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Comparison of positive surgical margin rates in high risk prostate cancer: open versus minimally invasive radical prostatectomy

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ABSTRACT

Objective: We compared positive surgical margin (PSM) rates for patients with high risk prostate cancer (HRCaP) who underwent open radical retropubic (RRP), robotic (RALP), and laparoscopic (LRP) prostatectomy at a single institution.

Materials and Methods: We performed a retrospective review of our prospectively maintained IRB approved database identifying prostate cancer patients who underwent RRP, RALP, or LRP between January 2000 and March 2010. Patients were considered to have HRCaP if they had biopsy or final pathologic Gleason score ≥ 8, or preoperative PSA ≥ 20, or pathologic stage ≥ T3a. A positive surgical margin (PSM) was defined by the presence of tumor at the inked surface of the specimen. Patients who received neoadjuvant hormonal therapy and those who underwent a perineal prostatectomy were excluded from the study.

Results: Of the 445 patients in this study, surgical technique for prostatectomy included RRP (n = 153), RALP (n = 152), and LRP (n = 140). PSM rate for the three groups were not different: 52.9% RRP, 50% RALP, and 41.4% LRP, (p = 0.13). The PSM rate did not differ when comparing RRP to a combined group of RALP and LRP (p = 0.16). Among patients with a PSM, there was no statistical difference between the three groups in terms of the number of patients with a pathologic stage of T3 or higher (p = 0.83). On univariate analysis, a higher preoperative PSA value was associated with a positive margin (p = 0.04).

Conclusion: In this HRCaP series, the PSM rate did not differ based on the surgical approach. On univariate analysis, patients with a higher preoperative PSA value were more likely to have a PSM.

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INTRODUCTION

In 2011, it was estimated that 240,890 men would be diagnosed with prostate cancer and 33,720 men would die of this disease (1). Prostate cancer encompasses a heterogeneous patient population with varying aggressiveness. Patients with high risk prostate cancer (HRCaP) represent a subset with a relatively high risk of death from prostate cancer (2). Standardized criteria to define HRCaP are lacking (3,4). D'Amico's high risk definition of PSA ≥ 20ng/mL, 1992 TNM ≥ cT2c, or biopsy Gleason score ≥ 8 is frequently referenced, although variations exist (5). Loeb et al. defined HRCaP using two definitions: [1] 1992 TNM of cT2b and biopsy Gleason score 8-10, or PSA ≥ 15ng/mL, and [2] those with 1992 TNM of cT3 (6). Others have

simply defined HRCaP based on digital rectal exam including 1992 TNM cT3 disease (7).

Surgical treatment options include open radical prostatectomy (RRP), robotic assisted laparoscopic prostatectomy (RALP), and laparoscopic radical prostatectomy (LRP). However, successful radical removal of the prostate for patients with HRCaP may be more challenging given the potential for local extension. Surgery aims to provide clean apical dissection, neurovascular bundle resection at the tumor bearing side, complete resection of the seminal vesicles and lymph nodes, with an adequate dissection at the bladder neck (8). The bladder neck is then reconstructed when necessary and the vesicourethral anastomosis performed. A positive surgical margin (PSM) has been established as an independent predictor for biochemical recurrence and has been shown to be associated with a 2.6-fold increased unadjusted risk of prostate specific cancer mortality (9-11). As such, the PSM rate may be a useful endpoint to compare efficacy of different surgical techniques employed for radical prostatectomy.

Minimally invasive surgery (MIS) purports to provide patients with shorter hospital stay, decreased postoperative analgesic requirement, and earlier convalescence compared to open surgery (12). RALP and to a lesser extent LRP are now widely used for radical prostatectomy. Establishing the oncologic efficacy of MIS compared to open surgery is paramount. The aim of this study was to compare PSM rates for HRCaP patients undergoing RRP, RALP, and LRP, at a single institution.

MATERIALS AND METHODS

We performed a retrospective review of our IRB approved prostate cancer database for patients undergoing RRP, RALP, or LRP between January 2000 and March 2010. Patients were considered to have HRCaP if they had biopsy or final pathologic Gleason score ≥ 8, or PSA ≥ 20, or pathologic stage of T3a or higher. Patient demographics included patient age, preoperative PSA value, clinical T stage, biopsy Gleason sum, number of positive biopsy cores, whether a pelvic lymph node dissection was performed, prostate size, final pathologic stage, and presence and location of PSM. Preoperative patient assessment included bone scan and CT scan to rule out metastatic disease. Since 2007, the majority of high risk patients had prostate MRI to assess for seminal vesical involvement or gross extra capsular extension. All patients had a detailed discussion about treatment alternatives prior to surgery as well as the possible need for adjuvant radiation therapy based on the possibility of treatment failure with surgical monotherapy.

