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Original article

OVERALL AND CANCER-SPECIFIC SURVIVAL OF HIGH-RISK PROSTATE CANCER – IMPACT OF ADJUVANT THERAPY AFTER RADICAL PROSTATECTOMY

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ABSTRACT

Purpose: The study examines the survival of patients with high-risk prostate cancer in order to find a relationship between survival and the type of postoperative therapy.

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. Postoperatively, some patients were additionally subjected to hormonal therapy (referred to as "dual therapy" in the text), and others to hormonal and radiotherapy (referred to as "triple therapy").

Results: Overall and cancer-specific survival of high-risk patients did not differ statistically significantly for the two types of postoperative therapy.

Conclusions: The optimal combination of radical prostatectomy, hormonal and radiotherapy in order to achieve maximum survival for patients with high-risk prostate cancer is still poorly defined.

Keywords: hormonal therapy, radiotherapy, Gleason score,

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. The high-risk group often postoperatively undergoes other therapies – hormonal and/or radiotherapy. The aim of the present study is to examine the survival of patients with high-risk PCa and to try to find a relationship between survival and the type of postoperative therapy.

MATERIALS AND 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. Postoperatively, the patients were followed in Oncology Hospital "Marko Markov - Varna", where some of them were additionally subjected to hormonal therapy (referred to as "dual therapy" in the text), and others to hormonal and radiotherapy (referred to as "triple therapy").

RESULTS

Patients with high-risk PCa were 491 (56.4% of all patients). Their age ranged from 48 to 81 years, median 67 (63 – 71) years. The Gleason score of patients in the group ranged from 4 to 10, median 7 (7 – 8); PSA ranged from 2 to 164 ng/ml, median 17 (10 – 26), and prostate volume ranged from 16 to 200 ml, median 50 (50 – 60). In this group, 152 (30.9%) of the patients were in T-stage 1 or 2, and the remaining 339 (69.1%) were in T-stage 3 (including the 2 patients in T-stage 4). Survival ranged from 0 to 19 years, median 4.0 (2–7). 143 (29.1%) of the patients died, of which 82 (16.7%) from the PCa.

Of all 491 patients in the high-risk group, 30 (6.1%) were treated only surgically.

Of all 491 patients in the high-risk group, 119 patients (24.2 %) were treated with dual therapy. Their age ranged from 50 to 81 years, median 67 (63 – 71). The Gleason score of the patients in the group ranged from 4 to 10, median 8 (7 – 8). PSA ranged from 4 to 75, median 20 (10 – 26), and prostate volume ranged from 40 to 100 ml, median 50 (50 – 60).

Of all 491 patients in the high-risk group, 342 (69.7 %) patients were treated with triple therapy. Their age ranged from 48 to 79 years, median 6 6 (63 – 71). 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 15 (10–25), and prostate volume ranged from 16 to 100 mL, median 50 (50–60).

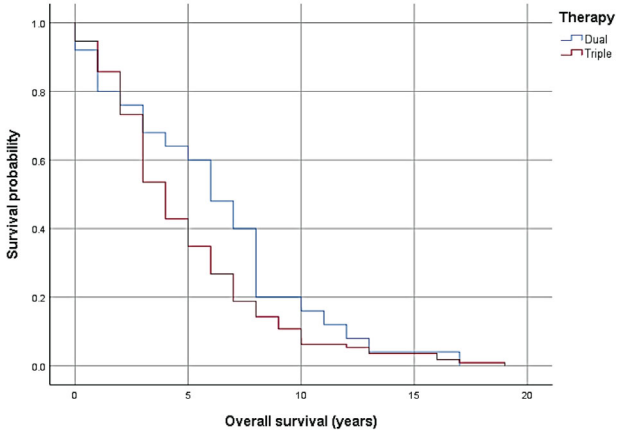
1. Overall survival of the high-risk group

Data on overall survival (OS) in this group were available for 137 (29.7%) patients - 25 (18.2%) were treated with double, and 112 (81.8%) were treated with triple therapy. We found a statistically significant association between the type of treatment and the probability of death (z = -2.411, p = .016, Mann-Whitney U Test). Dual therapy patients had a lower chance of dying than patients on triple therapy (OR = .546, 95%CI = .333 – .896).

OS for patients treated with dual therapy ranged from

0 to 17 years, median 6 (3–8) years, and for those treated with triple therapy, it ranged from 0 to 19 years, median 4 (2–7) years. Regardless of the difference in the median, the duration of OS did not differ statistically significantly for the two types of therapy (z = - 1.535, p = .125, Mann-Whitney U Test). This is confirmed by all three reliability tests (Log Rank, p = .140; Breslow, p = .132 and Tarone-Ware, p = .105) and by the Kaplan-Meier survival analysis and the resulting survival curves (fig. 1.).

