OUTCOMES OF ROBOTIC RADICAL PROSTATECTOMY IN HIGH-RISK PROSTATE CANCER PATIENTS: EXPERIENCE IN 60 PATIENTS WITH ONCOLOGICAL AND FUNCTIONAL OUTCOMES

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ABSTRACT

Introduction: In this retrospective study, we report outcomes of robot-assisted laparoscopic radical prostatectomy (RARP) in high-risk prostate cancer (HRPC), classified according to the D’Amico risk criteria and with a minimum follow-up of 1 year.

Methods: A total of 60 patients who had at least one preoperative HRPC feature and underwent RARP were included. Mean patient age and preoperative serum prostate-specific antigen level were 66.4±7.5 years and 13.4±11.0 ng/ml, respectively. Preoperatively, 3 (5.0%), 4 (6.7%), 17 (28.3%), 3 (5.0%), and 33 (55.0%) patients had prostate biopsy-proven Gleason scores of 5+4, 4+5, 4+4, 3+5, and <8, respectively. Bilateral neurovascular bundle (NVB)-sparing, unilateral NVB-sparing, and non-NVB-sparing surgery were performed in 44 (73.3%), 3 (5.0%), and 13 (21.7%) patients, respectively.

Results: Mean console time, intraoperative blood loss, duration of hospital stay, and urethral catheter removal time were 159.7±62.4 minutes, 210±201.9 ml, 3.9±1.9 days, and 10.9±5.3 days, respectively. During the perioperative period (Days 0-30), 7 minor and 5 major complications occurred as categorised using the modified Clavien classification. No complications were detected during postoperative Days 31-90. Postoperative pathological stages included pT0, pT2a, pT2b, pT2c, pT3a, and pT3b disease in 2 (3.3%), 8 (13.3%), 4 (6.7%), 14 (23.3%), 18 (30.0%), and 14 (23.3%) patients, respectively. The positive surgical margin rate was 26.7% and mean lymph node yield was 11.8±8.3 (range: 3-37). Mean follow-up was 27.8±11.1 months. Biochemical recurrence was detected in 13 (21.7%) patients. Of the total 60 patients, 26 (43.3%) were fully continent (0 pad/day), 15 (25.0%) wore a safety pad/day, 10 (16.7%) wore 1 pad/day, 5 (8.3%) wore 2 pads/day, and 4 (6.7%) wore >2 pads/day. Of the 27 patients with no preoperative erectile dysfunction (ED), 17 (63.0%) had no ED at a mean follow-up of 1 year. Trifecta and pentaefecta rates were 43.2% and 28.7%, respectively.

Conclusion: Based on our experience, RARP in HRPC is a relatively safe procedure with satisfactory oncolgical and functional outcomes.

Keywords: Robotic radical prostatectomy, high-risk prostate cancer, outcomes, minimally invasive surgery, robotic surgery.

INTRODUCTION

Prostate cancer (PrC) is the most common solid-organ cancer and a significant aetiology of cancer-associated death in the male population.1 Between 15-30% of patients diagnosed with PrC have high-risk, non-metastatic disease.2,3 The D’Amico risk-stratification system classifies non-
metastatic PrC into low, intermediate, or high-risk PrC according to initial serum prostate-specific antigen (PSA) level, clinical T stage, and biopsy-proven Gleason score (GS). High-risk PrC (HRPC) was classified as having any one of the following features: PSA >20 ng/ml, clinical T stage ≥T2c according to the American Joint Committee on Cancer criteria published in 1992, or Gleason 8-10 disease. The prognostic importance of preoperative PSA levels, clinical stage, and biopsy-proven GS is well known and previously verified. Treatment of HRPC includes a multimodality approach, including a combination of surgery, radiation therapy (RT), and androgen deprivation therapy (ADT).

Management of HRPC needs aggressive treatment or a multimodal therapy. The outcomes of the Swedish Registry Study showed that, for HRPC, the patient group receiving surgery displayed longer cancer-specific survival than the RT group. On the other hand, some reports favour the use of RT with ADT. The definitive treatment should be individualised according to the patient. Although open radical prostatectomy (RP) is the standard technique in the surgical management of patients with PrC, the robotic approach has come to dominate contemporary practice worldwide. However, the number of publications related to the use of robotic surgery in HRPC is very limited. We have previously published results from our initial robot-assisted radical prostatectomy (RARP) case series in HRPC. In our case series, all patients were operated on using a da Vinci-S four-arm surgical robot (Intuitive Surgical, Sunnyvale, California, USA). Overall, five surgeons performed RARP on HRPC patients. We previously described in detail the surgical technique that we applied, as well as the pre and postoperative follow-up of the patients upon whom we performed RARP. Mean patient age and preoperative serum PSA were 66.4±7.5 years and 13.4±11.0 ng/ml, respectively. Pelvic lymph node (LN) dissection was performed in patients who had >5% of LN involvement probability according to Partin’s tables. Biochemical recurrence (BCR) was defined as two consecutive serum PSA levels of >0.2 ng/ml. Statistical analyses were performed using the chi-squared test in SPSS version 22.0 (SPSS, Chicago, Illinois, USA).

