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Professional paper

Our Experiences in Treatment of Prostate Carcinoma in Patients over the Age of 70

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A B S T R A C T

The goal of our study was to present our long-standing experience of the treatment of prostate carcinoma in patients over the age of 70. During the 20 years period (from 1991 to 2010) we diagnosed the prostate carcinoma in 1998 patients. More than 58% of the patients were over 70 years old. The most frequent symptoms of the prostate carcinoma were frequent urination and backache. At the first examination 36% of the patients had both prostate lobes involved, and 27% of them had metastases. The most frequent ones (26%) were those in the bone system (pelvis and spine), while in only 1% metastases were found in solid organs (lungs and liver). According to the TNM classification, T1 and T2 were diagnosed in 818 (71%) patients. Histopathological examination discovered Gleason score 2 in 70% of patients and Gleason score 3 in 24% of them. Most often the combination of castration and antiandrogen therapy (in 68% of the patients) and the combination of castration and Estracyt therapy (in 19% of the patients) were applied. In conclusion, intensified efforts should be made in promoting preventive urological examinations because of the great number of patients (27%) with metastases at the first examination.

Key words: *antiandrogen therapy, metastasis, prostate carcinoma*

Introduction

The Nobel Prize winner Charles Brenton Huggins et al. laid the groundwork for the hormonal treatment of the prostate carcinoma in 1941, proving its androgens dependence[1].

Applying castration of the patients, i.e. oestrogen administration reducing the level of circulating testosterone resulted in dramatic tumour remission in those days. The initial enthusiasm, concerning the treatment results, quickly deflated due to ephemeral effects. This cognition resulted in development of additional treatment strategies such as adrenalectomy, surgical or medicamentous hypophysectomy, and production and use of new antiandrogens, antiprogestins and antiprolactins. These new additional methods decreased mortality and morbidity, but did not considerably contribute to the prolongation of patients' survivals.

Relatively small number of patients is detected in the initial stage of the disease, and they undergo radical treatment, while a greater number of patients show the signs of locally advanced disease or remote metastases at the time of making diagnosis. A significant number of patients with localized prostate carcinoma are not considered to be good candidates for the radical treatment because of their old age. Therefore, a large majority of patients with prostate carcinoma undergoes hormonal treatment achieving years-long remission of the disease in the significant number of cases[2]. However, the full health recovery is possible only by radical treatment, i.e. radical prostatectomy or radical radiotherapy. In spite of remarkable progress in the last decade, the basic propositions of diagnostics and treatment of the prostate carcinoma represent a series of negative cognitions even today: aetiology of the disease – unknown; hormonal therapy – palliative; basic diagnostics (palpatory finding and cytological biopsy) – unchanged in this century; ultrasound diagnostics – insufficiently reliable; monitoring of treatment results – without sufficiently exact parameters.

Patients and Methods

The purpose of the study was a prospective monitoring of patients with newly diagnosed prostate carcinoma at our Department of Urology during 1991–2010 period.

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Diagnostics, treatment and monitoring of patients were performed in accordance with the existing protocol of the Croatian Urologic Society. Diagnostic treatment consisted of digitorectal examination of the prostate, the abdominal or transrectal ultrasound of the prostate, intravenous urogram, x-ray of the skeleton, cytological transrectal biopsy, PSA analysis, CT and the scintigram of the skeleton. The clinical stage of the disease was evaluated on the bases of the results of the above examinations and expressed in TNM-system[3]. Tumours were classified according to the histological criteria (Gleason score) as well differentiated (Gleason 1), moderately differentiated (Gleason 2) and poorly differentiated (Gleason 3). The basic treatment of patients over the age of 70 at our department is the combination of castration and antiandrogens. At the beginning of our study we used castration and estrogens (Honvan) that were quickly abandoned because of cardiotoxic effects. Afterwards the Androcur and Prostandril or Flutamide were most frequently used with castration. Because of great number of patients with metastases the combination of castration and Estracyt are very successfully applied in such cases. The control examinations are done in 3-month intervals. The control treatment consists of digitorectal examination, ultrasound of the prostate and the kidneys, PSA analysis and x-ray of the bones and lungs, as well as scintigraphy of the skeleton in particular cases[4]. The shortest observation time is 6 months and the longest one is 20 years. During the observation we include in progression of the disease the appearance of metastases, progression of local finding or the increase of the PSA values.

