Predictors of Positive Surgical Margins After Laparoscopic Robot Assisted Radical Prostatectomy

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Abbreviations and Acronyms

BMI = body mass index
LRP = laparoscopic radical prostatectomy
PSA = prostate specific antigen
PSM = positive surgical margin
RALP = robot assisted laparoscopic radical prostatectomy
RP = radical prostatectomy
RRP = radical retropubic prostatectomy
TRUS = transrectal ultrasound

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Purpose: We identified the predictors of positive surgical margins in a series of patients undergoing robot assisted laparoscopic radical prostatectomy.

Materials and Methods: We prospectively collected data from 322 patients who underwent robot assisted laparoscopic radical prostatectomy for clinically localized prostate cancer between April 2005 and October 2008, and who had not received any prior hormonal therapy.

Results: Positive surgical margins were observed in 95 cases (29.5%). Specifically positive surgical margins were at the apex in 22 cases (6.8%), anterior in 5 (1.6%) and posterolateral in 68 (21%). Among the preoperative variables prostate volume on transrectal ultrasound (HR 0.420, p = 0.002) and cT stage (HR 2.217, p = 0.008) were independent predictors of the presence of any positive surgical margin in the cohort while cT stage (HR 2.070, p = 0.025) and biopsy Gleason score (p = 0.019) were predictors of posterolateral positive surgical margins. Considering pathological variables only extraprostatic extension of the primary tumor was an independent predictor of any positive surgical margin (HR 11.852, p <0.001) and posterolateral positive surgical margins (HR 7.484, p <0.001) in the series. Of those patients with organ confined disease positive surgical margins were present in 21 (10.6%). Only perineural invasion was an independent predictor of any positive surgical margin (HR 4.096, p = 0.028) while a not statistically significant trend was identified with regard to posterolateral positive surgical margins (HR 6.938, p = 0.067).

Conclusions: Pathological extension of the primary tumor was the most relevant predictor of positive surgical margins. In patients with organ confined disease the presence of perineural invasion was significantly associated with positive surgical margins.

Key Words: prostatic neoplasms, prostatectomy, robotics, neoplasm, residual

In RP specimens the presence of tumor cells at the inked margin may indicate incomplete cancer clearance in a high percentage of cases and PSMs are generally considered an adverse outcome in cases treated with RP. In most surgical series PSMs are an independent predictor of biochemical recurrence and local disease recurrence as well as the need for secondary cancer treatment. However, to our knowledge the impact of PSMs on more robust clinical end points such as metastatic progression or cancer specific survival has yet to be reported.[1] Nonetheless given the fact that long-term oncological followup for pure LRP and RALP is still un-

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available, the PSM rate has been considered an important early outcome in evaluating the oncological safety of new minimally invasive techniques.

In the most important and recent surgical series reporting data on margin status, PSM rates ranged from 11% to 37% after RRP, from 11% to 30% after LRP and from 9.6% to 26% after RALP. Moreover the available comparative studies did not show any significant differences among the various techniques.[2]

Surgical factors such as type of procedure, technique, surgeon volume and experience could have a more relevant impact on PSMs from iatrogenic capsular incision in organ confined tumors. In contrast, PSMs associated with extraprostatic extension of high grade tumors are more probably an expression of aggressive tumor biology. Moreover data from RRPs have demonstrated that the effect on biochemical disease-free survival was highly influenced by specific positive margin location, with the posterolateral site conferring the greatest probability of relapse.[3] However, little information is available regarding the predictors of this unfavorable PSM location. Currently few studies have evaluated the predictors of PSMs in RALP series.[4,5]

The primary objective of this prospective study was to identify the preoperative, surgical or pathological predictors of PSMs in a recent series of consecutive RALPs. Secondary objectives were the identification of factors predictive of the presence of PSMs in organ confined tumors as well as the presence of posterolateral and multiple PSMs.

MATERIALS AND METHODS

The clinical records of all patients who underwent RALP for clinically localized prostate cancer between April 2005 and October 2008 were prospectively collected in the Prostate Cancer Padua Database. All patients treated with neoadjuvant hormonal therapy before RP were excluded from this study. All procedures were performed by 2 surgeons using the same technique (WA and SC).

Surgical Technique

The ports of the 3-arm robot (da Vinci® Surgical System) and the traditional laparoscopic tools were placed as previously reported.[6,7] The anterolateral surface of the prostate was dissected following intrafascial or interfascial planes,[8] and the lateral pedicles were controlled using monopolar forceps using electrocautery as little as possible and as far as possible from the neurovascular bundles. Specifically in the intrafascial dissection the plane between the prostatic capsula and the thin surrounding periprostatic fascia was developed, while in the interfascial dissection a plane on to the periprostatic fascia was developed.[8] Every attempt was made to preserve the neurovascular bundles in those patients with cT1–cT2a prostate cancer, biopsy Gleason score 7 or less and preoperative International Index of Erectile Function score greater than 26 without significant comorbidities. Vesicourethral anastomosis was performed using a running suture as described by Van Velthoven et al.[9] In patients with an intermediate or high risk of lymph node involvement according to Partin table progression bilateral iliac and obturator lymphadenectomy was performed.[10]

Pathological Analysis of Specimens

The prostate specimen was formalin fixed in the standard manner. The whole mount sections were identified consecutively with capital letters, always starting from the section closest to the apex, making the whole specimen available for histological examination. The en face section was then processed as a single section. In particular, the paraffin embedded specimen was examined histologically in the form of 4 mm, whole mount, hematoxylin and eosin stained sections. A PSM was defined as the presence of tumor at the inked margin.

Clinical and Pathological Parameters

Every patient was evaluated for the parameters of age at diagnosis, comorbidity according to Charlson score,[11] BMI, preoperative total PSA, prostate volume estimate on preoperative TRUS, biopsy Gleason score, clinical stage according to the 2002 TNM system,[12] nerve sparing technique, prostate volume in the prostatectomy specimen, Gleason score in the prostatectomy specimen, focal or extensive capsular invasion, perineural invasion in the prostatectomy specimen, endovascular invasion in the prostatectomy specimen and pathological extension of the primary tumor according to the 2002 TNM system. Institutional review board approval is not usually needed in Italy for nonexperimental studies such as this one. However, all the patients signed an informed consent form authorizing data collection for scientific purposes.

Statistical Analysis

Mean and standard deviation were used to report continuous normally distributed variables, while median and IQR were used for the nonnormally distributed variables. The Pearson chi-square test was used to compare categorical variables and logistic regression was used to perform multivariate analysis. The Kaplan-Meier method was used to calculate survival functions and differences were assessed with the log rank statistic. A 2-sided $p < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS® v. 16.0.

RESULTS

During the study 341 consecutive RALPs were performed. A total of 19 patients (5.6%) were excluded from study because they had received neoadjuvant hormonal therapy before surgery. Table 1 summarizes the main characteristics of the 322 evaluated patients.

Mean patient age was 61.4 ± 6.6 years. Mean prostate volume was 42 ± 20.5 cc at preoperative TRUS while mean weight of prostate in the prostatectomy specimen was 40.9 ± 21.5 gm. Overall PSMs were observed in 95 cases (29.5%). Specifically PSMs were at the apex in 22 cases (6.8%), anterior