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# Outcomes of robot-assisted laparoscopic radical prostatectomy in high-risk prostate cancer patients: experience in 34 patients with oncologic and functional outcomes

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

**Methods:** A total of 34 patients who had at least one preoperative HRPC feature and who underwent RARP were included. Mean patient age and preoperative serum prostate-specific antigen levels were 62.6±6.4 years and 12.2±9.1 ng/mL, respectively. Preoperatively, two (5.8%), one (2.9%), eleven (32.3%), three (8.8%), and 17 (50%) patients had prostate biopsy 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 was performed in 16 (47%), five (15%), and 13 (38%) patients, respectively.

**Results:** Mean console time, intraoperative blood loss, duration of hospital stay, and urethral catheter removal time were 162.1±64.4 minutes, 232.2±255.1 cc, 4.1±2.1 days, and 12.6±6.2 days, respectively. During the perioperative period (0–30 days), three minor and five major complications occurred as classified using the modified Clavien classification. No complication was detected during postoperative 31–90 days. Postoperative pathologic stages included pT0, pT2a, pT2b, pT2c, pT3a, and pT3b disease in two (5.8%), five (14.7%), three (8.8%), six (17.6%), ten (29.4%), and eight (23.5%) patients, respectively. Positive surgical margin rate was 32.3%. Mean lymph node yield was 11.8±8.3 (range three to 37). Mean follow-up was 27.8±11.1 months. Biochemical recurrence was detected in nine (26.4%) patients. Of the patients, 17 (50%) were fully continent (zero pads/day), six (17.7%) wore a safety pad/day, six (17.7%) wore one pad/day, three (8.8%) wore two pads/day, and two (5.9%) wore more than two pads/day. Of the 24 patients with no preoperative erectile dysfunction, 15 (44.1%) had no erectile dysfunction at a mean follow-up of 1 year. Trifecta and pentafecta rates were 38% and 26%, respectively.

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

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

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## Introduction

Prostate cancer (PCa) accounts for almost 30% of all newly diagnosed cancers in men in the US and is the second most frequent cause of cancer death in men.[1] Almost 20%–30% of patients diagnosed with PCa still have high-risk, nonmetastatic disease.[2]



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D'Amico et al[3] proposed a three-group risk stratification system to predict posttreatment biochemical failure following radical prostatectomy (RP) and external-beam radiotherapy. This system classified nonmetastatic PCa into low-, intermediate-, and high-risk PCa according to initial serum prostate-specific antigen (PSA), clinical T-stage, and biopsy Gleason score. High-risk PCa (HRPC) was classified as having any one of the following features: 1992 American Joint Committee on Cancer stage ≥T2c, PSA >20 ng/mL, or Gleason disease score of 8–10.[3]

Currently, treatment of HRPC that includes a combination of surgery, radiation therapy, and androgen deprivation therapy as a multimodality approach is controversial.[4,5]

Management of HRPC requires aggressive treatment; otherwise, this disease might progress and cause serious symptoms and complications and eventually patient death.[6] The outcomes of the recently published Swedish Registry Study showed that surgery seems to be superior to radiation therapy and longer cancer-specific survival in the surgery group in patients with HRPC as per 15-year cancer-specific survival data[7] that suggested a trend toward performing RP in HRPC patients.[8]

Although open RP is the standard surgical technique in the surgical management of patients with PCa, a robotic approach has become the most common approach in the US.[9] However, the number of publications related to the use of robotic surgery in HRPC is very limited.

Herein, we report our experience in RARP and HRPC, including 34 patients classified according to a D'Amico risk group, with minimum 1-year follow-up.

## Materials and methods

Between February 2009 and September 2014, we performed almost 600 RARP procedures at our institution. All the data of the patients were recorded prospectively, and this database was used for our study. Of those, 68 patients were classified as having HRPC according to D'Amico risk groups. Of the patients with HRPC, 34 had at least 1-year follow-up who were included in the present retrospective study.

