ORIGINAL ARTICLE

Oncological outcomes in patients potentially eligible for active surveillance who underwent radical prostatectomy

C. Blázquez a,*, V. Hernández a, E. de la Peña a, F.J. Díaz a, M.D. Martin b, J.M. de la Morena a, C. Llorente a

a Servicio de Urología, Hospital Universitario Fundación Alcorcón, Madrid, Spain  
b Servicio de Medicina Preventiva, Hospital Universitario Fundación Alcorcón, Madrid, Spain

Received 18 November 2012; accepted 9 February 2013
Available online 23 November 2013

KEYWORDS
Prostatic neoplasms;  
Active surveillance;  
Clinical protocols

Abstract

Objective: To determine whether there are differences in the oncological outcomes after radical prostatectomy (adverse pathology and biochemical recurrence) based on clinical selection criteria used in two active surveillance (AS) protocols.

Materials and methods: 442 patients diagnosed with localized prostate cancer (CP) underwent radical prostatectomy at our institution between August 2003 and December 2009. We selected patients with low-risk CP, which could have been included in an AS program. Patients were divided into two groups: group i, those who met the most strict surveillance criteria described by Epstein (PSAD < .15; T1/T2a; < 2 positive core, Gleason ≤ 6, < 50% involvement of the core) and group ii, those meeting the more open criteria described by Klotz (PSA ≤ 10 or < 15 at age 70, Gleason ≤ 6 or < 7 [3 + 4] in over 70 years). We compared both groups to determine differences in pathological stage, positive surgical margins and biochemical recurrence after radical prostatectomy.

Results: Of the 442 patients 48% (213 patients) had low-risk PC, and become potential candidates for an AS program. Of the patients operated on 17% (76 patients) met the criteria for AS as of Epstein’s and 48% (213 patients) according to Klotz. Comparing patients in both groups there were no statistically significant differences in the presence of pT3 (7.9% vs 10.8%) P = .55, positive margins (22.4% vs. 28.3%) P = .41, nor in biochemical recurrence at 3 years (5.3% vs 5.6%) P = .86.

Conclusions: In our series of patients theoretically candidates for inclusion in a program of active surveillance, we found no differences in the percentage of patients with pathological stage pT3, positive margins and biochemical recurrence according to clinical inclusion criteria currently used.

© 2012 AEU. Published by Elsevier España, S.L. All rights reserved.


* Corresponding author.

E-mail addresses: cblazquezv@gmail.com, cristina_estopa@hotmail.com (C. Blázquez).

2173-5786/$ - see front matter © 2012 AEU. Published by Elsevier España, S.L. All rights reserved.
Resultados oncológicos en pacientes potencialmente candidatos a vigilancia activa sometidos a prostatectomía radical

Resumen

Objetivo: Determinar si existen diferencias en cuanto a seguridad oncológica tras prostatectomía radical (factores anatómicos y recidiva) en función de los criterios de inclusión empleados en 2 protocolos de vigilancia activa (VA).

Material y métodos: Cuatrocientos cuarenta y dos pacientes con cáncer de próstata (CP) localizado sometidos a prostatectomía radical laparoscópica en nuestro centro entre agosto de 2003 y diciembre de 2009. Seleccionamos pacientes con CP de bajo riesgo, potenciales candidatos a un programa de vigilancia activa. Se dividieron los pacientes en 2 grupos: grupo 1: cumplieron los criterios más estrictos descritos por Epstein (dPSA < 0,15; T1/T2a; < 2 cilindros positivos; Gleason ≤ 6; < 50% de afectación del cilindro) y grupo 2: cumplieron criterios más laxos descritos por Klotz (PSA < 10 o < 15 en mayores de 70 años, Gleason ≤ 6 o < 7 [3 + 4] en mayores de 70 años). Comparamos ambos grupos para determinar diferencias en cuanto a estadío patológico, márgenes positivos y recidiva bioquímica tras la prostatectomía radical.

Resultados: De los 442 pacientes un 48%(213 pacientes) habrían sido potenciales candidatos a un programa de VA. Del total de pacientes operados el 17% (76 pacientes) cumplían criterios según Epstein y un 48%(213 pacientes) según Klotz. Comparando los pacientes de ambos grupos no existieron diferencias estadísticamente significativas en la presencia de pT3 (7,9 vs 10,8%) p = 0,55, márgenes positivos (22,4 vs 28,3%) p = 0,41, ni recidiva bioquímica a 3 años (5,3 vs 5,6%) p = 0,86.

