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UNFAVORABLE CLINICOPATHOLOGICAL FEATURES IN RADICAL PROSTATECTOMY PATIENTS WHO WERE SPARED PELVIC LYMPHADENECTOMY

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SUMMARY – Pelvic lymph node dissection (PLND) during radical prostatectomy (RP) is the most accurate staging modality for lymph node assessment in patients with prostate cancer. It is recommended in all patients with intermediate or high-risk disease undergoing radical prostatectomy. The goal of our study was to assess unfavorable clinicopathological characteristics in patients with omitted lymphadenectomy (PLND) during radical prostatectomy based on the nomogram proposed by Briganti and colleagues. In 2011, 200 patients undertook radical prostatectomy in our institution. Among them 53 patients who fulfilled Briganti criteria and in whom we omitted lymphadenectomy based on current guidelines. Unfavorable clinicopathological features considered were: stage T3, positive surgical margins or biochemical relapse (BCR). We registered biopsy Gleason score 6 in 34 patients, and 19 patients had Gleason score 7. Stage pT2 was seen in 49 patients, and pT3 in 4. Gleason score after radical prostatectomy was upgraded from GS 6 to GS 7 in 20 patients (37%) and reduced in 1 patient (2%). After a median follow-up of 49 (44-56) months, there were 12 (22.6%) patients with BCR. Patients with biopsy Gleason score 6 (n=34) compared to biopsy Gleason 7 (n=19) patients showed no difference regarding positive margins (p=0.0738) and BCR (p=0,736) at 49 months follow-up. Thus, PLND according to current guidelines can be safely omitted in low-risk patients using Brigantinomogram.

Key words: *Radical prostatectomy (RP); Pelvic lymph node dissection (PLND); Brigantinomogram; Adverse clinicopathological features*

Introduction and objectives

Pelvic nodal involvement in prostate cancer (PCa) patients can only be precisely detected even in the modern era by pelvic lymphadenectomy (PLND)[1]. The goal of our study was to assess unfavorable clinicopathological characteristics in patients with omitted lymphadenectomy (PLND) during radical prostatectomy. Grounded on the Briganti nomogram, initially reported in 2006 and updated later in 2007 and 2012, the PLND may be safely neglected. in patients with a lymph node invasion (LNI) risk < 5% This matches the total Briganti score of 90 points, giving a negative predictive value of 98.6%[2,3].

Materials and methods

From the beginning to the end of 2011, 200 patients undertook radical prostatectomy in our institution. In this cohort 53 patients had a risk of nodal involvement < 5% and according to Briganti could safely be spared pelvic lymphadenectomy (Table 1). We evaluated the proportion of patients with omitted

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Table 1. Descriptive statistics of study cohort (N=53).

	MEAN	SD	MEDIAN	MIN	MAX
AGE (yr)	65	5.03	65	54	76
PSA (ng/ml)	6.32	1.89	6	2.80	9.95
#Cores	10.07	1.05	10	6	12
#Positive cores	2.28	1.44	2	1	6
%Cancer	27.65	21.59	22.50	5	80
Biopsy GS	6.35	0.48	6	6	7
Follow up	48.91	3.28	47.45	45	55

Table 2. Descriptive statistics of Gleason score 6 patients (N=34).

	MEAN	SD	MEDIAN	MIN	MAX
AGE (yr)	65.52	4.51	66.50	58	75
PSA (ng/ml)	6.23	1.81	5.85	3.10	9.95
#Cores	10.11	1.29	10	6	12
#Positive cores	2.29	1.42	3	1	5
%Cancer	18.25	15.20	10	5	50
Briganti score	31.86	13.45	28	45	58
Follow up	48.58	3.08	48	45	55

Table 3. Descriptive statistics of Gleason score 7 patients (N=19).

	MEAN	SD	MEDIAN	MIN	MAX
AGE (yr)	64.05	5.85	64	54	76
PSA (ng/ml)	6.50	2.05	6.10	2.80	9.90
#Cores	10	0	10	10	10
#Positive cores	2.30	1.49	2	1	6
%Cancer	2.30	1.49	50	1	6
Briganti score	60.50	24.21	46	28	90
Follow up	49.47	3.64	50	45	55

Table 4. Comparison of GS 6 vs GS 7 patients with respect to adverse findings and Briganti score.