All patients in our series were operated on using a da Vinci Surgical System four-arm surgical robot (Intuitive Surgical, Sunnyvale, CA, USA). Overall, five surgeons performed RARP on HRPC patients (AEC, AFA, SA, ZA, and MDB). We previously reported in detail patient preparation, surgical technique, and postoperative follow-up of patients on whom we performed RARP.[10]

Pelvic lymph node (LN) dissection was performed in patients who had >5% of LN involvement probability according to Partin's tables. Mean patient age and preoperative serum PSA were 62.6±6.4 years and 12.2±9.1 ng/mL, respectively.

Biochemical recurrence (BCR) was defined as two consecutive serum prostate-specific antigen (PSA) levels of >0.2 ng/mL.

Statistical analyses were performed with the chi-square test with use of the commercially available software Scientific Package for Social Sciences (SPSS), (version 10.0, Chicago, IL, USA). *P*-values smaller than 0.05 were considered statistically significant.

## Results

Preoperatively, two (5.8%), one (2.9%), eleven (32.3%), three (8.8%), and 17 (50%) patients had prostate biopsy Gleason scores of 5+4, 4+5, 4+4, 3+5, and <8, respectively. No patient had a Gleason score of 5+5 or 5+3. Bilateral neurovascular bundle (NVB)-sparing, unilateral NVB-sparing, and non-NVB-sparing surgery was performed in 16 (47%), five (15%), and 13 (38%) patients, respectively. Preoperative patient characteristics are presented in Table 1.

Mean console time, intraoperative blood loss, duration of hospital stay, and urethral catheter removal time were 162.1±64.4 minutes, 232.2±255.1 cc, 4.1±2.1 days, and 12.6±6.2 days, respectively. During the perioperative period (0–30 days), three minor (constipation/prolonged ileus [n=1], prolonged anastomotic leakage [n=1], and urinary tract infection [n=1]) and five major complications (intraoperative bladder injury [n=2] and rectum perforation [n=1], which were repaired intraoperatively, intensive care requirement [n=1], and abdominal hematoma [n=1]) occurred according to modified Clavien classification. No complication was detected during the postoperative 31–90 days.

Postoperative pathologic stages included pT0, pT2a, pT2b, pT2c, pT3a, and pT3b disease in two (5.8%), five (14.7%), three (8.8%), six (17.6%), ten (29.4%), and eight (23.5%) patients, respectively. No malignancy was detected in two (5.8%) patients' pathologic specimens. Positive surgical margin (PSM) rate was 32.3% (2.9% in pT2 and 29.4% in pT3 disease). Of the patients, 17 (50%) underwent extended pelvic LN dissection. Mean LN yield was 11.8±8.3 (range three to 37). One patient had LN metastasis.

Of the patients, four (11.8%) received adjuvant radiotherapy (ART) alone, four (11.8%) received hormone therapy (HT)

**Table 1** Preoperative patient characteristics

| | |
|---|---|
| Patients: n (%) | 34 (100) |
| Mean patient age (years) | 62.6±6.4 (27, 49–76) |
| Mean BMI (kg/m$^2$) | 26.7±2.6 (11, 23–34) |
| Mean serum PSA (ng/mL) | 12.2±9.1 (41, 3.4–45) |
| Mean prostate volume (cc) | 52.6±18.9 (73, 27–100) |
| Patients with prostate biopsy Gleason scores: n (%) | |
| 4+4 | 11 (32.3%) |
| 4+5 | 1 (2.9%) |
| 5+4 | 2 (5.8%) |
| 3+5 | 3 (8.8%) |
| <8 | 17 (50%) |
| 5+5 | 0 |
| Preoperative clinical stage: n (%) | |
| cT1 | 4 (11.7%) |
| cT2a | 8 (23.5%) |
| cT2b | 2 (5.8%) |
| cT2c | 20 (58.8%) |
| Mean ASA score: n (%) | |
| I | 11 (32.3%) |
| II | 21 (%) |
| III | 2 (%) |
| IV | 0 |
| Preoperative mean IIEF score | 36.6±22.4 (range 5–75) |
| No ED (IIEF score: 22–25): n (%) | 24 (70.5%) |
| Mild (IIEF score: 17–21): n (%) | 0 |
| Mild to moderate (IIEF score: 12–16): n (%) | 1 (2.9%) |
| Moderate (IIEF score: 8–11): n (%) | 1 (2.9%) |
| Severe (IIEF score: 5–7): n (%) | 8 (23.5%) |
| Preoperative mean IPSS score | 13.5±6.9 (range 2–28) |
| Patients with previous abdominal surgery: n (%) | 6 (17.6%) |
| Previous abdominal surgery history: n (%) | |
| Inguinal hernia repair | 1 (2.9%) |
| Appendectomy | 3 (8.8%) |
| Peptic ulcer perforation | 1 (2.9%) |
| TURP | 1 (2.9%) |