At our institution, radical prostatectomy specimens were submitted in their entirety. The right side of the specimen was inked blue and the left in black. The specimen serially sectioned transversely from the apex towards base perpendicular to the ink at 3 mm intervals. The specimen was reconstituted and lightly wrapped in gauze, then fixed in formalin. Next, the apical and shaved bladder margin was removed. Formalin fixed samples were submitted in cassettes and subjected to microwave tissue processing. The specimen weight, tumor volume, pathological stage according to the 1997 TNM classification, surgical margin status, and location of positive surgical margin were noted. PSM was defined by the presence of tumor at the inked surface of the specimen. A single genitourinary pathologist performed pathologic re-review of any questionable PSM or staging after final report was submitted.

All procedures were performed by attending surgeons (4 open, the same 3 surgeons for robotic and laparoscopic) with the assistance of a resident physician. Pelvic lymph node dissection was performed at the discretion of the surgeon. Patients who received neoadjuvant hormonal therapy and those who underwent a perineal prostatectomy were excluded from the study. Nerve preservation was performed at the discretion of the surgeon.

Mean age was compared between the three groups using an Analysis of Variance. The distribution of PSA and Gleason scores were compared between the three groups using the nonparametric Kruskal-Wallis test. Chi-square test was used to compare the distribution of clinical stage and the percentage of patients with a PSM between groups. Logistic regression was used to analyze for univariate associations of possible risk factors with a PSM. SAS software was used for analysis, version 9.2 (Copyright (c) 2002-2008 by SAS Institute Inc., Cary, NC, USA).

RESULTS

A total of 2,282 radical prostatectomy procedures were performed at our institution over the decade. We identified 513 (22.5%) patients with HRCaP. Sixty patients (12%) received neoadjuvant hormonal therapy while 8 (0.2%) patients underwent perineal prostatectomy, and were excluded from the analysis. The remaining 445 patients were included in our analysis. The surgical technique included RRP (n = 153), RALP (n = 152), and LRP (n = 140). Patient demographics and preoperative tumor characteristics are shown in Table-1. There was no significant difference in age among the three groups with mean ages of 59, 59, and 61 years respectively (p = 0.08). The median preoperative PSA was statistically equivalent, for patients undergoing RRP (5.6 ng/mL), RALP (6.0 ng/mL), and LRP (5.2 ng/mL), (p = 0.15). There was no statistical difference between groups in regards of clinical stage (p = 0.11). Eighty--nine patients (RRP = 28, RALP = 33, LRP = 28) had a biopsy Gleason sum of greater than or equal 8. However, there was no statistical difference between the three groups in terms of biopsy Gleason sum distribution (p = 0.34) (Table-1).

We assessed each group for Gleason score upgrading from 7 to ≥ 8 or downgrading from Gleason score 8 to ≤ 7 between biopsy and final pathology, and demonstrated that both occurred with equal frequency between groups. The Gleason score was upgraded in 15% RRP, 14% RALP, and 16% LRP (p = 0.90), and downgraded in 8% RRP, 9% RALP, and 7% LRP (p = 0.81). To further ensure that we were comparing three similar groups, we assigned each patient a score (one point for each included variable) for the number of high risk features based on our definition of HRCaP. Only one patient in the study had all four high risk features and the majority of patients in each group had only one high risk feature (RRP = 74%, RALP = 71%, LRP = 75%) (p = 0.71). Overall, there was a statistically significant higher percentage of patients in each group with pathologic T3 disease (RRP = 70%, RALP = 74%, LRP = 70%) compared to patients with T2 disease (RRP = 24%, RALP = 22%, LRP = 30%) (p = 0.04) (Table-2). Lymph node dissection was performed with similar frequency: 58% of RRP patients, 56% RALP patients, and 38% LRP patients.

