



EAU RISK GROUPS APPLIED ON PATIENTS TREATED WITH RADICAL PROSTATECTOMY - ANALYSIS OF PATHOLOGY SPECIMENS AND PATIENT SURVIVAL

Boyan Lazarov,

Clinic of Urology, Department of Surgery, Faculty of Medicine, MHAT "Sveta Anna-Varna", Medical University-Varna, Bulgaria.

ABSTRACT

Purpose: The European Association of Urology (EAU) classifies patients with prostate cancer into three risk groups - low-risk, intermediate- and high-risk depending on the probability of biochemical progression after treatment with curative intent (either radical prostatectomy or radiotherapy). The aim of the present study is to analyze our experience with patients who underwent radical prostatectomy and to look for the relationship between the pathological results from the operation and the distribution of patients into risk groups.

Material/Methods: A single-center, non-interventional study was conducted. The study was performed after analysis of patients undergoing radical prostatectomy (either open or laparoscopic) at the Clinic of Urology in St. Anna Hospital in Varna. The number of patients available for analysis was 201. Data were analyzed with IBM SPSS version 23.

Results: We found that high-risk patients had unfavorable results from the examination of the pathology specimens- patients with pT3a and pT3b were more often from the high-risk group. High-risk patients were also at increased risk of PSA progression and development of distant metastases.

Conclusions: The EAU-risk groups will probably undergo changes connected with the improved methods for the diagnosis of prostate cancer. But still, it is a valid tool which correctly predicts the unfavorable pathology of the removed specimen and also the risk of biochemical progression after radical prostatectomy.

Keywords: Overall survival, PSA-progression, lymph node metastases, extraprostatic extension, seminal vesicle involvement,

INTRODUCTION

The introduction of prostate-specific antigen (PSA) revolutionized the diagnostics and treatment of prostate cancer (PCa) [1]. It enabled much earlier diagnosis [2] and gave urologists a tool with which to follow the patients after treatment. After radical prostatectomy (RP) and radiotherapy, PSA progression (the so-called biochemical recurrence) is one of the key events that determine the effect of the treatment. Depending on the risk of biochemical recurrence after RP and radiotherapy the European Association of Urology (EAU) distributes patients with PCa into three risk groups - low-risk, intermediate- and high-risk. In Bulgaria, this classification is applied relatively rarely. Therefore, the aim of the present study was to analyze our experience with patients who underwent RP and to look for a relationship between the pathological results of the operation and the distribution of patients into risk groups.

MATERIAL AND METHOD

A single-center, non-interventional study was conducted. The study was performed after analysis of patients undergoing radical prostatectomy (either open or laparoscopic) at the Clinic of Urology in St. Anna Hospital in Varna. 468 prostatectomies were performed in the clinic for the period from January 2013 to May 2021. Data about overall survival, survival without biochemical progression, and the time to occurrence of metastases of patients in our sample were obtained from the registers of the oncology center "Marko Markov", Varna.

During the preliminary processing of the data, it was found that in a large number of cases until 2018, there was no information about Gleason's score from a prostate biopsy and/or prostatectomy; sometimes, even PSA was missing. Also, patients with preoperative hormonal therapy were excluded. As a result, the final number of patients available for analysis was 201.

Data were analyzed with IBM SPSS version 23. The frequencies of the category variables were compared by nonparametric tests (Pearson's χ^2). Correlation analysis was applied to determine the strength and direction of the dependencies (Spearman's Rho correlation coefficient for rank variables). The tests were performed at a significance level $\alpha = 0.05$ or $p < 0.05$.

RESULTS

The preoperative characteristics of the patients are shown in table 1. The low-risk group is named group 1, the intermediate-risk is group 2 and the high-risk - group is group 3.

