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Original article

DOES HIGH-RISK PROSTATE CANCER HAVE WORSE SURVIVAL AFTER RADICAL PROSTATECTOMY?

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

ABSTRACT

Purpose: We examine if the division of patients into low-, moderate- and high-risk groups also corresponds to different overall and cancer-specific survival after radical prostatectomy.

Materials/Methods: The object of the study were 872 patients who underwent radical prostatectomy in the Clinic of Urology in "St. Anna - Varna" Hospital for the period from April 17, 1996, until November 25, 2022.

Results: Overall and cancer-specific survival are lower in the high-risk group. When we divide the overall survival into two groups - up to and over 5 years after the operation, then low- and moderate-risk groups have better survival only after the fifth year of the operation.

Conclusions: High–risk prostate cancer has very good overall survival within 5 years after radical prostatectomy, which means that an operation is a reasonable option for the treatment of this type of tumor.

Keywords: EAU-risk groups, biochemical progression, Gleason score, ISUP grades,

INTRODUCTION

The European Association of Urology divides patients with prostate cancer (PCa) into low-, moderate- and high-risk according to the probability of biochemical progression after definitive treatment [1]. However, overall survival (OS) and cancer-specific survival (CSS) are more important for patients. We tried to examine if this division of patients into the three aforementioned risk groups also corresponds to different OS and CSS after radical prostatectomy (RP).

MATERIALS AND METHODS

The object of the study were 871 patients who underwent RP in the Clinic of Urology in "St. Anna-Varna" Hospital for the period from April 17, 1996, until November 25, 2022. Postoperatively, the patients were followed in Oncology Hospital "Marko Markov - Varna," from where data about OS and CSS were obtained. The low- and moderate-risk groups were combined into a control group, which was compared with the high-risk group.

RESULTS

The high-risk group included 491 (56.4%) patients. Their age ranged from 48 to 81 years, median 67 (63 – 71) years. The Gleason score of the patients in the group ranged from 4 to 10, median 7 (7 – 8); PSA ranged from 2 to 164, median 17 (10–26), and prostate volume ranged from 16 to 200, median 50 (50–60). In this group, 152 (30.9%) of the patients were in T-stage I or II, and the remaining 339 (69.1%) were in T-stage III (including the 2 patients in T-stage IV). Survival ranged from 0 to 19 years, median 4.0 (2–7). 143 (29.1%) of the patients died, of which 82 (16.7%) died from PCa.

The control group included 380 (43.6%) patients. Their age ranged from 49 to 79 years, median 66 (62 – 70) years. The Gleason score of the patients in the group ranged from 2 to 7, median 7 (6 – 7); PSA ranged from 2 to 19, median 10 (7 -12), and prostate volume ranged from 35 to 120, median 50 (50 – 60). Survival ranged from 0 to 25 years, median 8.0 (3 – 12). 108 (28.4%) of the patients died, of which 23 (6.1%) died from PCa.

Patients in the high-risk group had a larger prostate volume ($z = -2.263$, $p = .024$, Mann-Whitney U Test). No statistically significant difference was found in the age of the patients in the two groups ($z = -1.467$, $p = .142$, Mann-Whitney U Test). Patient survival data are presented in Table 1.

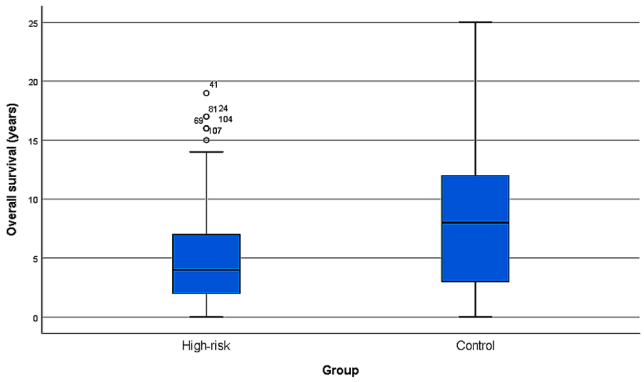
Table 1. Patient survival.