The PSM rate was not statistically different between RRP (52.9%), RALP (50%), and LRP (41.4%) (p = 0.13). Among patients with a PSM, the majority had pathologic T3 disease or higher (RRP = 85%, RALP = 88%, LAP = 88%) and the percentage with pathologic stage T3 did not significantly differ

Table 1 - Patient and clinical tumor characteristics.

	RRP	RALP	LRP	p-value
N	153	152	140	
Age	59.5 ± 6.5	61.3 ± 6.0	59.9 ± 6.9	p = 0.8
Pre-op PSA (median)	5.6	6	5.2	p = 0.15
Clinical Stage				
cT1	108 (71%)	91 (60%)	96 (69%)	
cT2	45 (29%)	61 (40%)	44 (31%)	p = 0.11
Biopsy Gleason Sum				p = 0.34
6	66 (43%)	52 (34%)	55 (39%)	
7	59 (39%)	67 (44%)	57 (41%)	
8,9,10	28 (18%)	33 (22%)	28 (20%)	
Prostate Size (gm)	39.6 ± 12.2	47.5 ± 14.5	44.5 ± 14.4	p < 0.001

Table 2 - Pathologic Features.

	RRP	RALP	LRP	p-value
# Patients	153	152	140	
Positive Margins	52.9% (81/153)	50% (76/152)	41.4% (58/140)	p = 0.13
Pathologic Stage				
T2	37 (24%)	33 (22%)	42 (30%)	
T3	107 (70%)	112 (74%)	98 (70%)	p = 0.04
T4	9 (6%)	7 (4%)	0	
Positive margins by p-stage				
pT2	12 (15%)	9 (12%)	7 (12%)	
pT3	60 (74%)	60 (79%)	51 (88%)	p = 0.83
pT4	9 (11%)	7 (9%)	0	
Positive margins by t-stage				
cT1	59 (73%)	46 (61%)	40 (69%)	
cT2	22 (27%)	30 (39%)	18 (31%)	
Node Positive	4 (2.6%)	5 (3.3%)	5 (3.6%)	p = 0.09

between the three groups (p = 0.83). When comparing PSM rate between open cases (RRP) and those done by a MIS approach (RALP + LRP), there was no statistical difference (p = 0.16). The percentage of patients in the open group with a PSM that had a pathologic stage of T3 or greater did not differ from the MIS group (p = 0.54) (Table-2). The location of a PSM was characterized as apex, bladder neck, postero-lateral, multiple sites, and other. The apex was the location of a PSM in 14 RRP, 16 RALP, and 19 LRP while the bladder neck was the location in 15 RRP, 10 RALP, and 7 LRP. The postero-lateral margin was positive in 27 RRP, 19 RALP, and 15 LRP. Patients with multiple PSMs were 19, 23, and 10 while other was the location in 6, 8, and 7 patients in the RRP, RALP, and LRP groups, respectively. Univariate analysis of preoperative patient variables demonstrated a higher preoperative PSA was associated with a PSM (Table-3). Other variables assessed including age, Gleason sum, and prostate size were not significant for this cohort of HRCaP.

DISCUSSION

Several treatment options exist for men with HRCaP including radiation therapy, androgen deprivation, and surgery. For some patients with HRCaP, surgical management may be an attractive option, as surgical monotherapy may provide cure for a portion of these patients (13-16). Radical resection may be optimal in younger patients with greater than 10-year life expectancy. Resection allows for use of adjuvant treatments if necessary. Some studies have advocated the use of multimodality therapy combining surgery and radiation (17-19). A high level of technical expertise is mandatory during radical prostatectomy for HRCaP as these cases may prove more challenging to achieve negative margins. Experienced surgeons have noted no increased morbidity in HRCaP patients when compared to a lower risk cohort (14,16). Theoretically, given the lack of tactile feedback associated with robotic assisted surgery, concern exists about the use of robotics

Table 3 - Univariate analysis assessing variable association with PSM rate.

% with PSM	RRP	RALP	LRP		p-value
	53	50	41		p = 0.12
Age (years)	**< 55**	**55-65**	**> 65**		
	47/85 (55%)	105/233 (45%)	63/127 (50%)		p = 0.25
PSA (ng/mL)	**< 5**	**5-10**	**> 10**		
	59/152 (39%)	105/206 (51%)	50/85 (59%)		p = 0.0071
Gleason Sum	**6**	**7**	**8-10**		
	90/173 (52%)	90/183 (49%)	35/89 (39%)		p = 0.14
Prostate Size (gm)	**≤ 35**	**35.1-45**	**45.1-55**	**> 55**	
	69/125 (55%)	57/137 (42%)	40/96 (42%)	30/70 (56%)	p = 0.66

for high risk prostate cancer. We set out to examine our single institution data to see if such a concern may be substantiated.