Table 1. Preoperative characteristics of the patients

		EAU risk group 1	EAU risk group 2	EAU risk group 3
Age years, mean		66.5	67.6	67.9
PSA ng/ml, mean		7.4	11.7	28.8
Prostate volume ml.		70.97	61.35	65.86
PSA density		0.12	0.23	0.48
DRE – palpable node Patients/total patients		4/38 (10.53%)	15/89 (16.85%)	16/74 (21.62%)
ISUP-grade from biopsy	1	38	33	9
	2		44	18
	3		12	5
	4			25
	5			17
ISUP-grade from RP	1	23	45	22
	2	11	18	20
	3	1	10	3
	4	2	9	13
	5	1	7	16

*DRE-digital rectal examination

EAU risk groups showed a correlation with the following postoperative pathological characteristics. With seminal vesicles involvement (stage pT3b), there were 32 (15,9%) patients. Their distribution by EAU risk groups is shown in table 2.

Table 2. Patient with seminal vesicle involvement

			Seminal vesicle involvement (pT3b)		Total
			No	Yes	
EAU risk groups	1 group	Patients (%)	36 (94,7%)	2 (5,3%)	38 (100,0%)
	2 group	Patients (%)	81 (91,0%)	8 (9,0%)	89 (100,0%)
	3 group	Patients (%)	52 (70,3%)	22 (29,7%)	74 (100,0%)
Total			169 (84,1%)	32 (15,9%)	201 (100,0%)

A statistically significant relationship was found between the risk groups and the presence of pT3b - seminal vesicles involvement ($X^2 = 16,961$; $p = ,000$) – with a weak positive correlation ($r_{(sp)} = ,268$; $p = ,000$). That is, patients with pT3b were more often from the high-risk group.

With lymph node metastases (pN1) were 11 (5,5%) patients. Their distribution by EAU risk groups is shown in table 3.

Table 3. Patients with lymph node metastases

			Lymph node metastases (pN1)		Total
			No	Yes	
EAU risk groups	1 group	Patients (%)	36 (94,7%)	2 (5,3%)	38 (100,0%)
	2 group	Patients (%)	87 (97,8%)	2 (2,2%)	89 (100,0%)
	3 group	Patients (%)	67 (90,5%)	7 (9,5%)	74 (100,0%)
Total			190 (94,5%)	11 (5,5%)	201 (100,0%)

No statistically significant association was found between the EAU risk groups and the presence of lymph node metastases ($X^2 = 4,164$; $p = 1,25$).

With extraprostatic tumor extension (stage pT3a) were 57 (28,4%) patients. Their distribution by EAU risk groups is shown in table 4.

Table 4. Patients with extraprostatic tumor extension

			Extraprostatic tumor extension (pT3a)		Total
			No	Yes	
EAU risk groups	1 group	Patients (%)	34 (89,5%)	4 (10,5%)	38 (100,0%)
	2 group	Patients (%)	64 (71,9%)	25 (28,1%)	89 (100,0%)
	3 group	Patients (%)	46 (62,2%)	28 (37,8%)	74 (100,0%)
Total			144 (71,6%)	57 (28,4%)	201 (100,0%)

A statistically significant relationship was found between the risk groups and the presence of pT3a -extraprostatic tumor extension ($X^2 = 9,224$; $p = 0,10$) - with weak positive correlation (r (Spearman) =, 211; $p = 0,003$). That is, patients with pT3a were more often from the high-risk group.

The postoperative follow-up of the patients is shown in table 5. Some patients were missing, which is why the total number here (129 men) is smaller than in the previous tables.