Results

We have discovered 1998 prostate carcinomas during the aforementioned period (Table 1). The number of newly detected patients with the prostate carcinoma with their annual distribution was presented in the Table 1. It is evident that most of the new patients were detected in the years 2001–2010[5]. Digitorectal examination of the prostate has been still the basic diagnostic method for detecting the prostate carcinoma. In case of suspicious palpatory finding a transrectal needle biopsy of the prostate follows, being successful in more than 70% of the patients[6]. In the last decade the investigations are directed to discover markers of the prostate carcinoma, like PSA, total and free. PSA was partially determined at our department of urology during particular time intervals, due to occasional lack of reagent in the course of research. There were 1158 (58%) patients older than 70 years. The dominant symptoms in their clinical picture were difficulties in urine discharge, backache and retention of urine. It is interesting that a great number of patients (26%) sought the medical help for the first time because of osseous symptoms[7]. Even 317 patients (27%) had metastases at the beginning of treatment. Their localisations were most frequently in the bone system (26%) and in solid organs (1%). The right prostate lobe was involved in 34% of our patients and the left one in 30% of them. Both prostate lobes were affected in 36% of the cases, thus proving the advanced stage of the disease.

For determination of the clinical stage of the disease we used the classification of the International Association for Anti-Cancer Campaign, the so called TNM classification and histological tumour gradation[3]. According to the TNM classification 818 patients developed T1 and T2 of the localised prostate carcinoma and 340 of them had the advanced carcinoma.

The patients with the localised prostate carcinoma are presented in the Table 2 according to the stage. The prevalence of the patients with stages T2c (26%) and T2b (22%) is evident.

TABLE 2
PATIENTS WITH LOCALISED PROSTATE CARCINOMA (N=818)

TNM classification	No. of patients (%)
T1bN0M0	23 (2%)
T1cN0M0	68 (6%)
T2aN0M0	178 (15%)
T2bN0M0	248 (22%)
T2cN0M0	301 (26%)

Domination of the T3a stage of the prostate carcinoma is shown in the Table 3. There were 177 (15%) patients with this stage.

TABLE 3
PATIENTS WITH ADVANCED PROSTATE CARCINOMA (N=340)

TNM classification	No. of patients (%)
T3aN0M1b	177 (15%)
T3bN0M1b	90 (8%)
T3cN1M1b	36 (3%)
T3cN1M1c	24 (2%)
T4aN2M1c	13 (1%)

TABLE 1
DISTRIBUTION OF 1988 PATIENTS WITH NEWLY DETECTED PROSTATE CARCINOMAS (1991–2010)

Year	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000
No. of patients	27	33	60	46	56	75	54	57	59	70
Year	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
No. of patients	137	128	131	148	150	200	191	200	91	85

TABLE 4
CLASSIFICATION OF THE PROSTATE CARCINOMA ACCORDING TO HISTOLOGICAL CRITERIA

Tumour grading	No. of patients (%)
G1	71 (6%)
G2	811 (70%)
G3	276 (24%)

The prevalence of moderately differentiated prostate carcinoma is evident in the Table 4. (Gleason 2) in 70% of the patients[3], followed by poorly differentiated carcinoma (Gleason 3) in 24% of patients, while a well differentiated carcinoma (Gleason 1) was found in only 6% of them.

It is evident from the Table 5. that the greatest number of our patients (68%) was treated with combination of castration and antiandrogen[8,9]. They were initially administered cyproterone acetate and flutamide over last few years[10,11].

