ResearchJet Journal of Analysis and Inventions
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MODERN APPROACHES IN DIAGNOSIS AND TREATMENT OF PROSTATE CANCER (LITERATURE REVIEW)

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Summary
Prostate cancer has one of the leading positions among the incidence of cancer and still has a higher position on the aggressiveness of the process. This research briefly analyzes the current condition of the issue of prostate cancer, assesses the modern aspects of early diagnosis, prognosis and complex treatment.

Key words: prostate cancer, adenocarcinoma, hormone treatment

According to the WHO, prostate cancer is one of the most important problems of oncourology and at the beginning of the 21st century has become one of the most common diseases among the male population in most countries of the world. In the United States, more than 174,650 new cases were reported in 2019, and the number of deaths exceeded 31,620. [20]. In the structure of the incidence of malignant neoplasms in the male population of Russia, prostate cancer increased 3.0 times from 2001 to 2016 (from 19.1 to 56.5 cases per 100 thousand population) [1]. So over the past 10 years, the mortality rate from prostate cancer ("rough" indicator) among the male population has increased by 39.0% from 12.9 in 2006. 18.42 cases per 100 thousand population in 2016, the average annual growth rate is -3.21% [1].

In the last 5 years in our country there is an increase in the number of patients with prostate cancer, in particular, in 2015 - 372, in 2016 - 443 and by 2019 the number of patients reached 483 (an increase of 23%). There is also an increase in the incidence rate, which in 2015 was 1.2 patients per 100 thousand population, and by 2019 this figure was 1.5 (Tillyashaykhov M.N. et al. 2020).

The mortality rate from prostate cancer is 8.09 per 100,000 population. Over the last decade, this figure has grown by 23.54%. (Al Shukri S.X. 2019). The sharp increase in the number of new diagnoses of prostate cancer and

mortality from disease over the past decade, it has necessitated improvements in the screening and treatment of these patients.

At present, early detection of oncological diseases to serves increase the effectiveness of treatment of patients. Through early diagnosis prostate cancer allows patients to undergo radical treatment and improve their life expectancy. Over the past 5 years, the rate of early detection of prostate cancer in the Republic of Uzbekistan (stages I and II) has improved, in particular, in 2015, 30.1% of patients were diagnosed at an early stage, and in 2019 this figure was 40.6%. (Tillyashayxov M.N. 2020).

Diagnosis of prostate cancer

As mentioned above, at the initial stage, prostate cancer has no pronounced clinical symptoms, which significantly complicates its diagnosis. Detection of prostate-specific antigen (PSA) in the 1980 led to a revolution in the early diagnosis of prostate cancer. The probability of having prostate cancer at a plasma PSA level of 2–4 ng / ml ranges from 23 to 26% [22]. The average probability of detecting prostate cancer based on the results of prostate biopsy with PSA in the "gray zone" is 20%, and the probability of having prostate cancer with PSA is in the range from 10 to 20% - 24% [12]. Discussion continues about the possibility of lowering the threshold value to 2.0-3.0 ng / ml. In this case, the detection of prostate cancer according to prostate biopsy data increases [12]. In accordance with the European recommendations of 2017, special attention is required for risk groups: patients over 40 years of age with PSA> 1 ng / ml and over 60 years of age with PSA> 2 ng / ml [22]. An increase in PSA levels is not always proof of prostate cancer. The sensitivity of this tumor marker is more than 95%, and the specificity is about 75%. That is, in 25% of cases, an increase in PSA levels is associated with other reasons: the presence of prostate adenoma, chronic inflammation in the prostate gland, etc. [12,14]

The "gold standard" for diagnosing locally advanced prostate cancer is a combination of digital rectal examination (DRE). If changes in one or another indicator are detected, a multifocal biopsy is performed under ultrasound control. This is a short, painless manipulation, during which a special automatic device inserted with an ultrasound probe into the rectum is used to collect several tissue fragments for histological examination.

The Glisson index turned out to be an extremely accurate prognostic criterion that determines the activity and characteristics of a tumor, in other words, the degree of its malignancy. The prognosis of the course of the disease and the

choice of treatment tactics depend on it. The localization of the tumor in the prostate gland, and the percentage of tumor tissue in the biopsy specimen, and confirmation of the defeat of the seminal vesicles, and of course, the growth of the tumor beyond the border of the prostate gland, are also important. In the literature, especially in Russia, this aspect has not been sufficiently studied. [18]

Magnetic resonance imaging with contrast (provides additional information on the localization of the tumor in the prostate and the possible spread of the tumor beyond the prostate capsule, as well as on the state of regional lymph nodes). Computed tomography and ultrasonography are of limited value in the diagnosis of prostate cancer. The ultimate goal of the examination is to determine the stage of the disease. With the help of currently existing diagnostic methods, it is difficult to correctly establish the stage of prostate cancer. Only the totality of all examination data makes it possible to accurately stage the tumor and give a prognosis with a high probability.