Conclusiones: En nuestra serie, en pacientes teóricamente candidatos a inclusión en un programa de vigilancia activa, no encontramos diferencias en cuanto a porcentaje de pacientes con estadío patológico pT3, márgenes positivos ni recidiva bioquímica en función de los criterios clínicos de inclusión empleados.

© 2012 AEU. Publicado por Elsevier España, S.L. Todos los derechos reservados.

Introduction

In Spain, the prostate cancer incidence is 19,107 new cases per year (82.27 cases per 100,000 men).1 Since the introduction of PSA screening, a substantial increase in prostate cancer diagnosis has been observed.2 Nowadays, a major remaining challenge is to find effective tools that enable the identification of only those high-risk, life-threatening tumors and to establish a standardized protocol for reducing overtreatment and its side effects. Thus, in recent years several active surveillance programs have been developed in order to avoid overtreatment of those patients with very low-risk tumors.3-4

These programs are not unified and show a wide variability in inclusion and follow-up criteria as well as in the indications for active treatment during clinical course. The Toronto (Sunnybrook Health Sciences Center, University of Toronto)5 and the Baltimore (The Johns Hopkins Hospital and National Institute on Aging, National Institutes of Health)6 are the two PC surveillance series with the longest follow-up and the largest number of patients.

The objective of this study is to determine whether there are differences in the oncological outcomes after radical prostatectomy (adverse pathology and biochemical recurrence) based on clinical inclusion criteria used in each of these active surveillance protocols.

Materials and methods

Between August 2003 and December 2009, 442 patients diagnosed of localized PC were undergone to laparoscopic radical prostatectomy in our center.

Of overall series of laparoscopic radical prostatectomy, those patients with low-risk prostate cancer, potentially eligible for inclusion in an active surveillance program, were chosen.

Patients were classified in 2 groups according to the 2 active surveillance (AS) protocols published.

Group 1 included those patients who met inclusion criteria defined by Epstein et al.: patients with PC findings on biopsy and non-palpable tumor (T1c clinical stage), with PSA density (PSAD) (defined as total PSA divided by transrectal ultrasonad – determined prostate volume) minor or equal to 0.15ng/ml/cm³, with favorable histological features on biopsy (Gleason ≤ 6, Gleason 4 or 5 are not included, no more than 2 positive cylinders, without involvement of more than 50% of the cylinder).5

Group 2 comprised those patients who met inclusion criteria defined by Klotz: patients younger than 70 years old must have a PSA < 10 and Gleason ≤ 6; patients older than 70 years old levels of PSA must be minor or equal than 15 and their Gleason score ≤ 7 (3 + 4).10

All surgery specimens were processed and assessed according standardized protocols by urological pathologists. According to whole-mount histological procedure, specimen was sliced from apex to base into 5mm-thick transverse slices15. In no case, pelvic lymphadenectomy were performed because patients were diagnosed of low-risk tumor.

After radical prostatectomy, demographical data as well pathological, clinical and biochemical course data were prospectively registered in our institutional database.

The follow-up was performed by digital rectal examination and PSA at month 3, 6, 12, 18 and 24 and then yearly.
Potentially eligible for active surveillance

Table 1  Baseline characteristics in two groups.

<table>
<thead>
<tr>
<th></th>
<th>Group I: 76 patients</th>
<th>Group II: 213 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63.44 (5.04)</td>
<td>63.86 (5.8)</td>
</tr>
<tr>
<td>PSA</td>
<td>5.29 (1.7)</td>
<td>5.99 (2.2)</td>
</tr>
<tr>
<td>PSA Density</td>
<td>0.11 (0.02)</td>
<td>NA</td>
</tr>
<tr>
<td>N. biopsy cylinders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 cylinders</td>
<td>49 (64.5)</td>
<td>NA</td>
</tr>
<tr>
<td>&gt;8 cylinders</td>
<td>27 (35.5)</td>
<td>NA</td>
</tr>
<tr>
<td>N. positive cylinders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 cylinder</td>
<td>45 (59.2)</td>
<td>NA</td>
</tr>
<tr>
<td>&gt;1 cylinder</td>
<td>31 (40.8)</td>
<td>NA</td>
</tr>
<tr>
<td>Clinical stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1c</td>
<td>76 (100)</td>
<td>198 (93)</td>
</tr>
<tr>
<td>T2a</td>
<td>NA</td>
<td>15 (7)</td>
</tr>
<tr>
<td>Gleason of the biopsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤6 (3+3)</td>
<td>76 (100)</td>
<td>200 (93.9)</td>
</tr>
<tr>
<td>7 (3+4)</td>
<td>NA</td>
<td>13 (6.1)</td>
</tr>
</tbody>
</table>

NA: not applicable. Selection criterion not included in this group.