Deceased patients:		Time to death		Total
		≤ 5 years	> 5 years	
High-riskgroup	Died of PCa	71	11	82
	Other cause of death	15	46	61
	Total	86	57	143
Controlgroup	Died of PCa	20	3	23
	Other cause of death	18	67	85
	Total	38	70	108
Total	Died of PCa	91	14	105
	Other cause of death	33	113	146
	Total	124	127	251

1. Overall survival – high-risk and control group

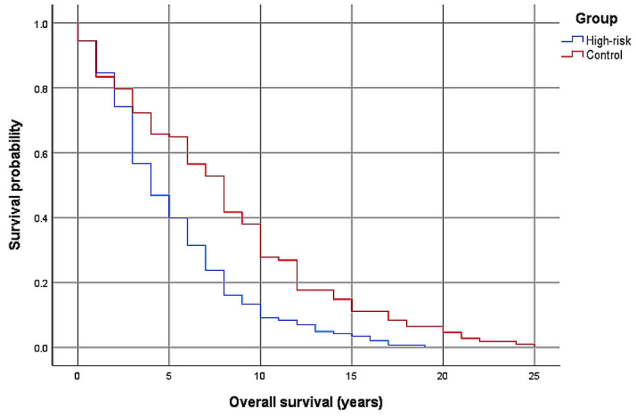
Survival data were available for 251 (28.8%) of all patients included in the study, of which 143 (57.0%) were in the high-risk group and 108 in the control group. The survival of patients from the high-risk group varies from 0 to 19 years, with a median of 4.0 (2 - 7) years, and that of the control group patients - from 0 to 25 years, with a median of 8.0 (3 - 12) years (fig. 1.).

Fig. 1. Descriptive statistics of overall survival in the high-risk and the control group.



Survival of patients in the risk group was lower than that of patients in the control group (z = 3.839, p < .001, Mann-Whitney U Test). This is also confirmed by the Kaplan-Meier survival analysis and the resulting survival curves. Statistical significance between the curves was confirmed by the three tests of reliability (Log Rank, p = .000; Breslow, p = .000 and Tarone-Ware, p = .000), (fig. 2.). However, it should be noted that even in the high-risk group, individual patients have a very long survival (6 persons ≥15.0 years).

Fig. 2. Overall survival in the high-risk and the control group.



2. Overall survival of the high-risk and the control group - up to and over 5 years after RP.

In the high-risk group, 86 patients (34.3% of all patients) survived ≤ 5 years, and 57 (22.7% of all) > 5 years after RP. In this group, the survival of patients ≤ 5 years ranged from 0 to 5 years, median 3.0 (1 – 4), and the survival of patients > 5 years ranged from 6 to 19 years, median 8.0 (7 – 10).

In the control group, 38 patients (15.1% of all patients) survived ≤ 5 years and 70 of the patients (27.9% of all) survived > 5 years after RP. In this group, the survival of patients ≤ 5 years ranged from 0 to 5 years, median 2.0 (1 – 3), and the survival of patients > 5 years ranged from 6 to 25 years, median 10.0 (8 – 14).

No statistically significant difference was found in survival ≤ 5 years of patients from the high-risk and the control groups (z = -1.946, p = .052, Mann-Whitney U Test). A statistically significant difference was found in survival > 5 years - the survival of patients in the high-risk group was lower than that of patients in the control group (z = -2.951, p = .003, Mann-Whitney U Test).

3. Cancer-specific survival – high-risk and control group.

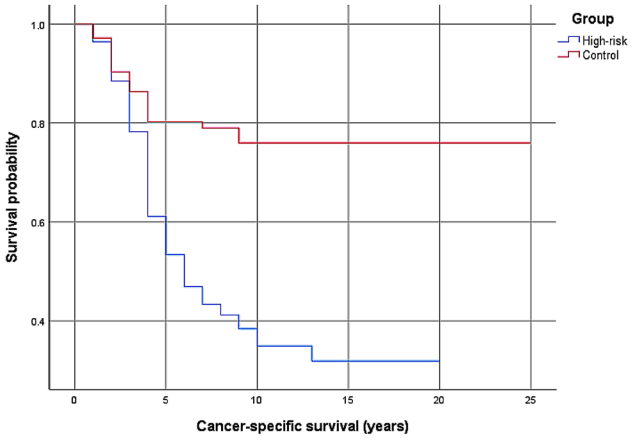
Of all 251 patients who died, 105 (41.8%) died of PCa and 146 of other diseases. The survival of those who died of PCa ranged from 0 to 12 years, with a median of 3 (2–4) years.

In the high-risk group, 143 (57.0%) patients died; 82 (57.3%) died of cancer, and 61 patients died of other causes. Survival of those who died from PCa ranged from 0 to 12 years, with a median of 3 (2–4), and that of those who died from other causes ranged from 0 to 19 years, with a median of 7 (6–10).

In the control group, 108 patients died, of which 23 (21.7%) died of PCa, and 85 died of other causes. Survival of those who died from PCa ranged from 0 to 8 years, with a median of 2 (1–3), and that of those who died from other causes varied from 0 to 25 years, with a median of 9 (6–12).