**Note:** Data shown mean ±SD (range).
**Abbreviations:** BMI, body mass index; PSA, prostate-specific antigen; ASA, American Society of Anesthesiologists; IIEF, International Index of Erectile Function; ED, erectile dysfunction; IPSS, International Prostate Symptom Score; TURP, transurethral resection of the prostate.

alone, and four (11.8%) received ART + HT postoperatively. Mean follow-up was 27.8±11.1 months. BCR was detected in nine (26.4%) patients. Of the 34 patients with 1-year follow-up, 17 (50%) were fully continent (zero pads/day), six (17.7%) wore a safety pad/day, six (17.7%) wore one pad/day, three (8.8%) wore two pads/day, and two (5.9%) wore more than two pads/day. Of the 24 patients with no preoperative erectile dysfunction (ED), 15 (44.1%) had no erectile dysfunction at a mean follow-up of 1-year. Trifecta and pentafecta rates were 38% and 26%, respectively.

Operative parameters (Table 2), NVB sparing and relation to PSM (Table 3), postoperative parameters and complications classified according to modified Clavien–Dindo classification (Table 4), postoperative pathologic outcomes (Table 5), oncologic outcomes (Table 6), postoperative urinary continence outcomes (Table 7), postoperative erectile function outcomes (Table 8), and trifecta and pentafecta outcomes (Table 9) are presented.

**Table 2** Operative parameters

| | |
|---|---|
| Mean surgery (console) time (min) | 162.1±64.4 (range 90–380) |
| Mean estimated blood loss (cc) | 232.2±255.1 (range 40–1,500) |
| APAs detected and preserved: n (%) | |
| Overall | 4 (11.7%) |
| Unilateral | 3 (8.8%) |
| Bilateral | 1 (2.9%) |
| Not preserved | 0 |
| NVB-preserving technique: n (%) | |
| Bilateral | 16 (47%) |
| Unilateral | 5 (15%) |
| Not performed | 13 (38%) |

**Abbreviations:** APA, accessory pudendal artery; NVB, neurovascular bundle.

## Discussion

RARP is increasingly being applied in the surgical management of PCa; however, number of publications related to experience in HRPC is limited. In this paper, we evaluated the outcomes of our RARP experience in 34 HRPC patients.

In our series, mean estimated blood loss was 232.2 cc. Similar to our study, Punnen et al[11] reported estimated blood loss as 217 cc in a series of 233 HRPC patients, respectively, who underwent RARP. Mean length of hospital stay was 4.1 days in our series. On the other hand, Punnen et al[11] and Gandaglia et al[12] reported a shorter length of hospital stay as 1.6 days and 1 day, respectively. In our study, mean length of hospital stay seems to be longer than that in Punnen et al[11] and Gandaglia et al.[12] We discharge patients when we remove the abdominal drain, generally on postoperative day 3 or 4, and when the patient passes flatus and initiates sufficient oral intake.