LRP and to a greater extent RALP have emerged and, or surpassed RRP as the most frequent surgical option in the United States. In 2010, approximately 70% of radical prostatectomies in the United States were performed with robotic assistance (20). Several publications aimed to compare outcomes of MIS to the open radical prostatectomy. Other investigators have compared outcomes between MIS prostatectomy and RRP and concluded that MIS approaches afford less blood loss, shorter hospital stay, equivalent complication rates, and earlier convalescence (21,22). In 2002, Menon et al. compared a group of 30 consecutive RRP to 30 initial RALP and found no difference in overall PSM rates (29% vs. 26%) (23). In an update of the series, comparing 100 RRP to 200 RALP performed at the same institutions, the authors demonstrated improved overall PSM rate with the robotic approach (9%) vs. the open procedure (26%) ($p < 0.05$) (12). Details relating to HRCaP comparison was not provided. In 2004, Ahlering et al. compared one surgeon's experience of 60 RRP with his last 60 RALP. The authors found margin rates were not statistically different between groups, 20 vs. 16.7% respectively (24). The PSM rate did not differ for patients with ≥ pT3a disease, although the number of patients was small (16 patients in each arm).

The Memorial Sloan Kettering group compared their PSM rates for LRP (n = 612) and (RRP n = 818) and found identical rates of 11%. Overall disease free progression did not differ between the two groups with a short median follow-up 1.5 years. Rather than provide PSM rate break down relative to preoperative risk stratification, the authors provide predicted probability of PSM based on a nomogram and correlation with final outcome. Based on their data, there was no difference between the two groups' true PSM rate with increasing nomogram likelihood of PSM. Unfortunately, this presentation style does not allow direct comparison with our data. Bahler et al. reported a 47% PSM rate in 119 patients with Gleason 8-10 prostate cancer treated with RRP as initial monotherapy, within the 15-54% PSM rate among previous reports for patients with pathologically confirmed high grade prostate cancer (13). As well, our PSM rate for pT2 disease of 12% in the RALP and LRP groups and 15% in RRP compares favorably.

To the best of our knowledge, only one other publication has compared PSM rates for RRP and RALP allowing for subgroup analysis of HRCaP (25). In this study, Smith et al. compared

200 consecutive RALP with 200 RRP performed at the same institution specifically comparing margin rate and location. Overall margin rates were lower for the RALP (15%) as compared to the RRP group (35%) ($p < 0.001$). However, a criticism of this study was the lack of similarity in the two arms with the robotic group having a higher percentage of low risk patients (65%), compared to the open group (47%) ($p < 0.001$). Using the D'Amico preoperative risk stratification, comparing the relatively small group of patients with HRCaP in this study reveals, 7/13 (58%) and 18/32 (56.3%) of the HRCaP patients had PSM ($p = 0.883$). Our HRCaP PSM of 52.9% RRP, 50% RALP, and 41.4% LRP compares favorably with this series as well as others in the literature (13,26-28).

Recently a small number of publications have focused on RALP for high risk malignancies. None of these studies have had comparative arms of LRP and RRP. Jayram et al. presented a series of 148 men having undergone RALP with HRCaP as defined by D'Amico. Overall PSM rate was 21%. There was no comparison arm in this study. However, the authors state that their overall oncologic and functional outcomes are comparable to published historical controls (29). Casey et al. reported on 35 patients who had pT3 disease after RALP. Only 10 patients met the D'Amico HRCaP definition. PSM rate was 20% in the pT3 group compared to 4.9% for pT2 ($p < 0.004$). Other perioperative and functional outcomes were similar between those with locally advanced cancer and those with confined prostate cancer (30).

