Therapies for Prostate Cancer and Treatment Selection

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Abstract: The number of patients with prostate cancer has been increasing rapidly as a result of the widespread use of prostate specific antigen (PSA) screening and the aging of society. In Japan, prostate cancer is now recording the highest rate of increase in prevalence amongst all types of cancer. Localized prostate cancer can be managed using various treatment options such as surgery, radiotherapy, and watchful waiting, and each of these therapies has further options. So long as patient selection is performed properly, the outcomes of these therapies are comparable. However, wide variations are seen in the effects of various therapies on complications and QOL. In addition, we must consider the fact that prostate cancer needs follow-up care for a relatively long period after treatment. Therefore, in choosing treatment options, we should consider not only the effects of treatment, such as survival, but also the changes in QOL after treatment. It is important to support patients through the provision of information concerning QOL, so that they can understand the treatment from a broader perspective.

Key words: Prostate cancer; Localized; PSA; QOL

Introduction

The number of patients with prostate cancer is increasing rapidly as a result of the widespread use of screening with prostate specific antigen (PSA), an effective tumor marker, and as a result of the aging of society. In the Japanese population, prostate cancer is now recording the highest rate of increase in prevalence among all types of cancer.

This article outlines the treatment options for prostate cancer, in particular early-stage cancer, showing a dramatic rate of increase in recent years.

Treatment Decision Processes with Patient Participation

Recent emphasis in the processes of cancer diagnosis and treatment has been placed on the
importance of patient participation in treatment decisions, predicated on the provision of medical information covering all aspects of the disease. In the case of prostate cancer, we can use this approach as discussed below.

After a definite diagnosis is made based on biopsy, the patient is told he has cancer, and receives information on prostate cancer in general. He receives an explanation concerning the need for staging examinations and a rough plan for treatment. Nowadays, many patients obtain information via the Internet. In our hospital, we not only provide patients with a written explanation, but also recommend them to access the Japanese version (http://www.ccijapan.com) of Physician Data Query (PDQ®) maintained by the National Cancer Institute (NCI) in the U.S. to provide cancer information for patients.

Next, the patient receives comprehensive information on his condition, including clinical staging, malignancy (Gleason score), and PSA. A detailed explanation is given concerning treatment options and their benefits and risks. A nomogram for estimating pathological staging from the above clinical parameters has been developed and introduced in clinical practice.1)

The patient chooses the optimal treatment for himself, based on comprehensive consideration of the information. During this process, physicians should evaluate the medical appropriateness of the patient’s choice and provide support toward treatment.

With these processes in mind, the following sections review therapies for early-stage prostate cancer and treatment selection.

Clinical Staging of Prostate Cancer

This section discusses important points regarding early-stage cancer as defined by clinical staging. Japanese Classification of Prostate Cancer and the TNM classification are illustrated. Conventionally, a cancer detected in the histopathological specimens from surgery for prostatic hyperplasia is classified as stage A in the former and stage T1 in the latter. This classification is specific to prostate cancer (Fig. 1).

Recently, a rapidly increasing number of cancers that are non-palpable on digital rectal examination are detected by needle biopsy performed because of abnormally elevated PSA. These cancers are collectively classified as B0 or T1c. Currently, many of the cancers detected by PSA screening and subjected to curative treatment are classified as T1c, and these cancers represent a considerable part of all prostate cancer cases.2)

Palpable cancers localized within the prostate are classified as stage B or T2 (Fig. 2). Of these, many of the cases with palpable cancer in both lobes of the prostate (T2b) are considered
treatment. If the disease is well-differentiated minute cancer in elderly patients, watchful waiting can be a good option for T1c cancer. Other cases are treated with curative therapies such as surgery and radiotherapy.

**Table 1 Treatment for Localized Prostate Cancer**

- Radical prostatectomy
  - Retropubic approach, perineal approach, laparoscopic approach
- Radiotherapy
  - External irradiation
  - 3D conformal radiation, intensity modulated radiation therapy
  - Brachytherapy
- Hormone therapy
- Watchful waiting

**Treatment Strategies According to Staging**

T1 and T2 cancers localized within the prostate are usually given curative treatment, such as radical prostatectomy and radiotherapy (Fig. 3). In locally advanced T3 cancer, the effectiveness of surgery or radiotherapy alone is limited, and a combination with hormone therapy is selected in many cases.