**Table 3** NVB sparing and relation to PSM

| | Bilateral NVB sparing | Unilateral NVB sparing | Non-NVB sparing |
|---|---|---|---|
| Overall N=34 | N=16, 47% | N=5, 15% | N=13, 38% |
| PSM | N=6, 40% | N=1, 20% | N=4, 30.7% |
| PSM location | | | |
| Apex | N=2, 13.3% | N=1, 20% | N=1, 7.6% |
| Prostate base | N=4, 26.6% | N=0 | N=2, 15.3% |
| Bilateral prostate laterale lobes | N=0 | N=0 | N=1, 7.6% |

**Abbreviations:** NVB, neurovascular bundle; PSM, positive surgical margin.

**Table 4** Postoperative parameters and complications classified according to modified Clavien–Dindo classification

| | | |
|---|---|---|
| Mean follow-up (months) | 27.8±11.1 (range 12–48) | |
| Mean abdominal drain removal time (days) | 3.1±2.0 (range 1–12) | |
| Mean urethral catheter removal time (days) | 12.6±6.2 (range 7–30) | |
| Mean duration of hospital stay (days) | 4.1±2.1 (range 2–12) | |
| **Type of complication** | **0–30 days** | **31–90 days** |
| Intraoperative (surgical) | | |
| Bladder perforation | 2 (Clavien 3b) | None |
| Rectum perforation | 1 (Clavien 3b) | None |
| Postoperative | | |
| Wound | None | None |
| Pulmonary | None | None |
| Neurologic | None | None |
| Gastrourinary | | |
| Urinary leakage | 1 (Clavien 1) | None |
| Infectious diseases | None | None |
| Urinary infection | 1 (Clavien 2) | None |
| Gastrointestinal | | |
| Constipation | 1 (Clavien 1) | None |
| Cardiac | None | None |
| Bleeding | | |
| Abdominal hematoma | 1 (Clavien 3b) | None |
| Thromboembolic | None | None |
| Uremia | None | None |
| Metabolic | None | None |
| Psychiatric | None | None |
| Miscellaneous | None | None |
| Intensive care requirement | 1 (Clavien 4) | None |
| **Grade of complications according to modified Clavien–Dindo classification: n** | **Overall complications: N=8** | **Overall complications: N=0** |
| 1 | 2 | 0 |
| 2 | 1 | 0 |
| 3a | 0 | 0 |
| 3b | 4 | 0 |
| 4 | 1 | 0 |
| 5 | 0 | 0 |
| Minor complication (grade 1 and 2): n | 3 | 0 |
| Major complication (grade 3–5): n | 5 | 0 |
| Readmission due to minor complications: n | 1 | 0 |
| Readmission due to major complications: n | 0 | 0 |

**Table 5** Postoperative pathologic outcomes

| | |
|---|---|
| Pathologic stage | N=34 (100%) |
| ASAP + HGPIN | 0 |
| pT0 | 2 (5.8%) |
| pT2a | 5 (14.7%) |
| pT2b | 3 (8.8%) |
| pT2c | 6 (17.6%) |
| pT3a | 10 (29.4%) |
| pT3b | 8 (23.5%) |
| Gleason score | N=34 (100%) |
| 2–6 | 7 (20.5%) |
| 3+4 | 10 (29.4%) |
| 4+3 | 6 (17.6%) |
| 8–10 | 9 (26.4%) |
| T0 | 2 (5.8%) |
| PSM rate | N=34 (100%) |
| Overall | 11 (32.3%) |
| pT2 | 1 (2.9%) |
| pT3 | 10 (29.4%) |

**Abbreviations:** ASAP, atypical small acinar proliferation; HGPIN, high-grade prostatic intraepithelial neoplasia; PSM, positive surgical margin.