Ham et al. divided their series of RALP into two groups based on digital rectal examination: 121 with "locally advanced": prostate cancer (≥ clinical stage T3a) and 200 patients with assumed "localized disease" (≤ clinical stage T2) (27). Using this definition, overall PSM rate was 33.3%, locally advanced group 48.8%, and low risk group 24%. No differences were noted in perioperative or complication outcomes. The major criticism is the study design with group designation based on digital rectal examination which may be inadequate. For example, one study demonstrated digital rectal examination did not detect extraprostatic extension in 30%-50% of exams (31). Finally, Engel et al. published their single surgeon experience with RALP and HRCaP with a modified D'Amico definition (lower threshold of PSA ≥ 10 ng/dL) (32). Of the 73 HRCaP patients identified, PSM rate was 38%. Short term PSA free recurrence appears to be similar to RRP series.

Our results suggest that using PSM rate as an early surrogate for cancer control, patients with HRCaP may be offered either open, robotic assisted, or laparoscopic radical prostatectomy. On univariate analysis, the factor affecting increased PSM rate was a higher PSA. This finding correlates with other studies which have indicated a higher PSA is associated with higher PSM rates (33). Limitations exist for the present study. Our single institution data may not be generalizable. All three MIS surgeons have extensive experience with prostatectomy. The retrospective nature of comparison may include inherent bias as related to patient selection that could not be controlled. We attempted to assess this possibility by evaluating patient characteristics between the three groups, which appear to be similar. Having more than one surgeon involved for each surgical type may introduce a lack of uniform approach to each surgery. However, the increased number of surgeons involved may also allow the results to be interpreted beyond just one surgeon's experience. We did not specifically study the effect of neurovascular preservation and functional outcomes results for this study. Studying such endpoints may aid in proving the equivalence between the open and the MIS technique. Although a prospective design would alleviate these concerns, carrying out such a study would be challenging. Finally, we did not evaluate the complication rates or functional outcomes between the three techniques although others have addressed these issues previously.

CONCLUSIONS

PSM rate does not statistically differ between MIS and open radical prostatectomy for patients with HRCaP. On univariate analysis, patients with a higher preoperative PSA value are more likely to have a PSM.

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ABBREVIATIONS

PSM = positive surgical margin
HRCaP = high risk prostate cancer
RRP = radical retropubic prostatectomy
RALP = robotic assisted laparoscopic prostatectomy
LRP = laparoscopic radical prostatectomy
MIS = minimally invasive surgery