	GS 6	GS 7	p value
Positive margins	10	1	0.0738
T3NxMx	2	2	0.6117
BCR	7	5	0.736
Follow up (months)	48.58	49.47	0.355
Briganti score	31.8	60.5	<0.0001

lymphadenectomy and their unfavorable clinicopathological features using pathology reports hospital records, and operative protocols. Unfavorable clinicopathological features were T3 stage of disease, positive surgical margins or biochemical relapse. Data were described as frequency tables. T-test was used for numerical variables that follow normal distribution, and Mann Whitney was used for data that do not follow normal distribution. Distribution of data was tested using Kolgomorov-Smirnov's test. Analysis was performed using StatView 5.0 (SAS Institute Inc, Cary, NC, USA). P value considered statistically significant was <0.05%.

Results

From the beginning to the end of 2011, 200 patients undertook radical prostatectomy. In 53 of them lymphadenectomy was neglected in line with the Eu-

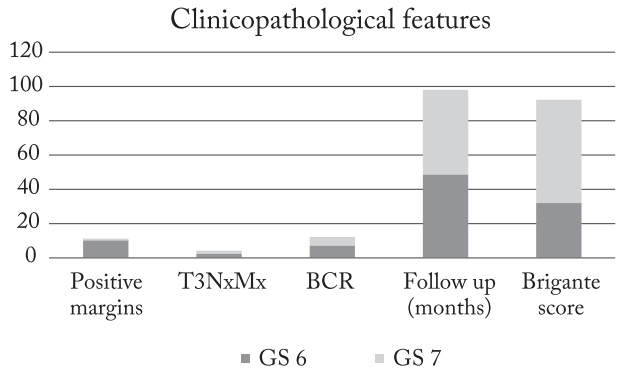

Figure 1.Frequency of adverse clinicopathological findings in GS 6 vs GS 7 patients.

ropean association of urology guidelines. Patients with neglected lymphadenectomy were 65.03±5.03 (54-76) years old, with mean PSA of 6.32±1.88 (2.8-9.95) ng/mL. The overall number of biopsy cores acquired was 10.07±1.05 (6-12), with mean positive biopsy cores of 2.28±1.44 (1-6) and mean maximum percent cancer in a single core of 27.65±21.58 (5-80) %. Out of the 53 patients, 34 patients had biopsy Gleason score 6 (Table 2), while 19 had Gleason score 7 (Table 3). Mean biopsy Gleason score was 6.36±0.48 (6-7). pT2 stage disease was found in 49 patients following radical prostatectomy, and 4 patients had pT3 stage disease. Gleason score in radical prostatectomy specimen was promoted from GS 6 to GS 7 in 20 patients (37%) and downgrade was seen in only 1 patient (2%). 11 (20%) patients had positive surgical margins. Biochemical relapse (BCR) was found in 12 (22.6%) patients after the median follow-up of 49 (44-56) months (Table 4). Biopsy Gleason score 6 patients (n=34) compared to the group with biopsy Gleason 7 (n=19) showed no difference regarding positive margins (p=0.0738) and BCR (p=0,736) after 49 months of follow-up (Figure 1).

Discussion

Pelvic lymph node dissection (PLND) during radical prostatectomy (RP) is the most accurate staging modality for lymph node assessment in patients with prostate cancer[1]. It is recommended in all patients with intermediate or high-risk disease undergoing radical prostatectomy. Several studies have tried to predict LNI in patients with localized prostate cancer using preoperative variables[2,3,4,5]. Godoy *et al.*[4] appraised their nomogram to contain only patients who had undertaken extended PLND and improved calibration with high discriminative accuracy. Briganti *et al.*[5] presented that biopsy pathology report data, such as the percentage of positive biopsy cores, enhanced the ability to predict nodal involvement when integrated in their nomogram. The updated Briganti nomogram was also validated by different European authors and showed good accuracy[2]. Nevertheless nomograms can safely be used only if the patients closely resemble the population from which the nomogram was originated. Whether the predictive model is appropriate to any patient population is still a matter of debate, as different patient characteristics may weaken the accuracy of a nomogram[6,7]. In the recent years a significant decline in the use of PLND has been observed[9]. Numerous reasons to explain this feature have been contemplated. Some considered increased use of robotic techniques in RP to be responsible for this trend; although both technical viability and safety of the procedure have been shown in recent studies[10,11], PLND was not usually performed in the early propagation of robotic RP. In addition, there is lack of evidence of an absolute therapeutic benefit of PLND, in patients with LN metastases[12-14]. Recent meta-analysis by Fossaty *et al.* systematically reviewed 66 studies including a total of 275,269 patients (44 full-text articles and 22 conference abstracts)[15]. The review showed a high risk of bias and confounding in most studies. Conflicting results appeared when biochemical and clinical recurrence was compared, while no significant survival differences were observed among groups. The majority of studies showed that the more extensive the PLND was accompanied by higher rate of complications. Unfavorable outcomes in terms of operating time, blood loss, length of stay, and postoperative complications were noted. Functional outcomes such as urinary continence and erectile function recovery were not significantly different. A low rate of LN metastases because of a stage migration may have also added to such a conclusion. Nevertheless, as the final judgement has not been reached it is necessary to estimate the risk of LN metastases. It would be against oncological principles to randomly skip PLND. The present study has its' limitations. The study is not a multi-institutional study, thus the study population may not resemble general population. Also, this is a retrospective study and the Briganti nomogram was not used by all surgeons. In this study, we wanted to make a single insti-

