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Communication

Predictor Factors for the Detection of Positive Nodes in Patients Undergoing Radical Prostatectomy and Lymph Node Dissection

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Abstract: Background: The detection of positive lymph nodes after a lymph node dissection changes the clinical prognosis; therefore, we evaluated what factors help us predict the presence of positive lymph nodes. Methods: A retrospective analysis of all radical prostatectomies and extended lymph node dissection performed from January 2010 to October 2018 in our centre was conducted. The variables included in the Briganti nomogram (preoperative PSA, Gleason biopsy, percentage of cores, and clinical stage) were considered, as well as perineural invasion and involvement of the seminal vesicles in the prostate biopsy; Results: A total of 110 lymph node dissections are obtained. Patient mean age is 64.18 years (46.55–75.91). Of the 110 lymphadenectomies performed, 16 patients (14.5%) presented positive nodes. Presenting infiltrated seminal vesicles, perineural invasion, higher PSA, higher clinical stage, higher Gleason biopsy and percentage of cores is more likely to have statistically significant lymph node involvement ($p < 0.05$). In the multivariate analysis, the percentage of positive core, together with the involvement of the seminal vesicles and Gleason ≥ 4 in the majority are predictor factors for positive nodes ($p < 0.01$); Conclusions: The percentage of positive cores, the involvement of the seminal vesicles, and the majority Gleason ≥ 4 are independent predictors of lymph node involvement in prostate cancer.

Keywords: lymphadenectomy; prostate cancer; lymph nodes

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1. Introduction

Currently, extended pelvic lymph node dissection (ePLND) is recommended when there is a risk of lymph node involvement in prostate cancer [1]. The risk of lymph node involvement can be calculated with various nomograms; the latest ones have included the results of multiparametric magnetic resonance imaging (MRI) [2–4].

There are discrepancies between the oncological results of ePLND. In a systematic review, no improvement in oncological outcomes was found [5], but other studies have shown an oncological benefit, especially when it is ePLND rather than limited PLND [6,7]. However, adequate lymph node staging is recognized by all authors.

Patients with prostate cancer and who are lymph node-positive have a higher risk of biochemical recurrence and worse oncological outcomes [8,9]. For this reason, it is important to know which patients will benefit from ePLND and what its predictive factors are.

2. Results

A total of 110 radical prostatectomies with ePLND were obtained from January 2010 to October 2018. The mean age of the patients at the time of the intervention was 64.18 years (46.55–75.91) and the preoperative PSA was 10.5 ng/mL (1.25–47.20). The approach to the interventions was laparoscopic, except in 19 (19.71%) cases where it was an open approach. 94 of the 110 (85.5%) ePLND did not detect positive nodes, and 16 were positive (14.5%). The clinical characteristics of the patients are listed in Table 1.

Table 1. Clinical and pathological characteristics.

Characteristic	Patients with pN0 (N = 94)	Patients with pN1 (N = 16)	*p*
PSA preoperative (ng/mL)	9.81 (2.16–47.2)	12.61 (1.25–38.40)	0.075
Age surgery (years)	64.19 (46.55–75.91)	64.11 (50.95–75.83)	0.96
Prostate volume (mL)	40.15 (14–116)	34.09 (20–60)	0.52
Biopsy GLEASON score			
3 + 3	8 (8.5%)	1 (6.25%)	0.003
3 + 4	35 (37.23%)	2 (12.5%)	
4 + 3	28 (29.78%)	3 (18.75%)	
4 + 4	18 (19.14%)	4 (25%)	
4 + 5	4 (4.25%)	5 (31.25%)	
Positive cores (%)	44.90 (6.25–100)	64.92 (25–100)	0.004
Clinical T stage			
cT1	38 (40.42%)	2 (12.5%)	0.000
cT2	44 (46.8%)	6 (37.5%)	
cT3	7 (7.4%)	8 (50%)	
Maximum core affectation (mm)	11.16 (0–29)	16 (5–30)	0.083
Perineural invasion in prostate biopsy			
YES	59	15 (93.75)	0.02
NO	32	1 (6.25)	
Seminal vesicles invasion in prostate biopsy			
NO	90 (95.75%)	11 (68.75%)	0.000
YES	4 (4.25%)	5 (31.25%)	

After surgery, the pathological characteristics of the patients were analyzed and are listed in Table 2. The median follow-up was 27.7 months (6–106). 21.8% (24 patients) presented biochemical recurrence (BCR), with a mean time to recurrence of 34.35 months (2.67–95.40). Of the 24 patients, 19 (79.16%) presented negative lymph node invasion and 5 (20.83) positive lymph node invasion. No statistically significant relationship was shown between the presence of positive lymph node involvement and biochemical recurrence.

Table 2. Pathological characteristic after lymph node dissection.

Characteristic	Patients with pN0 (N = 94)	Patients with pN1 (N = 16)	*p*
Briganti score	106.78 (43–227)	172.74 (106–251)	0.00
Lymph nodes removed	20.93 (9–55)	21.81 (8–38)	0.7
Positive lymph nodes	0	3.75 (1–22)	–
Pathological Gleason score			
3 + 3	3	0	0.01
3 + 4	43	1	
4 + 3	29	4	
4 + 4	10	4	
4 + 5	7	6	
Pathological stage T			
pT2	40	0	0.00
pT3a	43	4	
pT3b	11	11	
pT4	0	1	
Surgical margin			
Negative	54	6	0.17
Positive	39	10	

When performing the univariate analysis, the clinical stage, the perineural invasion, the involvement of the seminal vesicles, the Gleason score in the biopsy, and the percentage of affected cores present a higher probability of lymph node involvement with statistical significance ($p < 0.05$). In the multivariate analysis, the percentage of positive core, together with the involvement of the seminal vesicles and Gleason ≥ 4 in the majority are predictor factors for positive nodes ($p < 0.01$) (Table 3). The presence of $\geq$35% percentage of affected cores is related to lymph node involvement with a sensitivity of 75% and a specificity of 60%.