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Siegel R, Ward E, Brawley O, Jemal A: Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. CA Cancer J Clin. 2011; 61: 212-36.
2. Albertsen PC, Hanley JA, Fine J: 20-year outcomes following conservative management of clinically localized prostate cancer. JAMA. 2005; 293: 2095-101.
3. Cooperberg MR, Cowan J, Broering JM, Carroll PR: High-risk prostate cancer in the United States, 1990-2007. World J Urol. 2008; 26: 211-8.
4. Yossepowitch O, Eggener SE, Bianco FJ Jr, Carver BS, Serio A, Scardino PT, et al.: Radical prostatectomy for clinically localized, high risk prostate cancer: critical analysis of risk assessment methods. J Urol. 2007; 178: 493-9; discussion 499.
5. D'Amico AV, Whittington R, Malkowicz SB, Schultz D, Blank K, Broderick GA, 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.
6. Loeb S, Smith ND, Roehl KA, Catalona WJ: Intermediate-term potency, continence, and survival outcomes of radical prostatectomy for clinically high-risk or locallyadvanced prostate cancer. Urology. 2007; 69: 1170-5.
7. Hsu CY, Joniau S, Oyen R, Roskams T, Van Poppel H: Outcome of surgery for clinical unilateral T3a prostate cancer: a single-institution experience. Eur Urol. 2007; 51: 121-8; discussion 128-9.
8. Hsu CY, Joniau S, Van Poppel H. Radical prostatectomy for locally advanced prostate cancer:Technical aspects of radical prostatectomy. EAU Update Series. 2005; 3: 90-7.
9. Karakiewicz PI, Eastham JA, Graefen M, Cagiannos I, Stricker PD, Klein E, et al.: Prognostic impact of positive surgical margins in surgically treated prostate cancer: multi-institutional assessment of 5831patients. Urology. 2005; 66: 1245-50.
10. Swindle P, Eastham JA, Ohori M, Kattan MW, Wheeler T, Maru N, et al.: Do margins matter? The prognostic significance of positive surgical margins in radical prostatectomy specimens. J Urol. 2005; 174: 903-7.
11. Wright JL, Dalkin BL, True LD, Ellis WJ, Stanford JL, Lange PH, et al.: Positive surgical margins at radical prostatectomy predict prostate cancer specific mortality. J Urol. 2010; 183: 2213-8.
12. Tewari A, Srivasatava A, Menon M; Members of the VIP Team: A prospective comparison of radical retropubic and robot-assisted prostatectomy: experience in one institution. BJU Int. 2003; 92: 205-10.
13. Bahler CD, Foster RS, Bihrle R, Beck SD, Gardner TA, Sundaram CP, et al.: Radical prostatectomy as initial monotherapy for patients with pathologically confirmed high-grade prostate cancer. BJU Int. 2010; 105: 1372-6.
14. Boorjian SA, Blute ML: Surgical management of high risk prostate cancer: the Mayo Clinic experience. Urol Oncol. 2008; 26: 530-2.
15. Donohue JF, Bianco FJ Jr, Kuroiwa K, Vickers AJ, Wheeler TM, Scardino PT, et al.: Poorly differentiated prostate cancer treated with radical prostatectomy: long-term outcome and incidence of pathologicaldowngrading. J Urol. 2006; 176: 991-5.
16. Yossepowitch O, Eastham JA: Role of radical prostatectomy in the treatment of high-risk prostate cancer. Curr Urol Rep. 2008; 9: 203-10.
17. Gonzalez JR, Laudano MA, McCann TR, McKiernan JM, Benson MC: A review of high-risk prostate cancer and the role of neo-adjuvant and adjuvant therapies. World J Urol. 2008; 26: 475-80.
18. Lau WK, Bergstralh EJ, Blute ML, Slezak JM, Zincke H: Radical prostatectomy for pathological Gleason 8 or greater prostate cancer: influence of concomitant pathological variables. J Urol. 2002; 167: 117-22. Erratum in: J Urol. 2004; 171(2 Pt 1): 811.
19. Zincke H, Fleming TR, Furlow WL, Myers RP, Utz DC: Radical retropubic prostatectomy and pelvic lymphadenectomy for high-stage cancer of the prostate. Cancer. 1981; 47: 1901-10.
20. Singh I, Hemal AK: Robotic-assisted radical prostatectomy in 2010. Expert Rev Anticancer Ther. 2010; 10: 671-82.
21. Hoznek A, Salomon L, Olsson LE, Antiphon P, Saint F, Cicco A, et al.: Laparoscopic radical prostatectomy. The Créteil experience. Eur Urol. 2001; 40: 38-45.
22. Wilson T, Torrey R: Open versus robotic-assisted radical prostatectomy: which is better? Curr Opin Urol. 2011; 21: 200-5.

23. Menon M, Tewari A, Baize B, Guillonneau B, Vallancien G: Prospective comparison of radical retropubic prostatectomy and robot-assisted anatomic prostatectomy: the VattikutiUrology Institute experience. Urology. 2002; 60: 864-8.
24. Touijer K, Eastham JA, Secin FP, Romero Otero J, Serio A, Stasi J, et al.: Comprehensive prospective comparative analysis of outcomes between open and laparoscopic radical prostatectomyconducted in 2003 to 2005. J Urol. 2008; 179: 1811-7; discussion 1817.
25. Smith JA Jr, Chan RC, Chang SS, Herrell SD, Clark PE, Baumgartner R, et al.: A comparison of the incidence and location of positive surgical margins in robotic assisted laparoscopic radical prostatectomy and open retropubic radical prostatectomy. J Urol. 2007; 178: 2385-9; discussion 2389-90.
26. Bastian PJ, Gonzalgo ML, Aronson WJ, Terris MK, Kane CJ, Amling CL, et al.: Clinical and pathologic outcome after radical prostatectomy for prostate cancer patients with a preoperative Gleason sum of 8 to 10. Cancer. 2006; 107: 1265-72.
27. Ham WS, Park SY, Rha KH, Kim WT, Choi YD: Robotic radical prostatectomy for patients with locally advanced prostate cancer is feasible: results of a single-institutionstudy. J Laparoendosc Adv Surg Tech A. 2009; 19: 329-32.
28. Ploussard G, Salomon L, Allory Y, Terry S, Vordos D, Hoznek A, et al.: Pathological findings and prostate-specific antigen outcomes after laparoscopic radical prostatectomy for high-risk prostate cancer. BJU Int. 2010; 106: 86-90.
29. Jayram G, Decastro GJ, Large MC, Razmaria A, Zagaja GP, Shalhav AL, et al.: Robotic radical prostatectomy in patients with high-risk disease: a review of short-term outcomes from a high-volume center. J Endourol. 2011; 25: 455-7.
30. Casey JT, Meeks JJ, Greco KA, Wu SD, Nadler RB: Outcomes of locally advanced (T3 or greater) prostate cancer in men undergoing robot-assisted laparoscopicprostatectomy. J Endourol. 2009 ; 23: 1519-22.
31. Grossfeld GD, Chang JJ, Broering JM, Li YP, Lubeck DP, Flanders SC, Carroll PR: Under staging and under grading in a contemporary series of patients undergoing radical prostatectomy: results from theCancer of the Prostate Strategic Urologic Research Endeavor database. J Urol. 2001; 165: 851-6.
32. Engel JD, Kao WW, Williams SB, Hong YM: Oncologic outcome of robot-assisted laparoscopic prostatectomy in the high-risk setting. J Endourol. 2010; 24: 1963-6.
33. Punnen S, Meng MV, Cooperberg MR, Greene KL, Cowan JE, Carroll PR: How does robot-assisted radical prostatectomy (RARP) compare with open surgery in men with high-risk prostate cancer? BJU Int. 2013; 112: E314-20.