Variables expressed as mean (SD).

2 consecutive PSA values higher than 0.2 ng/dl were considered as biochemical relapse.

Statistical analysis

In statistical analysis, variables are expressed as means ± standard deviation if normally distributed and as medians with interquartile ranges for skewed distributions. Quantitative variables were compared by Student’s t test and analysis of variance. Categorical variables are expressed as percentages. Comparisons between categorical variables were performed using Pearson χ² test, with continuity corrections, or Fisher’s exact test as appropriate. Relapse and progression-free survival curves were constructed by Kaplan–Meier method. Non-cancer deaths were less than 5% of patients and were included in the analysis. Significance level of all hypothesis testing was 0.05. Statistical analysis was performed using SPSS 17.0 for Windows (SPSS Inc., Chicago, IL).

Results

213 of the 442 patients with localized prostate cancer were chosen because they met criteria for low risk. 17% of the patients (76 patients) met Epstein et al. criteria and were included in group I. 48% of the patients (213 patients) met Klotz criteria for AS and were included in group II (Tables 1 and 2).

In prostatectomy specimens there were no differences between the groups in Gleason score (≥7 or ≥8). Neither found differences regarding disease locally advanced (pT3). The percentage of patients with extracapsular extension (pT3a) was 7.9% vs 8.9%, and with seminal vesicles invasion was 0% vs 1.9% in groups I and II respectively, with no differences between groups.

In summary, 2.9% and 12.7% of patients of both groups (I and II respectively) showed adverse pathological factors in the surgical specimen (Gleason ≥8 or disease locally advanced).

Positive margins rate was 22.4% in group I and 28.3% in group II (p = 0.41). No significant differences had been found regarding 3-years biochemical relapse: 5.3% of the group I patients (4 patients) and 5.6% of the group II patients (12 patients). The median of follow-up was 42.7 (92.73) months and 39.06 (93.17) months in group I and II respectively.

Discussion

AS is a therapeutic alternative for low risk localized prostate cancer by preventing or delaying treatment complications without threatening the life of the patients. Lately, the use of this therapeutic option becomes increasingly widespread, and nowadays it is considered as a valuable alternative by clinical guidelines.13

Currently, multiple surveillance protocols have been described. In them, inclusion criteria vary according to clinical stage, PSA figures and pathological findings in prostate biopsy samples. By the moment, in the clinical guidelines specific recommendations are not described, however AS is considered as a viable option in men with low-risk tumours.13,14

The decision of which patients should be treated varies according to the different series. Pathological progression, as well as patient willing, is a criterion for active treatment for all of them.10 However, PSA progression is not a standardized criterion for all protocols. In the Klotz series11 the PSA doubling time at 3 years is a negative prognostic factor.

Several articles have been published analyzing the data of patients who have been undergone to radical prostatectomy. According to them, these patients should be theoretically candidates to be included in one of these AS
programs. Suardi et al.,15 according to Klotz inclusion criteria, have found extracapsular extension in almost 20% of the patients (15% pT3a, 3.2% pT3b and 1% n-positive). Mufarrij et al.,16 following Epstein criteria that are stricter than former have found extracapsular extension in less than 10% of the patients (7.8% pT3a, 0.48% pT3b). Their results are similar to ours.

It has been demonstrated that the more stringent are the inclusion criteria, the better are the pathological results of RP; but these criteria limit the number of patients who are potential candidates for one of these programs.15,17 In our study, no relationship have been found between oncological safety and strictness of inclusion criteria.

The major limitation of our study is that it is a retrospective study of patients who theoretically would have been candidates for active surveillance program; however the patients really included in these programs remain in follow-up during a time until they are undergone to curative treatment. As consequence, our pathologic results may be different to those results obtained in these series. Another study limitation is the type of biopsy. In our series, most of patients were operated after diagnosis using octant biopsy. Nowadays, active surveillance protocols recommend larger biopsies in order to select patients with very low risk tumors.

**Conclusions**

In our series of patients theoretically candidates for inclusion in a program of active surveillance, we found no differences in the percentage of patients with pathological stage pT3, positive margins and biochemical recurrence according to clinical inclusion criteria currently used.

**Conflict of interests**

The authors declare that they have no conflict of interest.

**References**