Table 3. Univariate and multivariate analysis.

Variable	Comparison	Univariate *p*	OR	CI 95%	Multivariate *p*
Biopsy Gleason score	≥4/<4	0.00	3.44	0.911–12.99	0.01
Positive cores (%)	≥35%/<35%	0.00	1.964	0.587–6.56	0.05
Seminal vesicles invasion in prostate biopsy	Yes/No	0.00	22.63	6.203–82.61	0.00

3. Discussion

EPLND is recommended in prostate cancer, especially in high-risk cases. The decision to perform ePLND is recommended when there is a 5% risk of lymph node involvement in the different available nomograms [3,4,9–13]. There are several nomograms to predict lymph node invasion: the Briganti nomogram, the Roach formula, or the Partin and MSKCC nomograms. A risk of lymph node invasion above 5% recommends the performance of ePLND [7–9].

In the current scientific literature, there are different works that note the positive oncological results and survival rates. However, other studies differ from these results [10–13].

For adequate staging, it is recommended to obtain at least 20 nodes during ePLND to perform adequate lymph node staging [3,14–16]. The new update of the nomograms incorporating multiparametric magnetic resonance (MRI) has managed to increase external validation; however, it is an operator-dependent technique [2]. The detection of positive nodes in prostate cancer modifies the prognosis. Although the value of the final oncological results is not clear, there is a consensus on the importance of the pathological staging that it provides, as well as the clinical information [1,5,6,9,17].

There are controversies regarding the repercussion of lymph node dissection in prostate cancer, although the data do show that it should be extended, in addition to the fact that the nomograms have provided insight into which patients will benefit from lymph node dissection. The items analyzed in the nomogram are PSA, percentage of affected core, Gleason, and clinical stage; in addition, the latest version has incorporated the data from the MRI [2].

Some authors have highlighted that a higher percentage of positive cores and a higher Gleason are directly related to a higher risk of BCR [18,19]. Likewise, the presence of positive nodes has been directly related to BRC in localized prostate cancer [8,20]. Therefore, many prognostic factors for lymph node invasion will be related to BCR. In our work, in addition to recognizing the items of the Briganti nomogram as factors of lymph node invasion, the presence of a higher percentage of cores as well as a higher Gleason score are independent risk factors for lymph node invasion. Though there are articles like this paper, they are primarily based on the validation of current nomograms. In this study, we wanted to refer to certain factors that, in isolation, can be defining factors for the performance of ePLND, such as the percentage of cores in the prostate biopsy. There is a paper that also marks the importance of the percentage of cores in the prostate biopsy [1]; this example is based on the fact that a more aggressive cancer with a greater tumor load can cause micrometastases that are not detected in the available imaging tests and are later detected as tumor progression [14,20].

This scenario justifies the position of some authors who have highlighted the benefit of lymph node dissection at the level of oncological results; thus, when lymph node

involvement is $\leq$2 and PSA < 0.1 ng/mL, one option is observation without the need to start treatment with antiandrogen therapy [1,6,7,9]. These scenarios open to the hypotheses of a scenario whereby localized prostate cancer with lymph node involvement can be cured, thanks to the performance of an ePLND and the impact of the predictive factors for its detection.

Among the limitations of our study, we note that it is a retrospective study in a single center with a limited population and a short follow-up time (27.7 months) compared to other studies and the need to follow-up with an analysis of overall survival.

4. Materials and Methods

Retrospectively, 110 patients who underwent radical prostatectomy and ePLND from January 2010 to October 2018 in our center have been analyzed. The variables analyzed are age, preoperative PSA, prostate volume, clinical stage, Gleason of prostate biopsy, Gleason of surgical specimen, percentage of affected cores in prostate biopsy, maximum core involvement, perineural invasion in prostate biopsy, involvement of vesicles in biopsy and surgical specimen, surgical margins, number of lymph nodes extracted, number of positive nodes, and subsequent biochemical recurrence. Biochemical recurrence was defined as PSA $\geq$ 0.2 ng/mL and confirmed with subsequent analysis.

Lymph node dissection was performed in patients who presented a $\geq$5% risk of lymph node involvement in the Briganti nomogram or 7% in the updated nomogram with MRI.

The surgical limits for performing ePLND were superior: bifurcation of common iliac artery; inferior: femoral canal to pelvic side wall; posterior: obturator and internal iliac vessels.

Surgical interventions were performed by two experienced urologists (>25 lymph node dissection per urologist). The anatomopathological analysis was performed by two different pathologists.

Data are expressed as means and range. The statistical tests used are Chi-square and t-student distribution. A logistic regression analysis was used for the multivariate analysis of the predictive factors of lymph node involvement. We are aware that there are not many events, but the factors that favor the presence of lymph node invasion have a high statistical power. A step by step process has been followed using a forward procedure. The AUC for the Briganti nomogram in our population is 0.878. The statistical program used has been SPSS v. 2.0.

5. Conclusions

The percentage of positive cores ($\geq$35%), the involvement of the seminal vesicles and the majority Gleason $\geq$ 4 are independent predictors of lymph node involvement in prostate cancer.

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