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EDITORIAL COMMENT

Treatment of prostate cancer in patients with high risk localized and locally advanced disease is still a controversial issue concerns to the indication for surgery or treatment with external beam radiotherapy associated with hormone therapy. The indication for surgery in locally advanced prostate cancer is growing especially after some results of long-term follow-up showing that 60-80% of patients can be free of clinical recurrence (1).

Recently a study of Mitchell et al. with a follow-up of 20 years after open radical prostatectomy in 843 patients with preoperative diagnosis of locally advanced disease, confirmed by the pathologist, showed disease-free survival of 81%, 76% free of local recurrence and 72% free of systemic recurrence (2).

In this scenario, some reports comparing the learning curve period of minimally invasive techniques (laparoscopic and robotic) to conventional surgery reported that open surgery promotes better control and fewer positive margins (3,4).

Nowadays minimally invasive radical prostatectomy is standart of care in many centers around the world (5). As experience was gained the indications has been amplified including patients with localized high risk preoperatively.

As we demonstrate in a previous video section of this periodic, in this clinical scenario is really important to respect oncological principals trying to resect all tumor to achieve negative margins, performing extended pelvic lymphadenectomy and preserving of neurovascular bundles only in selected situations (6).

There are only few series concerning laparoscopic or robotic as oncological effective and safe approachs in surgical treatment of locally advanced disease.

Casey et al. (7) reported in 2009 the results of robotic radical prostatectomy in 35 patients with pT3 in pathological anatomy not diagnosed preoperatively. The positive margin rate was similar to open surgery (20%), surgical time and postoperative recovery were similar to patients operated with pT2 tumors and the rate of continence at 1 year was 100%, 71% remained free of recurrence although the follow-up was only 13 months.

Jayram et al. (8) in 2011 reported another study with 148 high-risk patients undergoing RARP by two high-volume robotic surgeons. D'Amico's criteria for high-risk prostate cancer were prostate-specific antigen ≥ 20 ng/mL or clinical stage ≥ T2c or preoperative Gleason grade ≥ 8. Rate of positive surgical margins was 20.9%. Final pathology demonstrated extra-capsular disease in 54.1% of patients and 12.3% had lymph node involvement. At 2 years of follow-up, 21.3% of patients had experienced biochemical recurrence or had persistent disease after treatment. Authors conclude that RARP does not compromise oncologic outcome in patients with high-risk prostate cancer. Although long-term study is necessary data suggest that the presence of high-risk disease is not a contraindication to a minimally invasive approach for radical prostatectomy at experienced centers.

A systematic review of the literature was recently performed showing that positive surgical margin rates are at least equivalent between open and robotic, but firm conclusions about biochemical recurrence and other oncologic end points are difficult to draw because the follow-up in existing studies is relatively short and the overall experience with RARP in locally advanced PCa is still limited and Further research is needed to clarify the actual role of RARP in patients with locally advanced disease (9).