TABLE 5
TYPES OF TREATMENT FOR PROSTATE CARCINOMA

Types of treatment	No. of patients (%)
Castration+Estrogens	21 (1.8%)
lmult1Castration+Antiandrogens	795 (68%)
Castration+Estracyt	220 (19%)
Castration	32 (3%)
Antiandrogens	45 (4%)
Estracyt	24 (2%)
Transurethral resection of the carcinoma	21 (1.8%)

Discussion

Metastases were found in great number of patients at the first examinations. Therefore, they underwent castration in combination with Estracyt as the therapy[12]. This combination was applied in 19% of the patients. It should be pointed out that we achieved good results with this medicine and it has been still in use, in spite of its slow abandonment.

In the first years of this study we used the combination of castration and oestrogen (Honvan) in 2% of the patients[13].

Radiotherapy is used as radical, adjuvant and palliative treatment in patients with the prostate carcinoma. Radical radiotherapy is introduced as the alternative procedure in patients in T1 and T2 stage of the disease, being a therapy of choice in T3 and partly in T4 stages of the disease.

We rarely decided to apply radiotherapy in single cases of the advanced prostate carcinoma as an adjuvant and palliative procedure due to particular technical and organisational problems at the department of radiotherapy and oncology.

In order to eliminate the obstruction and to create the „water way“ we carried out TUR of the prostate carcinoma in only 2% of patients during the first years of this research. Because of rapid progression of the disease after TUR, with early lethal outcome in these patients, we rarely chose TUR of the prostate carcinoma in later course of the study[14].

During the treatment progression of the disease developed in 182 (16%) patients. The progression was manifested by the increase of the PSA markers and the occurrence of metastases. Metastases appeared most frequently within one year after the initial treatment (112 patients – 10%).

Conclusion

The prostate carcinoma is a disease of males in their older age – 1158 patients (58%) in this study were over 70 years old. Metastases were found in the initial treatment in 317 (27%) patients. Diagnostics included digitorectal examination PBP, PSA, ultrasound, x-ray, scintigraphy of the skeleton and CT. Greatest number of our patients (68%) was treated with combination of castration and antiandrogen[8,9]. During the treatment progression of the disease most frequently occurred after one year (112 patients – 10%). There is still a great number of patients with the prostate carcinoma metastases detected at the first examination (27%), and intensified efforts should be made in promoting the preventive urological examinations.

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NAŠA ISKUSTVA U LIJEČENJU KARCINOMA PROSTATE U DOBI IZNAD 70 GODINA

S A Ž E T A K

Cilj rada je prikazati naša višegodišnja iskustva u dijagnozi i liječenju raka prostate kod bolesnika u dobi iznad 70 godina. Tijekom 20 godina (1991.–2010.) kod 1998 bolesnika dijagnosticirali smo karcinom prostate. Više od 58% (1158) bolesnika bili su u dobi iznad 70 godina. Najčešći simptomi karcinoma prostate bili su učestalo mokrenje i križobolja. Kod prvog pregleda oko 36% bolesnika imala su zahvaćena oba lobusa prostate, a kod 27% bolesnika nađene su metastaze. Najčešće su metastaze (26%) u koštanom sustavu (kosti zdjelice i LS kralješnica), a samo u 1% bolesnika našli smo ih u solidnim organima (pluća i jetra). Po TNM klasifikaciji stadiji T1 i T2 su dijagnosticirani kod 818 (71%) bolesnika. Patohistološkim pregledom kod 70% bolesnika nađen je Gleason score 2, a Gleason score 3 kod 24%. Najčešće smo primjenjivali kombinaciju kastracije i antiandrogena (68%) bolesnika i kombinaciju kastracije i Estracyta (19%) bolesnika. U zaključku možemo konstatirati da imamo još uvijek velik broj bolesnika (27%), koji su kod prvog pregleda već imali metastaze,zato moramo pojačati rad na popularizaciji preventivnih uroloških pregleda.