ORIGINAL ARTICLE

Incidence of positive surgical margins after robotic assisted radical prostatectomy: Does the surgeon’s experience have an influence on all pathological stages?


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Abstract

Objective: The aim of this study is to analyze the clinical and surgical features of patients who underwent robotic-assisted radical prostatectomy (RARP) at our institution, and the impact of the surgeon’s experience in the oncological results related to pathological stage.

Material and methods: An analysis of 300 RARP consecutively performed by the same urologist was conducted. Patients were divided into 3 groups of 100 patients in chronological order, according to surgery date. All patients had organ-confined clinical stage. Variables which could impact in positive margins rates were analyzed. Finally, positive surgical margins (PSM) in regard to pathological stage and surgeon’s experience were compared and analyzed.

Results: No significant differences were found in variables which could impact in PSM rates. The overall PSM rate was 21%, with 28% in the first group, 20% in the second, and 16% in the third (P = .108). Significant linear decreasing tendency was observed (P = .024). In pT2 patients, the overall PSM rate was 16.6%, with 27%, 13.8%, and 7.3% in each group respectively (P = .009). A significant difference was found between group 1 and group 3 (P = .004). In pT3 patients, the surgeon’s experience was not significantly associated with margin reductions with an overall PSM rate of 27.7% (28.2%, 28.6%, and 26.7% in each group respectively).

Conclusions: Clinical and surgical features in our patients did not vary over time. We found a significant reduction of PSM related to surgeon’s experience in pT2 patients. Contrariwise, the margin status remained stable despite increasing experience in pT3 patients.

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Introduction

Since Young first described it last century, radical prostatectomy (RP) has been an ever-evolving technique. Robotic-assisted radical prostatectomy (RARP) was described by Binder and Kramer in 2001, and it has gained rapid acceptance among surgeon urologists ever since. In 2005, 20% of the RPs performed in the US were performed with this system, and by 2007 the percentage increased to 50%. Although immediate benefits have already been shown, such as decreased blood loss, hospitalization, and postoperative pain, there is controversy as regards the long-term oncological results, since the recent introduction of this technology.

Traditionally, the positive surgical margin (PSM) has been used as an indicator of oncological results related to the technique. The PSM is uniformly associated with an increased risk of biochemical recurrence, local relapse, and the need for adjuvant therapies. It is estimated that the risk of biochemical recurrence after the radical prostatectomy is two to four times higher in patients with PSM and the time to relapse is shorter for patients with PSM. Different factors are influencing the incidence of PSM, such as Gleason score, high prostate-specific antigen (PSA), the involvement of the seminal vesicles, the preoperative clinical stage, and the extent and location of positive biopsies. All these factors are inherent to the patient and their condition, and therefore, they cannot be changed. One factor affecting the incidence of PSMs that can be controlled is the surgical technique used, since the PSM may be due to the incision into the prostate or it may be the result of an extra-prostatic tumor involvement that extends beyond the limits of resection.

We have submitted our results of the first 100 RARPs, where we have observed significant differences with all the other techniques as regards PSMs. Our institution has had a Robotic Surgery Program since 2008. Since then, there have been over 400 RARPs. Out of 400, 300 were performed by the same surgeon (W.V).

The purpose of this study is to discuss the clinical and surgical characteristics of this population and the impact of the surgeon’s experience on the incidence of PSMs according to the pathologic stage.

Materials and methods

We analyzed our prospective database of RARPs including the first 300 performed at our institution, all by the same surgeon (W.V.). The patients were divided into 3 groups of 100 in chronological order, in accordance with the surgery date. All patients had organ-confined clinical stage. Staging was completed with abdomen and pelvis CT scan, and whole-body bone scintigraphy. Patients who received neoadjuvant hormone blockade were excluded from the analysis.

We used our prospective RARP database and we analyzed in each group the following variables:

1. Preoperative variables: age, total PSA, Gleason score, rectal examination (RE), D’Amico score.
2. Intra-operative variables: preservation of neurovascular bundles (NVB), dividing patients into those with bilateral
preservation, unilateral preservation, or no preservation.
3. Post-operative variables: pathologic stage according to the 2009 International Union Against Cancer (UICC) TNM classification,\textsuperscript{13} and prostate volume.

Finally, each group was subdivided into patients with organ-confined disease (pT2c or less), and patients with extra-prostatic disease (pT3a or more), and the PSMs were discussed.

Surgical technique

The 5-port technique described by Patel et al.\textsuperscript{14} was used in every case. Lymphadenectomy was performed in patients with Gleason > 6 or PSA > 10 ng/mL or T2a clinical stage or greater.

The criteria used for the preservation of NVB were: RE (if the tumor is palpable, preservation on that side is avoided), in intermediate and high risk tumor, according to the D’Amico classification, with more than 50% of positive biopsy cores excluding preservation on that side. The intra-operative variables were the presence of indurations and adhesions between the prostate and the neurovascular pedicles after incising the lateral pelvic fascia. In all cases of preservation, the dissection of neurovascular bundles was performed athermally.