**RESULTS**

Preoperatively, 3, 4, 17, 3, and 33 patients had a prostate biopsy GS of 5+4, 4+5, 4+4, 3+5, and <8, respectively.

Mean console time, intraoperative blood loss, duration of hospital stay, and urethral catheter removal time were 159.7±62.4 minutes, 210±201.9 ml, 3.9±1.9 days, and 10.9±5.3 days, respectively. Bilateral neurovascular bundle (NVB)-sparing, unilateral NVB-sparing, and non-NVB-sparing surgeries were performed in 44 (73.3%), 3 (5.0%), and 13 (21.7%) patients, respectively. During the perioperative period (Days 0-30), 7 minor complications (urinary tract infection that required hospitalisation [n=2], constipation [n=2], anastomotic urinary leakage [n=2], intra-abdominal bleeding that required transfusion without causing abdominal haematoma [n=1]), and 5 major complications (bladder perforation that was repaired intraoperatively [n=4], postoperative 1-day intensive care unit requirement [n=1]) occurred as categorised using the modified Clavien classification. No complication was detected during postoperative Days 31-90.

Postoperative pathological stages included pT0, pT2a, pT2b, pT2c, pT3a, and pT3b disease in 2, 8, 4, 14, 18, and 14 patients, respectively. The overall positive surgical margin (PSM) rate was 26.7%, and the mean LN yield was 11.8±8.3 (range: 3-37). Mean follow-up was 27.8±11.1 months. A total of 13 patients experienced BCR. Of the total 60 patients, 26 (43.3%) were fully continent (0 pad/day), 15 (25.0%) wore a safety pad/day, 10 wore (16.7%) 1 pad/day, 5 (8.3%) wore 2 pads/day, and 4 (6.7%) wore >2 pads/day. Of the 27 patients with no preoperative erectile dysfunction (ED), 17 (28.3%) had no ED at a mean follow-up of 1-year. Trifecta and pentafecta rates were 43.2% and 28.7%, respectively.

**METHODS**

Between February 2009 and February 2015, we performed 678 RARP procedures at our institution. All the data from patients were recorded prospectively and this database was used in the current study. A total of 100 patients were classified as HRPC according to D’Amico risk criteria. Of the 100 patients with HRPC, 60 had at least 1 year of follow-up and were included in the current retrospective study.

In our case series, all patients were operated on using a da Vinci-S four-arm surgical robot (Intuitive Surgical, Sunnyvale, California, USA). Overall, five surgeons performed RARP on HRPC patients. We previously described in detail the surgical technique that we applied, as well as the pre and postoperative follow-up of the patients upon whom we performed RARP. Hyperthermic intraperitoneal chemotherapy (HIPEC) was performed in patients with peritoneal disease or peritoneal carcinomatosis. The prognostic importance of preoperative PSA levels, clinical stage, and biopsy-proven GS is well known and previously verified. The definitive treatment should be individualised according to the patient.

Although open radical prostatectomy (RP) is the standard technique in the surgical management of patients with PrC, the robotic approach has come to dominate contemporary practice worldwide. However, the number of publications related to the use of robotic surgery in HRPC is very limited. We have previously published results from our initial robot-assisted radical prostatectomy (RARP) case series in HRPC. In the current study, we report mid-term functional and oncological results from our contemporary RARP case series in HRPC.
DISCUSSION

Within the published literature, experience with RARP in HRPC is limited. In this study we evaluated the outcomes of our RARP experience in 60 HRPC patients. In our case series, mean intraoperative blood loss was 210 ml. Similar to our study, Punnen et al. reported mean intraoperative blood loss as 217 ml in a series of 233 HRPC patients who underwent RARP. Mean length of hospital stay was 3.9 days in our series, which is longer than some previously reported series.

In our case series, 34 patients (56%) underwent extended pelvic lymph node dissection (ePLND) and mean LN yield was 11.8±8.3. Two patients had LN metastasis. We performed bilateral ePLND in those with an at least 5% risk of pelvic LN involvement by PrC according to Partin’s tables. The PSM rate was 26.7% in our series. Pierorazio et al. reported a PSM rate of 8.3% in pT2 disease, and Gandaglia et al. reported a PSM rate of 60% in pT2 and pT3a disease. Others reported overall PSM rates between 12-48.8%. Our PSM rates seem to be similar to the published literature.