Cases with metastasis are treated with hormone therapy using LH-RH agonists, antiandrogens, or castration. However, hormone therapy is palliative. After a period of response, many cases develop into a condition of hormone-resistant cancer. Few chemotherapy regimens are effective for prostate cancer. While some are effective, none has been reported to contribute to the elongation of survival.

Minute T1 cancers are classified as T1a, and most of these do not require treatment. Non-palpable cancers that are detected only by abnormal PSA levels, i.e., T1c cancers, include a wide spectrum of conditions from non-life-threatening minute cancer to locally advanced cancer. The treatment for T1c cancers, therefore, has many options, and it is important for us to understand characteristics of each treatment. If the disease is well-differentiated minute cancer in elderly patients, watchful waiting can be a good option for T1c cancer. Other cases are treated with curative therapies such as surgery and radiotherapy.

**Treatment for Localized Prostate Cancer**

The main treatment options are radical prostatectomy, radiotherapy, and watchful waiting (Table 1). Hormone therapy is not a curative therapy; it should always be considered as a palliative treatment. Hormone therapy is often selected for exacerbation after watchful waiting and recurrence after curative treatment.

As mentioned above, watchful waiting is an important treatment option for suspected well-differentiated minute cancer and for elderly patients. In this case, regular PSA tests are essential. It may be said that watchful waiting is a viable treatment option owing to the ability of simple PSA tests to predict disease progression.

The recent progress of radiotherapy has also been remarkable. As for external irradiation, conventional rotation therapy and pendulum irradiation are being replaced by new methods, such as 3-D conformal radiation and intensity modulated radiation therapy (IMRT). In these methods, careful preplanning of the field of irradiation to fit the shape of the prostate enables high-dose irradiation to the organ.
with the primary cancer while minimizing the dose to surrounding organs. These methods achieved an enhancement of anticancer efficacy and a marked reduction of bladder and rectal disturbances.

Brachytherapy, which uses small radioactive sources placed in the prostate, is gaining support recently. This treatment is being performed as frequently as surgery in the U.S. Brachytherapy was approved in Japan in 2003, and its use as a low-invasive treatment is expected to expand.

As for surgery, radical prostatectomy is the most widely used treatment for early-stage prostate cancer. Operation methods have improved greatly in the last 10 years, and very stable outcomes are reported nowadays. In view of the invasiveness of treatment and its contribution to survival, patients considered for surgery should have at least 10 years of life expectancy.

Types of Surgical Therapy

A number of methods have been developed for radical prostatectomy, and each has various advantages.

The retropubic approach is the one used most frequently, and this method is well established. The perineal approach, as the name implies, does not involve surgical operation on the lower abdomen, and thus is less surgically invasive. The use of this method is also slowly increasing in Japan.

Laparoscopic radical prostatectomy is a newly developed method in which all procedures are performed using video assistance. Its advantages are small surgical wounds and quick postoperative recovery. However, much is left for future evaluation with respect to complete cancer elimination and functional recovery. Because laparoscopic radical prostatectomy has not been covered by national health insurance, patients who desire this surgery must bear the cost of treatment.

Anatomical Features of the Prostate and Treatment Complications

In discussing the characteristics of curative therapies for prostate cancer, it is important to understand the anatomy of the prostate and surrounding structures (Fig. 4). During surgery, the prostate and the seminal vesicle are removed as a mass, and the bladder is anastomosed to the urethra. The apical portion of the prostate is in contact with the external urethral sphincter. Along the posterior and lateral aspects of the prostate run the rectum and the cavernous nerves of the penis, the so-called “erection nerves.”

As seen from the anatomic locations of these structures, curative therapies for prostate cancer must be viewed from 2 aspects: (1) complete resection or disappearance of the prostate and (2) preservation of the important function of surrounding structures. With the increasing knowledge of pelvic anatomy, treatment techniques have been improved, and surgery that spares the erection nerves is extensively performed. The advance in preservation of function has been remarkable.

On the other hand, prostate cancer often develops in the posterior-lateral aspect of the prostate, i.e., in the vicinity of the erection nerves. Because the complete cure of cancer is
the priority in surgery, the appropriateness of nerve-sparing surgery must be determined carefully based on information such as preoperative tumor localization.

For these anatomical reasons, each type of therapy for localized prostate cancer may cause characteristic complications (Table 2).

Curative radical prostatectomy has been reported to cause postoperative urinary incontinence, sexual dysfunction (erectile dysfunction; ED), stenosis of vesicourethral anastomosis, and other specific complications, in addition to wound infection and other general surgery complications. Thanks to the improvement in methods of operation, urinary incontinence is rarely severe and disabling. It usually occurs transiently after surgery, and improves with the passage of time.