In our series, 17 patients (50%) underwent extended pelvic LN dissection and mean LN yield was 11.8. One patient had LN metastasis. We performed bilateral extended pelvic LN dissection in those with an at least 5% risk of pelvic LN involvement by PCa according to Partin's tables.[13] Harty et al[14] (n=152), Pierorazio et al[15] (n=105), Punnen et al[11] (n=233), Busch et al[16] (n=110), and Gandaglia et al[12] (n=806) performed pelvic LN dissection in 56%, 97.1%, 63%, 94.5%, and 68% of the cases, respectively. Mean LN yield was reported between six and 24.[11,15–22]

PSM rate was 32.3% (2.9% in pT2 and 29.4% in pT3 disease) in our series. Harty et al[14] reported PSM rates as 12% and 79% in pT2 and pT3 disease, respectively. Pierorazio et al[15] reported PSM rate as 8.3% in pT2 disease, and Gandaglia et al[12] reported PSM rate as 60% in pT2 and pT3a disease. Others reported overall PSM rates between 12% and 48.8%.[8,12,14–19] Our PSM rates seem to be similar to those in the published literature. Interestingly, pT0 disease was reported in two patients, and the pathology slides were re-reviewed by the pathology department without any change in the final diagnosis (Table 5).

In our series, at a mean follow-up of 27.8 months, BCR was detected in nine (26.4%) patients. Punnen et al[11] reported BCR as 79% at 2-year and 66% at 4-year follow-up. Busch et al[16] reported BCR as 41.4% at 3-year follow-up. Of the 34 patients in our study, four (11.8%) received ART alone, four (11.8%) received HT alone, and four (11.8%) received ART+HT postoperatively. Gandaglia et al[12] reported that 21.2% of 353 HRPC

**Table 6** Oncologic outcomes of patients

| Follow-up | First month | Third month | Sixth month | Ninth month | First year |
|---|---|---|---|---|---|
| Available patients: N=34 (100%) | | | | | |
| BCR: 9 (26.4%) | | | | | |
| Overall | 5 | 1 | 1 | 0 | 1 |
| pT2 | 0 | 0 | 0 | 0 | 1 |
| pT3 | 5 | 1 | 1 | 0 | 0 |

**Abbreviation:** BCR, biochemical recurrence.

**Table 7** Postoperative urinary continence outcomes of the patients at follow-up

| | Preoperative | First day | First month | Third month | Sixth month | Ninth month | First year |
|---|---|---|---|---|---|---|---|
| n (%) | 34 (100) | 34 | 34 | 34 | 34 | 34 | 34 |
| Zero pads | 34 (100) | 1 | 4 | 10 | 14 | 15 | 17 |
| Safety pad | 0 | 16 | 10 | 9 | 9 | 8 | 6 |
| 1 pad/day | 0 | 8 | 14 | 10 | 7 | 7 | 6 |
| 2 pads/day | 0 | 5 | 2 | 2 | 2 | 2 | 3 |
| >2 pads/day | 0 | 4 | 4 | 3 | 2 | 2 | 2 |

patients who underwent RARP required additional cancer therapy after surgery. Of those, 15.9% required radiotherapy and 13.9% required androgen deprivation therapy.[12] Currently, the mean follow-up time is limited in our series, and the need for additional therapy might change as follow-up increases.

In our series, during the perioperative period (0–30 days), three minor (constipation/prolonged ileus [n=1], prolonged anastomotic leakage [n=1], and urinary tract infection [n=1]) and five major complications (intraoperative bladder injury [n=2] and rectum perforation [n=1], which were repaired intraoperatively, intensive care requirement [n=1], and abdominal hematoma [n=1]) complications occurred according to modified Clavien classification. We experienced rectal injury in one patient in our series, which we repaired intraoperatively. Postoperative follow-up was uneventful for this patient. No complication was detected during postoperative 31–90 days. Other authors reported complication rates between 4% and 30% in HRPC patients who underwent RARP.[17,19,21,23] In these studies, lymphocele, ileus, anastomotic leakage, deep vein thrombosis, and rectal injury were among the reported complications. Ham et al[19] reported rectal injury rate as 1.7%. Lymphocele formation was reported between 2.5% and 6.6% in other studies.[19,21]