In our series, the mean follow-up was 27.8±111 months and BCR was detected in 13 patients (21.7%), which are similar to results reported by Punnen et al. Busch et al. reported BCR as 41.4% after 3 years of follow-up. Of the 60 patients, 6 (10.0%) received adjuvant RT (ART) alone, 6 (10.0%) received hormone blocking treatment (HT) alone, and 8 (13.3%) received ART+HT postoperatively. Gandaglia et al. reported that 21.2% of 353 HRPC patients who underwent RARP required additional cancer therapy after surgery. Of those, 15.9% required RT and 13.9% required ADT. Currently, the mean follow-up time is limited in our series and the need for additional therapy might change as the follow-up time increases.

In our case series and during the perioperative period (Days 0-30), 7 minor and 5 major complications occurred as categorised using the modified Clavien classification. No complications were detected during postoperative Days 31-90. Other authors reported complication rates between 4-30% in HRPC patients who underwent RARP.

The functional outcomes following RARP are urinary continence and erectile function. Currently, the information about functional outcomes following RARP in HRPC patients is limited in the literature. Yuh et al. reported 1-year urinary continence rates (0-1 safety pad/day) between 78-95% and erectile function recovery rates between 52-60%. Yee et al. reported their

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Table 1: Operative parameters.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean surgery (console) time, min</td>
<td>159.7±62.4</td>
</tr>
<tr>
<td>Mean Intraoperative blood loss, ml</td>
<td>210±201.9</td>
</tr>
<tr>
<td>APAs detected and preserved, n (%)</td>
<td>Overall: 5 (8.3) Unilateral: 4 (6.7) Bilateral: 1 (1.7)</td>
</tr>
<tr>
<td>NVB-preserving technique, n (%)</td>
<td>Bilateral: 44 (73.3) Unilateral: 3 (5.0) Not performed: 13 (21.7)</td>
</tr>
<tr>
<td>Mean lymph node yield</td>
<td>11.8±8.3 (range: 3-37)</td>
</tr>
</tbody>
</table>

APA: accessory pudetal artery; NVB: neurovascular bundle.

Table 2: Post-operative pathological outcomes.

<table>
<thead>
<tr>
<th>Pathological stage</th>
<th>Frequency, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAP+HGPIN</td>
<td>0</td>
</tr>
<tr>
<td>pT0</td>
<td>2 (3.3)</td>
</tr>
<tr>
<td>pT2a</td>
<td>8 (13.3)</td>
</tr>
<tr>
<td>pT2b</td>
<td>4 (6.7)</td>
</tr>
<tr>
<td>pT2c</td>
<td>18 (30.0)</td>
</tr>
<tr>
<td>pT3a</td>
<td>14 (23.3)</td>
</tr>
<tr>
<td>pT3b</td>
<td>14 (23.3)</td>
</tr>
<tr>
<td>Gleason score</td>
<td></td>
</tr>
<tr>
<td>2-6</td>
<td>15 (25.0)</td>
</tr>
<tr>
<td>3+4</td>
<td>11 (18.4)</td>
</tr>
<tr>
<td>4+3</td>
<td>17 (28.3)</td>
</tr>
<tr>
<td>8-10</td>
<td>15 (25.0)</td>
</tr>
<tr>
<td>T0</td>
<td>2 (3.3)</td>
</tr>
<tr>
<td>PSM rate</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>16 (26.7)</td>
</tr>
<tr>
<td>pT2</td>
<td>4 (6.7)</td>
</tr>
<tr>
<td>pT3</td>
<td>12 (20.0)</td>
</tr>
</tbody>
</table>

ASAP: atypical small acinar proliferation; HGPIN: high-grade prostatic intraepithelial neoplasia; PSM: positive surgical margin.
1-year pad-free continence rate as 84% in HRPC patients who underwent RARP. Preoperative erectile function status of the patient, postoperative adjuvant treatment requirement, NVB-sparing (unilateral or bilateral), bladder neck preservation, and urethral length should all be considered seriously in the evaluation of postoperative functional outcomes. Limited sample size, inclusion of more than one surgeon’s experience, and being a retrospective and non-comparative study are the main limitations of our study.

In conclusion and according to our experience, RARP in HRPC is a relatively safe procedure with satisfactory oncological and functional outcomes in both the short and mid-term.

REFERENCES