progressed or died from PCa. Progression was defined as BCR. In the AS cohort treated with TP (12 of 32), tumor volume $\leq 20\%$ was reported in 100% of the patients and a positive margin in 3 of 12 patients. All patients were free of SVI, and one patient had EPE (Fig. 1).

As in other reported studies [19,20], neither PSA DT nor PSA velocity was an indication for treatment in our cohort. Increase in Gleason score or tumor volume was the threshold to urge treatment. Even though our mean post-TP follow-up is only 27 mo (range: 2–47; median: 35), we are cautiously optimistic that the prognosis will likely be as good as those with initial TP. Change in clinical stage coupled with a rising PSA level triggered treatment in older patients (> 80 yr of age after being followed) who elected HT. Only one patient elected treatment because of distress over living with untreated PCa.

Waning sexual function may be a common disease-specific concern for patients with PCa [21,22]. Beginning in 2007, all men with a diagnosis of PCa were asked to complete the SHIM. Of this subset of our AS cohort, 44% (first SHIM) and 56% (last SHIM) had at least moderate (≤ 16) ED. The significant increase in ED was seen in three of four age groups. The median follow-up was < 3 yr; thus, age may not be the significant factor that affects ED in this AS cohort (Table 3).

Why are few men offered AS, and of those patients who are, why do so few choose it as an alternate strategy? There appears to be a lack of acceptance for AS [23]. In a study of 110 of our AS cohort, 67% reported that the physician who diagnosed their PCa did not offer AS as an alternative to treatment. This offer is critical because it was reported that as many as 57–70% of patients chose treatment based on physician recommendation [24].

Before PSA screening, nearly half of PCa patients were diagnosed with advanced disease (T3–T4) [10] and had a poor prognosis. The problem, therefore, is not in diagnosing PCa but in educating patients about risk-adapted alternatives. Patients have the right to know they have LRPC, and physicians should not feel compelled to treat every PCa patient. With comprehensive educational information and supportive care from the physician, as many as 45% of PCa patients could postpone treatment—maybe indefinitely [1].

Our study has some limitations. AS patients with no ED were evaluated to see whether repeated biopsies might alter erectile function, as suggested by Fujita et al [25]. Because we only started collecting data on QoL objectively in 2007, we are lacking sufficient data to draw conclusions because of the short time span and the small number of repeated biopsies between the first and last questionnaire. Another limitation of our study is the small number of patients treated with TP. A larger number of patients treated

and longer follow-up are essential to better define the outcome of treatment following AS. Merging the data from multiple institutions might provide the most accurate outcome of treated AS patients.

5. Conclusions

Our data suggest that if the guidelines for AS are narrowly defined to include only those patients with Gleason score 6, PSA levels ≤ 10 , and tumor volume $\leq 20\%$ in two or fewer cores, a lower percentage of AS patients will likely require treatment when compared to other AS series. In our experience, the PFS appears to be equivalent to those who initiated treatment at diagnosis. With careful selection and close monitoring of LRPC, the dilemma regarding overtreatment and its impact on HRQoL, which may already be impaired at diagnosis, may be less of a dilemma—if and when AS is accepted as a viable alternative.

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Study concept and design: M. Soloway, Manoharan.

Acquisition of data: C. Soloway, Eldefrawy, Acosta.

Analysis and interpretation of data: C. Soloway, Eldefrawy.

Drafting of the manuscript: M. Soloway, C. Soloway, Eldefrawy.

Critical revision of the manuscript for important intellectual content: Kava.

Statistical analysis: C. Soloway, Eldefrawy.

Obtaining funding: None.

Administrative, technical, or material support: Acosta.

Supervision: Manoharan, M. Soloway.