Pathological evaluation

All preoperative biopsies were reported or reviewed (if already performed in another institution) by the same pathologist from our institution (M. I.) as with the prostatectomy specimens.

The surgical specimens were fixed in 10% formalin and painted with India ink to assess margins. The end of the urethra and the bladder neck was separated, and then 3 mm axial slices were made. It is important to highlight that the entire piece was included in the review. We used hematoxylin and eosin stain. In the radical prostatectomy specimens, the following were analyzed:

- Gland weight in grams (g).
- Histological type and pathological stage according to the 2009 UICC TNM classification.\textsuperscript{13}
- Gleason score.
- Surgical margins.

Surgical margins were defined as positive when there was minimum contact of tumor cells and India ink. The extra-capsular extension was defined as the existence of tumor cells in the periprostatic fat tissue with or without negative margins.

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**Table 1** Preoperative variables.

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>p =</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean Age (SD)</strong></td>
<td>61.18 (7.1)</td>
<td>60.52 (6.4)</td>
<td>60.23 (6.8)</td>
<td>0.607</td>
</tr>
<tr>
<td><strong>Median PSA ng/ml (range)</strong></td>
<td>7.2 (2.5–38)</td>
<td>7.5 (2.3–36.1)</td>
<td>7.1 (1.8–40)</td>
<td>0.743</td>
</tr>
<tr>
<td><strong>Median Prostate Weight (range)</strong></td>
<td>45.5 (16–88)</td>
<td>42 (16–110)</td>
<td>46 (23–105)</td>
<td>0.027</td>
</tr>
<tr>
<td><strong>Gleason Score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 (3+3)</td>
<td>25</td>
<td>28</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>7 (3+4)</td>
<td>33</td>
<td>32</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>7 (4+3)</td>
<td>20</td>
<td>17</td>
<td>13</td>
<td>0.507</td>
</tr>
<tr>
<td>8 (4+4)</td>
<td>15</td>
<td>18</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>9 (4+5)</td>
<td>7</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>9 (5+4)</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Rectal Examination</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1c</td>
<td>66</td>
<td>56</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>T2a</td>
<td>21</td>
<td>21</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>T2b</td>
<td>8</td>
<td>20</td>
<td>15</td>
<td>0.163</td>
</tr>
<tr>
<td>T2c</td>
<td>4</td>
<td>2</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
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<tr>
<td><strong>D’Amico Classification</strong></td>
<td></td>
<td></td>
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<tr>
<td>Low</td>
<td>12</td>
<td>22</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>65</td>
<td>48</td>
<td>56</td>
<td>0.122</td>
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<tr>
<td>High</td>
<td>23</td>
<td>30</td>
<td>23</td>
<td></td>
</tr>
</tbody>
</table>

* SD: standard deviation.

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**Table 2** Intra-operative variable.

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>p =</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NVB\textsuperscript{*} Conservation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>20</td>
<td>15</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Unilateral</td>
<td>32</td>
<td>38</td>
<td>32</td>
<td>0.431</td>
</tr>
<tr>
<td>Bilateral</td>
<td>48</td>
<td>47</td>
<td>53</td>
<td></td>
</tr>
</tbody>
</table>

* NVB: neurovascular bundle.
Statistical analysis

The continuous variables with normal distribution are expressed as mean and standard deviation (SD). Otherwise, they can be expressed as median and range. The categorical variables are expressed as absolute value and percentage. In order to compare variables with normal distribution, a means comparison test was used with ANOVA of one factor. In order to compare the other variables, the chi-square test was used. In cases where such test assumptions were violated, Fisher’s exact test was used. In cases of findings of global significant values, individual comparisons were performed by adjusting the p value with the Bonferroni method. Differences were considered significant with $p < 0.05$. The SPSS 17.0 software was used for the statistical analysis.

Results

When analyzing preoperative variables (Table 1), no significant differences were found among the three groups. Mean age was 60 years, and median PSA was 7 ng/mL. In the three groups, the most frequent Gleason score was 7 (3+4), while most of the patients had a normal RE. In accordance with the D’Amico classification, the intermediate risk was the most frequent one in the three groups analyzed.

It can be noted that the percentage of patients with normal RE (T1c) declined among groups (66%, 56%, and 52%, respectively).

When the intra-operative variable was assessed (Table 2), the preservation of neurovascular bundles, no differences were found among the groups ($p = 0.431$), although a bilateral preservation was performed in more patients in the third group (53%) compared to the first and the second groups (48 and 47% respectively).

When comparing the post-operative factors (Table 3), no significant statistical differences were found compared to the local extension (pT) ($p = 0.819$), with the pT2c being the most frequent stage in the three groups. In addition, prostate weight was not different among the three groups ($p = 0.321$).

When surgical margins were assessed, a total of 64 PSMs (21%) with 28% was found in the first group, 20% in the second group, and 16% in the third group. The difference was not significant among the groups ($p = 0.108$), although a significant linear decline tendency was observed ($p = 0.024$).