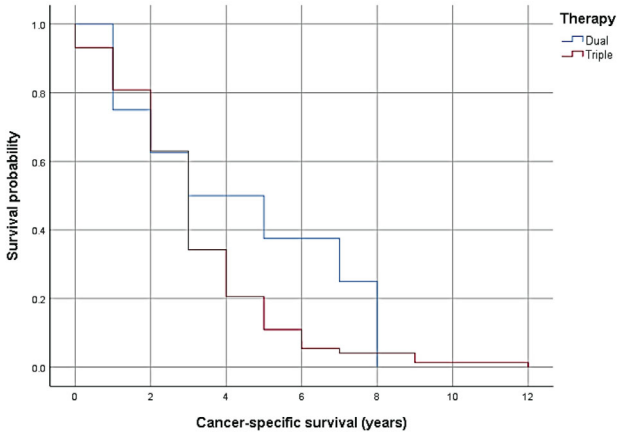
Fig. 1. Overall survival of those treated with dual and triple therapy



2. Cancer-specific survival of the high-risk group

Data on cancer-specific survival (CSS) in this group were available for 81 (17.6%) patients - 8 (9.9%) were treated with dual, and 73 (90.1%) were treated with triple therapy. CSS of patients treated with dual therapy ranged from 1 to 8 years, median 4 (1.50 - 7.50) years, and for those treated with triple therapy, it ranged from 0 to 12 years, median 3 (2 - 4) years. Regardless of the difference in the median, it was not statistically significant for the two types of therapy (z = - .900, p =.368, Mann-Whitney U Test). This is confirmed by all three tests of reliability (Log Rank, p =.247; Breslow, p =.375 and Tarone-Ware, p =.256) and by the Kaplan-Meier survival analysis and the resulting survival curves (fig. 2.).

Fig. 2. Cancer-specific survival of those treated with dual and triple therapy

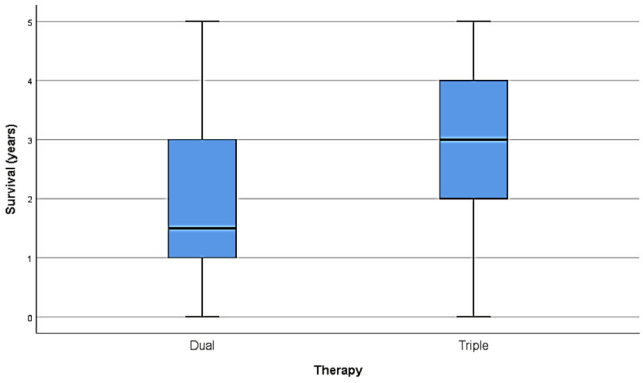


3. Overall survival under and over 5 years of the high-risk group

When dividing OS into groups up to and over 5 years, 83 (60.6%) survived ≤ 5 years, and 54 (39.4%) – > 5 years. Of all patients with OS - data, 10 (7.3%) patients with dual therapy and 73 (53.3%) patients with triple therapy survived ≤ 5 years, and 15 (10.9%) patients with dual therapy and 39 (28.5%) patients with triple therapy survived > 5 years.

In the group with OS ≤ 5 years, the overall survival of patients with dual therapy ranged from 0 to 5 years, median 1.5 (1 – 3), and that of patients with triple therapy ranged from 0 to 5 years, median 3 (2 – 4) (fig. 3.).

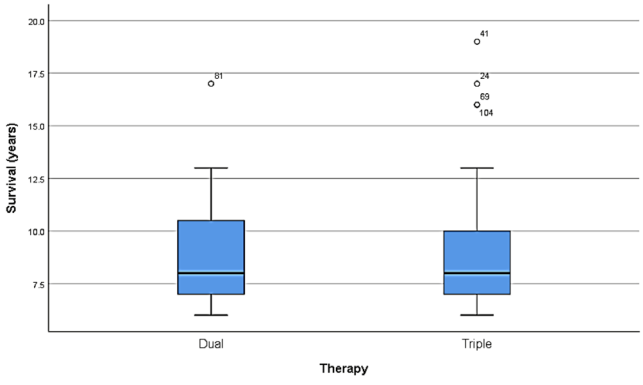
Fig. 3. Descriptive statistics of overall survival ≤ 5 years in those treated with dual and triple therapy in the high-risk group



Despite the apparent difference in OS in favour of triple therapy, this difference was not statistically significant (z = - 1.349, p = .177, Mann-Whitney U Test). This was confirmed by all three reliability tests (Log Rank, p = .261; Breslow, p = .145 and Tarone-Ware, p = .187) and by the Kaplan-Meier survival analysis.

In the group with a survival of > 5 years, there are 54 patients, of which 15 are with dual and 39 with triple therapy. OS of patients with dual therapy ranged from 6 to 17 years, median 8 (7–11), and that of patients with triple therapy ranged from 6 to 19 years, median 8 (7–8) (fig. 4.).