Table 5. Survival of the patients

	EAU risk group 1	EAU risk group 2	EAU risk group 3
Overall survival: survivors/all patients	20/24 (83.33%)	56/58 (96.55%)	38/47 (80.85%)
Time to death (mean months)	27.5	55.5	38.6
PSA-progression: patients with progression/all patients	10/24 (41.67%)	20/58 (34.48%)	25/47 (53.19%)
Time to progression (mean months)	13.6	7.8	9.5
Patient with metastasis/all patients	1/24 (4.17%)	2/58 (3.45%)	6/47 (12.77%)
Time to metastasis (mean months)	20	28	14.7
All patients available for follow-up 129	24	58	47

DISCUSSION

Overall survival is the most important indicator when discussing the treatment and the prognosis of patients with tumors. But for PCa, overall survival can be very long (at least 10-15 years for men after RP) [3], and it is more convenient to examine the progression-free sur-

vival, determined by the increase of PSA at a certain point. The EAU risk groups present the risk of biochemical progression after treatment with curative intent – either RP or radiotherapy. They are based on D'Amico's classification [4], published in 2005. Here, the probability of PSA recurrence after the treatment is calculated using the fol-

lowing parameters – PSA, Gleason score, clinical T-stage. The classification has been externally validated [5-8] and is now widely accepted – the guidelines of the EAU also recommend it. But the system itself is far from perfect. First, the Gleason score used in it is taken from the biopsy, and it is well-known that the Gleason score from the RP differs quite often [9]. Second, the T-stage is determined with rectal examination. If a different result is found from the biopsy or Magnetic Resonance Imaging (MRI) (for example, a bilateral disease that is palpated unilaterally), it is reported separately. In our days, with the introduction of MRI, Prostate-Specific Membrane Antigen (PSMA) Positron Emission Tomography, Computed Tomography (PET/CT) scan and improved biopsy (e.g., an increasing number of systematic biopsy cores, targeted biopsy), it is not unthinkable that changes in this classification are eminent [10].

We analyzed patients treated with RP in our clinic [11]. The aim was to find if high-risk patients also have unfavorable results from the examination of the pathology specimens. This eventually would transfer into earlier PSA recurrence after RP [12]. From the preoperative characteristics of the patients, an interesting result is the size of the prostate in the low-risk group – here, the prostate is the biggest. PSA density increases from group 1 to 3. A well-known fact is that the higher the PSA density is, the more likely it is that the PCa is clinically significant [13]. Also higher is the probability of having a palpable nodule in the prostate in the high-risk group. It is worth mentioning that 15 patients from the low-risk group also have ISUP-upgrade after RP stage 2 (11 patients), stage 3 (1 patient), stage 4 (2 patients), and stage 5 (1 pa-

tient). In 6 patients, the biopsy proved that the PCa is found actually in both lobes. For the intermediate-risk group of 12 patients, the biopsy proved that the PCa is found in both lobes.

The statistical analysis proved that patients with pT3a and pT3b were more often from the high-risk group. No statistically significant association was found between the EAU-risk groups and the presence of lymph node metastases. This is probably connected with our only 11 (5,5%) patients (out of 201) with positive lymph nodes. Patients preparing for RP are selected in advance, and those with a high risk of lymphatic metastases often do not undergo surgery but are treated with other methods.

The postoperative follow-up of the patients confirmed that high-risk patients are at increased risk of PSA progression. Biochemical progression is found in 41.67% of the patients from the low-risk group compared to 53.19% of the high-risk group. The risk for the development of metastases also increases. Much more complicated is the analysis of the results of overall survival – already explained why.

CONCLUSION

European Association of Urology classifies patients with PCa into three risk groups - low-risk, intermediate and high-risk. We found that high-risk patients have unfavorable results from the examination of the pathology specimens- patients with pT3a and pT3b were more often from the high-risk group. High-risk patients are also at increased risk for PSA progression and the development of distant metastases.