Postoperative ED is inevitable when nerves are not preserved. With nerve-sparing surgery, functional recovery can be expected to some extent. Recovery of sexual function can be expected even with unilateral nerve sparing procedures. When recovery of erection is insufficient, the use of Viagra® is likely to achieve recovery of sexual function in more than half of all cases.4

Complications of radiotherapy typically include anorectal injury (diarrhea, bloody stools, anal pain) and bladder dysfunction (increased urinary frequency, micton pain, difficulty in urinating) resulting from radiation exposure of adjacent organs. Many cases improve gradually with the passage of time after treatment. As a peculiarity of radiotherapy, rectal injury or ED can develop late after treatment. Recent development of 3-D conformal radiation and intensity modulated radiation therapy has reduced the occurrence of these complications.

In contrast with the above 2 types of curative therapies, watchful waiting cannot cause any direct complications. On the other hand, prolonged observation without treatment may cause a certain amount of psychological stress to the patient and a risk for stage progression during observation.

### Therapies for Early-Stage Prostate Cancer and QOL

Based on the points discussed above, we compare the patient’s QOL after surgery and radiotherapy in the treatment for early-stage prostate cancer (Table 3).

No difference is reported to occur between the effects of surgery and radiotherapy on general health-related QOL. Including physical function, mental health, social life, and daily role function.

On the other hand, there are marked differences in disease-specific QOL directly related to prostate cancer treatment.5 With respect to urinary incontinence, radiotherapy provides better QOL outcomes than surgery. However, because surgery removes the prostate with hyperplasia, it dramatically improves lower urinary tract symptoms such as difficulty in

### Table 2 Therapies for Localized Prostate Cancer and Complications

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Complications</th>
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<tbody>
<tr>
<td>Curative radical prostatectomy</td>
<td>Urinary incontinence, sexual dysfunction (ED), stenosis of vesicourethral anastomosis, general complications of surgery</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>Anorectal injury, bladder dysfunction, late radiation injury</td>
</tr>
<tr>
<td>Watchful waiting</td>
<td>Psychological stress, stage progression</td>
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</tbody>
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### Table 3 Therapies for Early-Stage Prostate Cancer and QOL

<table>
<thead>
<tr>
<th>General health related QOL</th>
<th>Surgery vs. Radiotherapy</th>
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<tr>
<td>Disease-specific QOL:</td>
<td>Surgery vs. Radiotherapy</td>
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<tr>
<td>Urinary continence</td>
<td>Surgery &lt; Radiotherapy</td>
</tr>
<tr>
<td>Lower urinary tract symptoms</td>
<td>Surgery &gt; Radiotherapy</td>
</tr>
<tr>
<td>Sexual function</td>
<td>Surgery &lt; Radiotherapy</td>
</tr>
<tr>
<td>Bowel function</td>
<td>Surgery &gt; Radiotherapy</td>
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Good > Poor
urinating and increased urinary frequency. Radiotherapy often causes transient aggravation of urination symptoms shortly after treatment, as a result of inflammation and other effects of irradiation. With respect to sexual function, surgery tends to result in poorer QOL because of the risk for surgical damage to erection nerves. Since surgery has almost no effect on the rectum, it provides better QOL related to bowel function than radiotherapy.

As summarized above, the 2 representative methods of curative treatment provide characteristic QOL outcomes after treatment. It is important that patients understand these differences. We also need to pay attention to the fact that this scheme on QOL may change with progress after treatment. Finally, it should be noted that recent remarkable developments in both surgery and radiotherapy have been reducing these differences in QOL outcome.

Conclusion

This paper outlines the therapies for prostate cancer and the process of treatment selection focusing particularly on localized prostate cancer, which is often detected by PSA tests. The treatment for localized prostate cancer has many options, including surgery, radiotherapy, and watchful waiting, and each of these therapies also includes many options. As long as patient selection is performed properly, the outcomes of these therapies are comparable. Wide variations are seen in the effects of various therapies on complications and QOL. In addition, we must consider the fact that prostate cancer needs followup care for a relatively long period after treatment.

Therefore, in choosing treatment options, we should consider not only treatment effects such as survival but also the changes in QOL after treatment. It is important to support patients through the provision of information concerning QOL, so that they can understand the treatment from a broader perspective.

REFERENCES