The prostate cancer clinic is characterized by three groups of symptoms:

1. Dysuria due to impaired outflow of urine due to obstruction of the bladder neck.
2. Symptoms characteristic of local tumor extension (hematuria, low back pain, ureteral obstruction, hydronephrotic transformation of the kidneys).
3. Clinic of metastases. The main targets of hematogenous disseminates of prostate cancer are the bones of the skeleton, and, first of all, the pelvic bones. It should be especially emphasized that prostate cancer is characterized by the osteoblastic nature of metastases (98% of cases). Osteolysis and pathological fractures in this pathology are quite rare (2% of cases). The clinic of lymphogenous metastases, as a rule, is reduced to limb lymphostasis and enlargement of the inguinal lymph nodes [18]. Typical complications of prostate cancer are acute or chronic urinary retention, unilateral or bilateral ureterohydronephrosis, priapism, lymphostasis of the lower extremities, profuse hematuria and bladder tamponade, anemia.

Non-acinar prostate cancer in radical prostatectomy material accounts for 5-10% of cases of primary prostate cancer. For the first time in the WHO classification (2016) it is highlighted: The most common form of prostate cancer is acinar adenocarcinoma, however, attention should be paid to rare (special) forms. Ductal carcinoma of the prostate accounts for less than 1% of prostate cancer. Urothelial carcinoma accounts for up to 3% of prostate cancer. Squamous prostate cnacer is a rare variant (less than 0.5%) [16.9]. It

is constituted a group of poor prognosis, since they demonstrate absolute hormone resistance and, as a consequence, uncontrollability. Prognostic significant gradation of adenocarcinoma of the prostate gland according to the degree of differentiation of cellular elements: G1 - the tumor is well differentiated, G2 - moderately differentiated, G3 - poorly differentiated.

Prostate cancer treatment

The choice of treatment method is determined by the PSA level, histological gradation and degree of tumor differentiation, the patient's age, concomitant disease and life expectancy. The goal of treatment may be:

- Active surveillance
- Local therapy (aimed at cure)
- Systemic therapy (aimed at shrinking or limiting the tumor) [28]

Over the past decades, radical prostatectomy (RP) has remained one of the most effective treatments for localized and locally advanced prostate cancer (PC) [3,6]. Prostatectomy is performed using the retropubic, perineal or laparoscopic approach. Omitting technical details, we will only report the results of surgical treatment. Postoperative mortality ranges from 3% to 12% and is mainly associated with thromboembolic complications.

The method of radical prostatectomy proposed in 1982 by Walsh and Doncer made it possible to widely use this method of treatment in localized prostate cancer (PC). [25,30]. The volume of the prostate gland before RP was from 21 to 102 cm3. The average age is 62 (46–68) years. The PSA level before the HIFU session varied from 0.4 to 18.0 ng / ml [2.4].

The goal of RP in localized prostate cancer is to eliminate the malignant process while preserving urinary retention and, if possible, erectile function. Some cases of disabling late complications include urinary incontinence, urinary retention, urethral stricture, erectile dysfunction, and rectourethral fistula [23,30]. According to the largest meta-analysis conducted in 2015, the likelihood of developing stress urinary incontinence after RP is 66% [6,27]. According to a meta-analysis, the likelihood of postoperative urethral stricture in patients with RP is 8%. [6] The results of the study show that 25-75% of patients develop erectile dysfunction (ED) after RP [29]. Postoperative mortality according to most foreign authors is 1-2% [8].

Pelvic lymphadenectomy, according to most authors, is more of a diagnostic than a treatment procedure that corrects the stage of cancer. The frequency of registered lymphometastases varies at T1 from 0 to 24%, at T2 - from 5 to 43%, at T3 - from 44 to 60%, at G1 from 15 to 19%, at G2 - from 39 to 56%, at

G3 - from 60 to 77%. [24] The procedure is considered indicated not only for the surgical treatment of localized PC, but also before radiation therapy for locally advanced stage 3 PC. Obturator, hypogastric, external and common iliac, presacral lymph nodes are subject to removal. [10,21, 24]

Radical prostatectomy can provide excellent local control in patients with localized prostate cancer. However, some patients with aggravating factors (extracapsular tumor spread (pT3a), invasion of seminal vesicles (pT3b) or the presence of tumor cells in the resection line (R1), etc.) will require postoperative radiation therapy [5]. Before irradiation, CT is performed, on the basis of which the radiation fields are determined. Radiation therapy is given 5 days a week for 1.5 months. The radiation may cause frequent painful urination, blood in the urine (radiation cystitis), as well as frequent painful bowel movements, blood in the stool (radiation rectitis). With a high intensity of these side effects, a break is made in radiation treatment until the symptoms of cystitis and rectitis subside [26]. External beam radiation therapy for localized prostate cancer can achieve satisfactory long-term results, which are practically not inferior to radical surgical treatment.