Fig. 4. Descriptive statistics of overall survival > 5 years in those treated with dual and triple therapy in the high-risk group

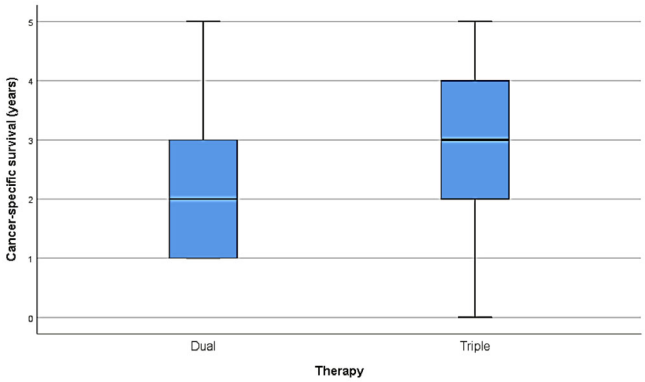


No statistically significant difference was found in the OS of patients treated with double and triple therapy in the group with survival > 5 years (z = - .313, p = .754, Mann-Whitney U Test). This was confirmed by all three reliability tests (Log Rank, p = .944; Breslow, p = .756 and Tarone-Ware, p = .817) and by the Kaplan-Meier survival analysis.

4. Cancer-specific survival under and over 5 years in the risk group

In the group with CSS ≤ 5 years, there are 70 patients, of which 5 patients had dual and 65 - triple therapy. CSS of patients with dual therapy ranged from 0 to 5 years, median 2 (1–3), and that of patients with triple therapy ranged from 0 to 5 years, median 3 (2–4) (fig. 5.).

Fig. 5. Descriptive statistics of cancer-specific survival ≤ 5 years in those treated with double and triple therapy in the high-risk group



Despite the apparent difference in CSS in favor of triple therapy, this difference was not statistically significant (z = - .561, p = .575, Mann-Whitney U Test). This was confirmed by all three reliability tests (Log Rank, p = .809; Breslow, p = .560 and Tarone-Ware, p = .649) and by the Kaplan-Meier survival analysis.

In the group with CSS of > 5 years, there were 11 patients, of which 3 patients had dual and 8 - triple therapy. CSS of dual therapy patients ranged from 7 to 8 years, median 8 (7–8), and that of triple therapy patients - from 6 to 9 years, median 6.5 (6–9) years.

No statistically significant difference was found in CSS > 5 years between those treated with dual and triple therapy (z = - .526, p = .599, Mann-Whitney U Test). This was confirmed by all three reliability tests (Log Rank, p = .827; Breslow, p = .610 and Tarone-Ware, p = .865) and by the Kaplan-Meier survival analysis.

DISCUSSION

Throughout the Guidelines of the European Association of Urology, the EAU-risk group classification is extensively used [1]. This classification is based on the grouping of patients with a similar risk of biochemical recurrence after radical prostatectomy or external beam radiotherapy. Methods of treatment of low- and intermediate-risk patients are relatively well specified. This is not the case with the treatment of high-risk PCa. Nowadays, radical prostatectomy is considered to be a reasonable first choice [2], although radiotherapy is also widely advocated [3] - which of the two methods is preferable in practice is currently an unsolved problem. The advantages of surgical treatment are that, firstly, it reduces the tumor burden, and secondly, we have a more accurate staging of PCa postoperatively. Already in 2012, Bolla draws attention to the fact that in 20% of cases, there is an improvement in the T-stage (from 3 to 2) [4]. The situation is similar with the Gleason score, currently reported according to the ISUP classification [5], which in 30% also improves postoperatively [6-8].

The postoperative treatment of patients with high-risk PCa is also a problem - very often, they undergo multimodal adjuvant treatment, including hormonal therapy (with or without radiotherapy) [9-10]. The exact combination of these methods is not strictly fixed, and this prompted us to look at the survival of the patients operated in our clinic. Biochemical progression-free survival is most often discussed [11], but in fact, overall and cancer-specific survival are most important to the patients. Therefore, we paid attention to them in our study. The only difference between dual and triple therapy was a statistically significant association between the type of treatment and the probability of death (z = -2.411, p = .016, Mann-Whitney U Test). Dual therapy patients had a lower chance of dying than patients on triple therapy (OR = .546, 95%CI = .333 – .896). Probably, this is connected with the side effects of the adjuvant treatment.

Unfortunately, a detailed analysis of these parameters showed no differences in the duration of survival between dual and triple adjuvant therapy. In our analysis, both the median survival was examined - it did not differ statistically significantly for the two therapies as well as three reliability tests (Log Rank, Breslow, and Tarone-Ware), and a survival analysis by Kaplan- Meier was performed. Survival itself, in addition to being calculated as an absolute value (measured in years), was also studied as two categories - under and over 5 years. This also did not lead to the finding of differences between dual and triple therapy.

CONCLUSION

Our results show that currently, the treatment of high-risk PCa remains poorly defined. The optimal combination of radical prostatectomy, hormonal and radiotherapy is unclear.

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