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References

- [1] O'Donnell H, Parker C. What is low-risk prostate cancer and what is its natural history? *World J Urol* 2008;26:415–22.
- [2] Cooperberg MR, Moul JW, Carroll PR. The changing face of prostate cancer. *J Clin Oncol* 2005;23:8146–51.
- [3] Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. *CA Cancer J Clin* 2009;59:225–49.
- [4] Savage CJ, Lilja H, Cronin AM, Ulmert D, Vickers AJ. Empirical estimates of the lead time distribution for prostate cancer based on two independent representative cohorts of men not subject to prostate-specific antigen screening. *Cancer Epidemiol Biomarkers Prev* 2010;19:1201–7.
- [5] Albertsen PC, Hanley JA, Fine J. 20-year outcomes following conservative management of clinically localized prostate cancer. *JAMA* 2005;293:2095–101.
- [6] Bastian PJ, Carter BH, Bjartell A, et al. Insignificant prostate cancer and active surveillance: from definition to clinical implications. *Eur Urol* 2009;55:1321–32.
- [7] Dall'Era MA, Cooperberg MR, Chan JM, et al. Active surveillance for early-stage prostate cancer: review of the current literature. *Cancer* 2008;112:1650–9.
- [8] Klotz L. Active surveillance for favorable risk prostate cancer: rationale, risks, and results. *Urol Oncol* 2007;25:505–9.
- [9] Neulander EZ, Duncan RC, Tiguert R, Posey JT, Soloway MS. Deferred treatment of localized prostate cancer in the elderly: the impact of the age and stage at the time of diagnosis on the treatment decision. *BJU Int* 2000;85:699–704.
- [10] D'Amico AV, Whittington R, Malkowicz SB, et al. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. *JAMA* 1998;280:969–74.
- [11] Nieder AM, Soloway MS. It's not a radical prostatectomy, it's a total prostatectomy. *Eur Urol* 2008;54:715–6.
- [12] Cappelleri JC, Rosen RC. The Sexual Health Inventory for Men (SHIM): a 5-year review of research and clinical experience. *Int J Impot Res* 2005;17:307–19.
- [13] Avery K, Donovan J, Peters TJ, Shaw C, Gotoh M, Abrams P. ICIQ: a brief and robust measure for evaluating the symptoms and impact of urinary incontinence. *Neurourol Urodyn* 2004;23:322–30.
- [14] Roemeling S, Roobol MJ, Kattan MW, van der Kwast TH, Steyerberg EW, Schroder FH. Nomogram use for the prediction of indolent prostate cancer: impact on screen-detected populations. *Cancer* 2007;110:2218–21.
- [15] Martin RM, Gunnell D, Hamdy F, Neal D, Lane A, Donovan J. Continuing controversy over monitoring men with localized prostate cancer: a systematic review of programs in the prostate specific antigen era. *J Urol* 2006;176:439–49.
- [16] Ploussard G, Xylinas E, Salomon L, et al. The role of biopsy core number in selecting prostate cancer patients for active surveillance. *Eur Urol* 2009;56:891–8.
- [17] van den Bergh RCN, Roemeling S, Roobol MJ, et al. Outcomes of men with screen-detected prostate cancer eligible for active surveillance who were managed expectantly. *Eur Urol* 2009;55:1–8.
- [18] Rajinikanth A, Manoharan M, Soloway CT, Civantos FJ, Soloway MS. Trends in Gleason score: concordance between biopsy and prostatectomy over 15 years. *Urology* 2008;72:177–82.
- [19] Schröder FH, Roobol MJ, van der Kwast TH, Kranse R, Bangma CH. Does PSA velocity predict prostate cancer in pre-screened populations? *Eur Urol* 2006;49:460–5, discussion 465.
- [20] O'Brien MF, Cronin AM, Fearn PA, et al. Pretreatment prostate-specific antigen (PSA) velocity and doubling time are associated with outcome but neither improves prediction of outcome beyond pretreatment PSA alone in patients treated with radical prostatectomy. *J Clin Oncol* 2009;27:3591–7.
- [21] Helgason AR, Adolfsson J, Dickman P, Fredrikson M, Arver S, Steineck G. Waning sexual function—the most important disease-specific distress for patients with prostate cancer. *Br J Cancer* 1996;73:1417–21.
- [22] Soloway MS, Soloway CT, Williams S, Ayyathurai R, Kava B, Manoharan M. Active surveillance; a reasonable management alternative for patients with prostate cancer: the Miami experience. *BJU Int* 2008;101:165–9.
- [23] Tseng KS, Landis P, Epstein JI, Trock BJ, Carter HB. Risk stratification of men choosing surveillance for low risk prostate cancer. *J Urol* 2010;183:1779–85.
- [24] Zeliadt SB, Ramsey SD, Penson DF, et al. Why do men choose one treatment over another?: a review of patient decision making for localized prostate cancer. *Cancer* 2006;106:1865–74.
- [25] Fujita K, Landis P, McNeil BK, Pavlovich CP. Serial prostate biopsies are associated with an increased risk of erectile dysfunction in men with prostate cancer on active surveillance. *J Urol* 2009;182:2664–9.