tution validation of current guidelines and we showed that in low-risk patients PLND can be safely omitted using the Briganti nomogram, but we suggest a close follow-up of all patients.

Conclusion

While patients with omitted lymphadenectomy according to EAU recommendations are thought to have favorable risk disease, they may still have adverse pathologic findings. Despite being the most precise staging procedure, PLND is associated with worse intraoperative and perioperative outcomes, while a direct therapeutic effect are still debatable. The presence of pathologically unfavorable disease in patients appropriate for omitting lymphadenectomy suggests the need for close follow-up. In the face of these conflicting findings,the EAU Prostate Cancer Guideline Panel suggests that, due to its recognized staging benefits, ePLNDshould be undertaken using a risk-stratified approach (15).

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Sažetak

NEPOVOLJNE KLINIČKO-PATOLOŠKE ZNAČAJKE U BOLESNIKA S IZOSTAVLJENOM LIMFADENEKTOMIJOM TIJEKOM RADIKALNE PROSTATEKTOMIJE

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Zdjelična limfadenektomija u vrijeme radikalne prostatektomije (RP) trenutno je najpouzdaniji način otkrivanja metastaza u limfne čvorove u bolesnika s rakom prostate. Cilj našeg istraživanja bio je procijeniti nepovoljne kliničko-patološke značajke u bolesnika s izostavljenom limfadenektomijom tijekom radikalne prostatektomije temeljene na Briganteovom nomogramu. U 2011. godini, u našoj je ustanovi 200 bolesnika podvrgnuto radikalnoj prostatektomiji. Identificirali smo 53 bolesnika koji su ispunili Brigantijeve kriterije te su prema aktualnim smjernicama bili pošteđeni zdjelične limfadenektomije. Nepovoljnim kliničko-patološkim značajkama smatralo se bilježenje stadija T3 bolesti, pozitivni kirurški rubovi ili biokemijski relaps. Na patohistološkom (PH) nalazu biopsije Gleason zbroj 6 verificiran je u 34 pacijenta, a 19 je pacijenata imalo Gleason zbroj 7. Na konačnom PH nalazu nakon učinjene radikalne prostatektomije 49 bolesnika je imalo pT2 stadiji bolesti, a 4 su bolesnika imala pT3. Konačni Gleason zbroj nakon radikalne prostatektomije povećan je u 20 bolesnika na GS 7 (37%) i smanjen kod jednog bolesnika (2%). Nakon srednjeg praćenja od 49 (44-56) mjeseci, bilo je 12 (22,6%) bolesnika s biokemijskim relapsom (BR). Usporedba bolesnika s biopsijskim nalazom Gleason zbroja 6 (n = 34) i bolesnika s Gleason zbrojem7 (n = 19) nije pokazala značajnu razliku u odnosu na pozitivne kirurške rubove (p = 0,0738) i BR (p = 0,736) nakon 49 mjeseci praćenja. Stoga se zdjelična limfadenektomija prema aktualnim smjernicama može sigurno izostaviti u bolesnika s procijenjenim niskim rizikom koristeći Briganteov nomogram.

Ključne riječi: *Radikalna prostatektomija (RP); Zdjelična limfadenektomija; Briganteov nomogram; Nepovoljne kliničko-patološke značajke*