The authors achieve important contribution to this article by adding more data with respect to control margins comparing the gold standard method (open radical prostatectomy) to the newer minimally invasive methods, supporting the idea that positive margins are similar to the 3 techniques. Although the purpose of the article is not a comparison of postoperative functional data, the exploration of this data may be interesting in order to consolidate the effectiveness of minimally invasive procedures.

Another point of extreme interest that can be explored in the future is the association between the preservation of neurovascular bundles (NVB) in these patients with increasing

number of positive margins. Some contemporary data suggest that NVB can be safely preserved in selected cases.

Lavery et al. (10) reported last year 123 high-risk patients submitted to robotic assisted radical prostatectomy. Interfascial nerve-sparing was performed whenever oncologically feasible. Bilateral, unilateral, and non-nerve-sparing on 58%, 15%, and 27%, respectively. On final histopathology, 42% were organ confined; 55 patients had extraprostatic extension, and 35 had seminal vesicle invasion. Positive surgical margins occurred in 31%: 15% focal and 16% extensive. Favorable pathologic outcomes (organ-confined and negative surgical margins) were observed in 40%. Biochemical recurrence occurred in 20%. When controlling for adverse pathologic features, nerve-sparing was not associated with higher rates of positive surgical margins or biochemical recurrence. At a median follow-up of 13 months, 78% were continent and 56% were potent. The "trifecta" of continence, potency, and freedom from recurrence was achieved in 28 patients (23%). Histopathologic and short-term oncologic outcomes at 13-month median follow--up are comparable to those obtained in open surgery. Authors concluded that nerve-sparing robotic-assisted laparoscopic prostatectomy can be safely performed in patients with preoperatively high risk prostate cancer.

Spite of small number of cases and articles available initial results are encouraging. Some studies suggest that surgeon quality is more related to results that the technique "per se". For experienced surgeons that adopt strict oncological principles MIRP can be utilized with efficacy to selected patients with high risk localized and locally advanced prostate cancer. More studies and long term data would support our actual thoughts.

REFERENCES

1. Okajima E, Yoshikawa M, Masuda Y, Shimizu K, Tanaka N, Hirayama A, et al.: Improvement of the surgical curability of locally confined prostate cancer including non-organ-confined high-risk disease through retropubic radical prostatectomy with intentional wide resection. World J Surg Oncol. 2012; 10: 249.
2. Mitchell CR, Boorjian SA, Umbreit EC, Rangel LJ, Carlson RE, Karnes RJ: 20-Year survival after radical prostatectomy as initial treatment for cT3 prostate cancer. BJU Int. 2012; 110: 1709-13.
3. Lepor H: Open versus laparoscopic radical prostatectomy. Rev Urol. 2005 Summer; 7: 115-27.
4. Raman JD, Dong S, Levinson A, Samadi D, Scherr DS: Robotic radical prostatectomy: operative technique, outcomes, and learning curve. JSLS. 2007; 11: 1-7.
5. Wilson T, Torrey R: Open versus robotic-assisted radical prostatectomy: which is better? Curr Opin Urol. 2011; 21: 200-5.
6. Tobias-Machado M, Starling ES, Carlos AS, Pompeo AC, Romanelli P, Nishimoto R: Laparoscopic radical prostatectomy for high risk localized and locally advanced disease. Int Braz J Urol. 2012; 38: 430; discussion 431.
7. Casey JT, Meeks JJ, Greco KA, Wu SD, Nadler RB: Outcomes of locally advanced (T3 or greater) prostate cancer in men undergoing robot-assisted laparoscopic prostatectomy. J Endourol. 2009; 23: 1519-22.
8. Jayram G, Decastro GJ, Large MC, Razmaria A, Zagaja GP, Shalhav AL, et al.: Robotic radical prostatectomy in patients with high-risk disease: a review of short-term outcomes from a high-volume center. J Endourol. 2011; 25: 455-7.
9. Montorsi F, Wilson TG, Rosen RC, Ahlering TE, Artibani W, Carroll PR, et al.: Best practices in robot-assisted radical prostatectomy: recommendations of the Pasadena Consensus Panel. Eur Urol. 2012; 62: 368-81.
10. Lavery HJ, Nabizada-Pace F, Carlucci JR, Brajtbord JS, Samadi DB: Nerve-sparing robotic prostatectomy in preoperatively high-risk patients is safe and efficacious. Urol Oncol. 2012; 30: 26-32.

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