Urinary continence and erectile function are the functional outcomes following RARP. Currently, the information about functional outcomes following RARP in HRPC patients is limited in the literature. Yuh et al[24] reported 1-year urinary continence (zero to one safety pads/day) rate between 78% and 95% and erectile function recovery rate between 52% and 60%. Yee et al[25] reported their 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. In our series, bilateral and unilateral NVB sparing was performed on 47% and 15%, respectively. Only 13 patients (38%) did not undergo NVB sparing. Of the 34 patients with 1-year follow-up, 17 (50%) were fully continent (zero pads/day), six (17.7%) wore one pad/day, three (8.8%) wore two pads/day, and two (5.9%) wore more than two pads/day. Of the 24 patients with no preoperative erectile dysfunction, 15 (44.1%) had no erectile dysfunction at a mean follow-up of 1-year. Trifecta and pentafecta rates were 38% and 26%, respectively. Preservation of the NVBs and postoperative adjuvant therapy administration are expected to affect functional outcomes.

Tissue characteristics might be different in HRPC patients compared with low-risk disease during performing of RARP. In addition, possibility of losing tissue of dissection might exist, and sufficient surgical experience might be essential. Therefore, we suggest gaining sufficient surgical experience in low-risk cases initially. Bulky disease and involvement of seminal vesicles or bladder neck could challenge the console surgeon. We demonstrated surgical differences comparatively in high-risk versus low-risk disease during performing of RARP (supplementary video).

Limited sample size, inclusion of more than one surgeon's experience, and being a retrospective and noncomparative study are the main limitations of our study.

**Table 8** Postoperative erectile function outcomes of the patients at follow-up

| IIEF scores | Preoperative n (%) | First month | Third month | Sixth month | Ninth month | First year |
|---|---|---|---|---|---|---|
| n (%) | 34 (100) | | | | | |
| No ED (IIEF score 22–25) | 24 (70.5) | 0 | 5 (14.7) | 9 (26.4) | 10 (29.4) | 15 (44.1) |
| Mild (17–21) | 0 (0) | 0 | 3 (8.8) | 6 (17.6) | 6 (17.6) | 4 (11.7) |
| Mild to moderate (12–16) | 1 (2.9) | 1 (2.9) | 4 (11.7) | 2 (5.8) | 1 (2.9) | 0 |
| Moderate (8–11) | 1 (2.9) | 0 | 2 (5.8) | 1 (2.9) | 1 (2.9) | 1 (2.9) |
| Severe (5–7) | 8 (23.5) | 33 (97) | 20 (57.1) | 16 (47) | 16 (47) | 14 (41.1) |

**Abbreviations:** IIEF, International Index of Erectile Function; ED, erectile dysfunction.

**Table 9** Trifecta and pentafecta outcomes

| | Proportion of patients | % |
|---|---|---|
| Trifecta outcomes at 1 year | 13 | 38 |
| Fully continent (no pad usage) | 17 | 50 |
| No ED* | 15 | 44 |
| BCR-free state** | 31 | 91 |
| Pentafecta outcomes at 1 year | 9 | 26 |
| No perioperative complications*** | 26 | 76 |
| Negative SMs | 23 | 68 |

**Notes:** *Potency was defined as the ability to achieve and maintain satisfactory erections firm enough for sexual intercourse in >50% of attempts, with or without the use of phosphodiesterase type 5. If patients required a vacuum erection device, penile injections, or transurethral alprostadil for intercourse, they were not considered to be potent; **BCR was defined as two consecutive serum prostate-specific antigen levels of >0.2 ng/mL; ***according to modified Clavien–Dindo classification.
**Abbreviations:** ED, erectile dysfunction; BCR, biochemical recurrence; SM, surgical margin.

## Conclusion

In conclusion, according to our experience, RARP in HRPC is a safe procedure with satisfactory oncologic and functional outcomes in the short term.

## Disclosure

This study was presented by Dr Canda as a poster during the European Robotic Urology Symposium (ERUS), which was held on 17–19 September 2014 in Amsterdam, the Netherlands. Dr Canda is a member of the Robotic Urology Working Group of the Young Academic Urologists (YAU) of the European Association of Urology (EAU). The other authors report no conflicts of interest in this work.

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