To improve the results of radiation therapy, hormone therapy is prescribed for most patients before, during, and for 2 years after radiation.

Brachytherapy is a modern, high-tech, effective, relatively safe and easily reproducible method of treating prostate cancer, with a low rate of complications and mortality. However, at present, the long-term results of treatment with brachytherapy have not been studied, a qualitative comparison has not been made with other treatments for localized and locally advanced PC and therefore it has not been determined whether brachytherapy can be considered as a real alternative to external beam radiation therapy and radical prostatectomy.

Types of hormone therapy for prostate cancer:

1. Surgical castration - orchiectomy

Despite the fact that orchiectomy is an operation, its main effect is associated with hormonal changes. During the operation, the surgeon removes the testicles, which produce 90% of the androgens. After removing the source of androgens, over time, their concentration in the blood decreases and tumor growth stops or shrinks.

Surgical castration is the easiest and cheapest way to lower blood androgen levels.

2. Medication hormone therapy for prostate cancer

The question of the need for hormone therapy before surgery remains controversial. There is a theoretical basis for preoperative hormone therapy, which includes the following.

1. In 40-50% of cases of clinically localized tumor process (T1-T2), postoperative pathomorphological examination reveals extracapsular invasion (pT3) (Zincke et al., 1994).
2. In an animal experiment (hormone-sensitive tumor Shionogi), non-adjuvant hormone therapy leads to a 50% reduction in local recurrence and cancer mortality (Gleave et al., 1996). [13]

The following groups of drugs can be used in the treatment of prostate cancer:

 Luteinizing releasing hormone analogs or agonists

Thanks to the use of these drugs, an effect similar to that of surgical castration is achieved, i.e. there is a decrease in the level of androgens in the blood. This is the so-called medical castration. The essence of the action of luteinizing releasing hormone blockers analogs is that due to the similarity of their chemical structure with the true hormone, the analogs bind to the hypothalamic receptors, but do not stimulate, but rather reduce the secretion of LH. This ultimately leads to a decrease in the level of testosterone in the blood.

Antiandrogens although the testes are the main site for testosterone production, a small portion (10%) is produced in the adrenal glands. Therefore, blocking the production of androgens in the testes does not always completely reduce their concentration in the blood, which means that it is necessary to block androgens formed in the adrenal glands. According to the results of several studies, there was no difference in survival between patients in whom hormone therapy for prostate cancer was carried out with luteinizing releasing hormone agonists and antiandrogens, although several studies indicate a lower efficacy of antiandrogens.

Most often, antiandrogens are used in combination with orchiectomy or luteinizing releasing hormone agonists. This treatment is called combined androgen blockade.

The following drugs belong to the group of antiandrogens: cyproterone acetate, flutamide, bicalutamide.

In many countries, the use of cyproterone acetate is limited due to its pronounced side effects, especially severe liver damage after prolonged use of the drug. However, in some cases, treatment with cyproterone is justified, despite the side effects. Many men complain of diarrhea associated with

flutamide. Flutamide and high doses of bicaluamide are less likely to cause erectile dysfunction and other side effects than luteinizing releasing hormone agonists. But these drugs are more likely to cause breast swelling and weakness [19].

 Luteinizing releasing hormone blockers

Luteinizing releasing hormone blockers - they block the production of LH by the pituitary gland, which in turn stops testosterone synthesis. The effect of the drugs is similar to that of luteinizing releasing hormone agonists, but unlike agonists, antagonists lead to a more rapid decrease in testosterone levels in the blood and do not cause flare-ups.

Estrogens

The use of estrogens - female hormones - is an alternative to orchiectomy in men with advanced prostate cancer. The multidirectional action of estrogens (suppression of luteinizing releasing hormone secretion, deactivation of androgens, etc.) leads to a decrease in the level of testosterone in the blood.

Follow-up - during the entire treatment and after its completion, all patients need careful dynamic monitoring. PSA is a very sensitive test that allows early detection of prostate cancer, monitoring the effectiveness of treatment and monitoring after its completion. Therefore, a prerequisite for all follow-up visits to the doctor is the control of the PSA level.

Conclusion

Analysis of the literature data available to us shows the imperfection of methods for diagnosing and treating prostate cancer. Since the proposed diagnostic methods have a low or medium degree of specificity and sensitivity. Medical measures, despite a number of complications and unusual actions, are not ordered according to the stages of implementation. One or another measure and proved that the minimum and maximum "standard" is sufficient to achieve satisfactory results.

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