By analyzing each of the groups according to the local extension, pT2 or less vs. pT3 or more, we found no differences between them ($p = 0.691$) (Table 4).

In patients with organ-confined disease (pT2c or less), the overall incidence of PSM was 16.6% (n 29/174). The difference in the PSM percentage was statistically significant between the 3 groups, being 27.9%, 13.8%, and 7.3%, respectively ($p = 0.009$). The significant difference was found in group 1 and group 3 with $p = 0.004$. In addition to this subgroup of pT2 patients, a significant linear decline tendency ($p = 0.004$) was evidenced. This can be observed in Table 5.

The overall incidence of PSMs in patients with pT3a or more was 27.7% (n 35/126). There were no differences among the groups, the percentage being 28.2%, 28.6%, and 26.7%, respectively, $p = 0.978$ (Table 6).
Discussion

The PSM prevention continues to be a fundamental objective of radical prostatectomy. There are many factors that influence the oncological outcome, and this does not make it easy to obtain homogeneous and comparable samples to draw conclusions exclusively inherent to the surgical technique used. Some factors have been shown to have independent predictive value such as the preoperative PSA, rectal examination, clinical stage (cT), pathologic stage (pT), prostate volume, D’amico risk classification, and Gleason score on biopsy.6,15,16 When assessing these variables in our series, we did not observe any statistically significant differences among the three groups.

Another factor that involves a theoretical risk of PSMs is the preservation of NVBs. The role of the preservation of NVBs on the incidence of PSMs is currently controversial, since recent publications have not found any association between these two variables,6,16 while other publications did find a relationship.17 Regardless of this controversy, when assessing our populations, we did not evidence any differences in the three groups with regard to the preservation of nerve structures and the incidence of PSM.

The incidence of PSMs varies widely among current publications. In a recent study where over 8,000 RARPs were analyzed in multiple institutions, an overall 15.7% incidence of PSMs was found, 9.45% for pT2 stages, and 37.2% for pT3 or more stages.6 It is important to highlight that it is difficult to homogenize samples because these results include surgeries performed in different sites by different surgeons. In another study, Narula et al. assessed the last 500 RARPs performed by the same surgeon, and they reported an overall incidence of 7.4%, although they made it clear that in their first 250 surgeries, the overall incidence was 21.2%.16 Ficarra et al. reported an overall incidence of 29.5%.15 Our series does not differ from these results, with an overall incidence of PSM of 21.3%.

The surgeon’s experience has been well documented as a major factor in the presence of PSMs, and every surgical procedure requires a number of initial cases for specific skills known as learning curve.15 For the robotic surgery, this number varies widely according to different publications.3,14,18,20 These studies normally take the results of the retropubic RP as a parameter to determine the number of patients of the curve. For Sammon et al., for example, the number of patients to obtain the curve was 25 cases, and the method used was an industry standardized statistical method.13 Patel et al. reached the same conclusions.14 It is important to highlight that when assessing inherent oncological results of robotic surgery, although the curve to achieve the results of the open RP ranges from 20 to 25 cases, RARP margins continue to decline. Narula et al., for example, when comparing their first 250 cases with the next 500, found a reduction of the overall PSMs of 21.2% to 7.4%.16 Ahlering et al. also found a 36% to 16.7% reduction when comparing the first 50 RARPs with the next 90.20 In our experience, we had similar findings with a reduction of the overall PSM of 28% in the first 100 RARPs to 16% in the last 100, with a significant linear decline tendency (p = 0.024).

In general, the comparison of margins among series is difficult due to the heterogeneity of the populations, but the PSMs in patients with organ-confined disease (pT2) should be similar.20 This subpopulation is ideal for studying the PSMs associated with the surgical technique errors since the tumor has not exceeded the limits of the prostate. It can be inferred that PSMs in pT2 should decline with the surgeon’s experience. Ahlering et al. published a reduction in this subset of 27.3% to 4.7% (p = 0.003). When comparing cases with extra-prostatic disease (pT3 or more), no significant reduction was found.20 In our series, we also found a reduction in PSMs in pT2 patients from 27.9% to 7.3% (p = 0.004), and also an significant linear decline tendency (p = 0.004). Contrarily, no reduction was found in pT3 or more patients, despite the increasing surgeon’s experience (p = 0.978).

The advantage of the present study is that all the RARPs were performed by the same surgeon, and the pathological study was performed by the same pathologist, at the same institution, thus eliminating the biases that may arise from interpersonal and inter-institutional differences.

Conclusion

The three groups studied did not differ in terms of factors that, a priori, could vary the oncological results of the technique. Therefore, we can conclude that our groups were homogeneous and statistically comparable.

We have found a significant reduction in PSMs associated with the surgeon’s experience for patients with organ-confined disease (T2), but not for T3 or more patients, where PSMs were stable. PSM rates in our study are consistent with current publications.

Conflict of interest

The authors declare that they have no conflict of interest.

References