REFERENCES:

1. Petkova L, Ganey T, Stelov T, Evtimov N. Prostate-Specific Antigen PSA: its Role in Diagnosis and Screening of Prostate Cancer *Varna Medical Forum* 2014 Dec;3(2):29-32.
2. Ganey T, Petkova L, Stelov T, Evtimov N. [To screen or not to screen for prostate cancer?] [in Bulgarian] *J Med*. 2012 Aug;367:595-605.
3. Hamdy FC, Donovan JL, Lane JA, Mason M, Metcalfe C, Holding P, et al. 10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer. *N Engl J Med*. 2016 Oct 13;375(15):1415-1424. [PubMed]
4. Cooperberg MR, Pasta DJ, Elkin EP, Litwin MS, Latini DM, Du Chane J, et al. The University of California, San Francisco Cancer of the Prostate Risk Assessment score: a straightforward and reliable preoperative predictor of disease recurrence after radical prostatectomy. *J Urol*. 2005 Jun; 173(6):1938-42. [PubMed]
5. Ishizaki F, Hoque MA, Nishiyama T, Kawasaki T, Kasahara T, Hara N, et al. External validation of the UCSF-CAPRA (University of California, San Francisco, Cancer of the Prostate Risk Assessment) in Japanese patients receiving radical prostatectomy. *Jpn J Clin Oncol*. 2011 Nov;41(11):1259-64. [PubMed]
6. May M, Knoll N, Siegsmond M, Fahlenkamp D, Vogler H, Hoschke B, et al. Validity of the CAPRA score to predict biochemical recurrence-free survival after radical prostatectomy. Results from a european multicenter survey of 1,296 patients. *J Urol*. 2007 Nov;178(5):1957-62. [PubMed]
7. Cooperberg MR, Freedland SJ, Pasta DJ, Elkin EP, Presti JC Jr, Amling CL, et al. Multiinstitutional validation of the UCSF cancer of the prostate risk assessment for prediction of recurrence after radical prostatectomy. *Cancer*. 2006 Nov 15; 107(10):2384-91. [PubMed]
8. Zhao KH, Hernandez DJ, Han M, Humphreys EB, Mangold LA, Partin AW. External validation of University of California, San Francisco, Cancer of the Prostate Risk Assessment score. *Urology*. 2008 Aug;72(2): 396-400. [PubMed]
9. Goel S, Shoag JE, Gross MD, Al Hussein Al Awamlh B, Robinson B, Khani F, et al. Concordance Between Biopsy and Radical Prostatectomy Pathology in the Era of Targeted Biopsy: A Systematic Review and Meta-analysis. *Eur Urol Oncol*. 2020 Feb;3(1):10-20. [PubMed]
10. Ploussard G, Manceau C, Beauval JB, Lesourd M, Almeras C, Gautier JR, et al. Decreased accuracy of the prostate cancer EAU risk group

classification in the era of imaging-guided diagnostic pathway: proposal for a new classification based on MRI-targeted biopsies and early oncologic outcomes after surgery. *World J Urol.* 2020 Oct;38(10):2493-2500. [PubMed]

11. Evtimov N, Ganev T. S002: Urethro – vesicale anastomate after

laparoscopic radical prostate - ectomy single versus continued suture Evtimov. N. department of urology St. Ann. Hospital, Varna Bulgarian. *European Urology Supplements.* 2014 Nov;13(7):e1408. [Crossref]

12. Hinev A, Ganev T, Radical prostatectomy in cases of locally advanced prostatic carcinoma. *Scripta*

scient med. 1997; 29(Suppl 4):57-61.

13. Omri N, Kamil M, Alexander K, Alexander K, Edmond S, Ariel Z, et al. Association between PSA density and pathologically significant prostate cancer: The impact of prostate volume. *Prostate.* 2020 Dec;80(16):1444-1449. [PubMed]

Please cite this article as: Lazarov B. EAU risk groups applied on patients treated with radical prostatectomy - analysis of pathology specimens and patient survival. *J of IMAB.* 2024 Jan-Mar;30(1):5392-5396. [Crossref - <https://doi.org/10.5272/jimab.2024301.5392>]

Received: 26/09/2023; Published online: 28/02/2024



Address for correspondence:

Boyan Lazarov

Multiprofile Hospital for Active Treatment “Sveta Anna-Varna”- Clinic of urology, Department of surgery, Medical University-Varna, 100, Tzar Osvoboditel Blvd., Varna, 9000, Bulgaria

E-mail: boyanlazarov@yahoo.com,