A statistically significant relationship was found between belonging to a high-risk or control group and dying from PCa (z = -5.721, p < .001, Mann-Whitney U Test). The risk of a patient from the high-risk group dying from PCa is 1.8 times higher than that of a patient from the control group (RR = 1.869, 95%CI = 1.505 – 2.321). This is also confirmed by the Kaplan-Meier survival analysis and the resulting survival curves. The statistical significance between the curves was confirmed by the three tests of reliability (Log Rank, p = .000; Breslow, p = .000 and Tarone-Ware, p = .000), (fig. 3.). There was no difference between the high-risk group and the control group regarding the occurrence of death from another (outside PCa) cause (Log Rank, p = . 194; Breslow, p = . 890 and Tarone-Ware, p = . 525).

Fig. 3. Cancer-specific survival in the high-risk and the control group.



4. Cancer-specific survival of the high-risk and the control group - up to and over 5 years after RP.

91 (36.3%) patients have a CSS ≤ 5 years after RP, and 14 (5.6%) patients have a CSS > 5 years.

In the high-risk group, CSS of 86 (60.1 %) patients was ≤ 5 years after RP, and of 57 (39.9 %) – > 5 years. Of them, 71 (82.6%) patients died of PCa in the period ≤ 5 years, and 11 (13.4%) – in the period > 5 years.

In the control group, the CSS of 38 (35.2 %) patients was ≤ 5 years, and of 70 (64.8 %) – > 5 years. Of them, 20 (87.0%) died of PCa in the period ≤ 5 years, and 3 (13.0%) - in the period > 5 years.

A statistically significant relationship was found between the cause of death ≤ 5 years and whether the patients belonged to a high-risk or control group (z = -3.362, p < .001, Mann-Whitney U Test). The risk of a patient from the high-risk group dying from PCa in the first 5 years is 1.7 times higher than that of a patient from the control group (RR = 1.716, 95%CI = 1.163 – 2.534).

The risk of a patient from the high-risk group dying from PCa > 5 years is 1.9 times higher than that of a patient from the control group (RR = 1.930, 95%CI = 1.357 – 2.746).

DISCUSSION

Tumor classification systems combine patients with similar clinical outcomes into separate groups– in this way, we can propose different treatment options according to the severity of the disease. TNM – classification [2] is the most widely used (and most universal), but for PCa, there are some unique systems. The degree of differentiation of the PCa is determined by the so-called Gleason score, which is based on how the prostate glands look under a microscope with low magnification. This is a histological classification in which the cytological features of the individual cells are not taken into account. Now, the ISUP grades (a version of the Gleason score) are used [3, 4].

Another important classification of PCa is the EAU risk group classification [5]. Here the tumors are divided into low-, intermediate- and high-risk groups depending on patient PSA [6], ISUP grade and the extent of the tumor (based on the digital rectal examination). The three groups have different biochemical progression-free survival – one of the most common indicators of the effectiveness of the treatment [7]. The problem discussed in our article is whether this difference (in survival without PSA-progression) also leads to different OS and CSS. The answer is essential because PSA progression is just a number from a laboratory study, but survival is what matters to the patient.

The analysis of the patients operated in our clinic shows that both OS and CSS are lower in the high-risk group. This is confirmed also when we divide the patients into two groups – with survival up to and over 5 years after RP. Yet there are some important details. Firstly, even in the high-risk group, there are patients with very long OS (6 persons ≥ 15.0 years). Secondly, no statistically significant difference was found in OS ≤ 5 years after RP between the high-risk and the control group. A difference was found in OS > 5 years after RP. This means that even patients with bad pathology have good results from RP – survival of 5 years is considered an excellent result for many other malignancies.

The treatment of high-risk PCa is a controversial topic [8]. Probably in our days, the key to success is the multimodal treatment [9, 10], which combines RP, followed by hormonal- and radiotherapy (if necessary). A major

drawback in our study is the lack of division of the patients according to the type of postoperative therapy. This is not done because of the insufficient data – on when and which type of therapy was applied at a given level (which level?) of PSA. Still, we think that our data give a good general view of what happens with the patients after RP regarding the two most important parameters – OS and CSS.

CONCLUSION

OS and CSS are lower in the high-risk group after PR. The difference appears to be due to the longer survival of low- and moderate-risk groups after the fifth year of the operation. Still, the high–risk PCa has a very good OS within 5 years after RP, which means that an operation is a reasonable option for the treatment of this type of tumor.

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Address for correspondence:
Assoc. Prof. Tosho Ganev, MD, PhD,
Clinic of urology, MHAT "Sveta Anna-Varna" - Department of surgery, Medical University - Varna;
100, Tzar Osvoboditel Blvd., Varna, 9000, Bulgaria.
E-mail: dr_ganev@yahoo.com,