The American Urological Association
Prostate Cancer Clinical Guidelines Panel

The Management of Localized Prostate Cancer

A Patient's Guide

Prostate Cancer Clinical Guidelines Panel

Members:
Richard G. Middleton, MD, Co-Chair
Ian M. Thompson, MD, Co-Chair
Mark S. Austenfeld, MD, Facilitator
William H. Cooner, MD
Roy J. Correa, Jr., MD
Robert P. Gibbons, MD
Harry C. Miller, Jr., MD
Joseph E. Oesterling, MD
Martin I. Resnick, MD
Stephen R. Smalley, MD
John H. Wasson, MD

Consultants:
Claus G. Roehrborn, MD
Hanan S. Bell, PhD
Brent Blumenstein, PhD
Scott Optenberg, Dr. PH
Patrick M. Florer
Curtis Colby, Editor

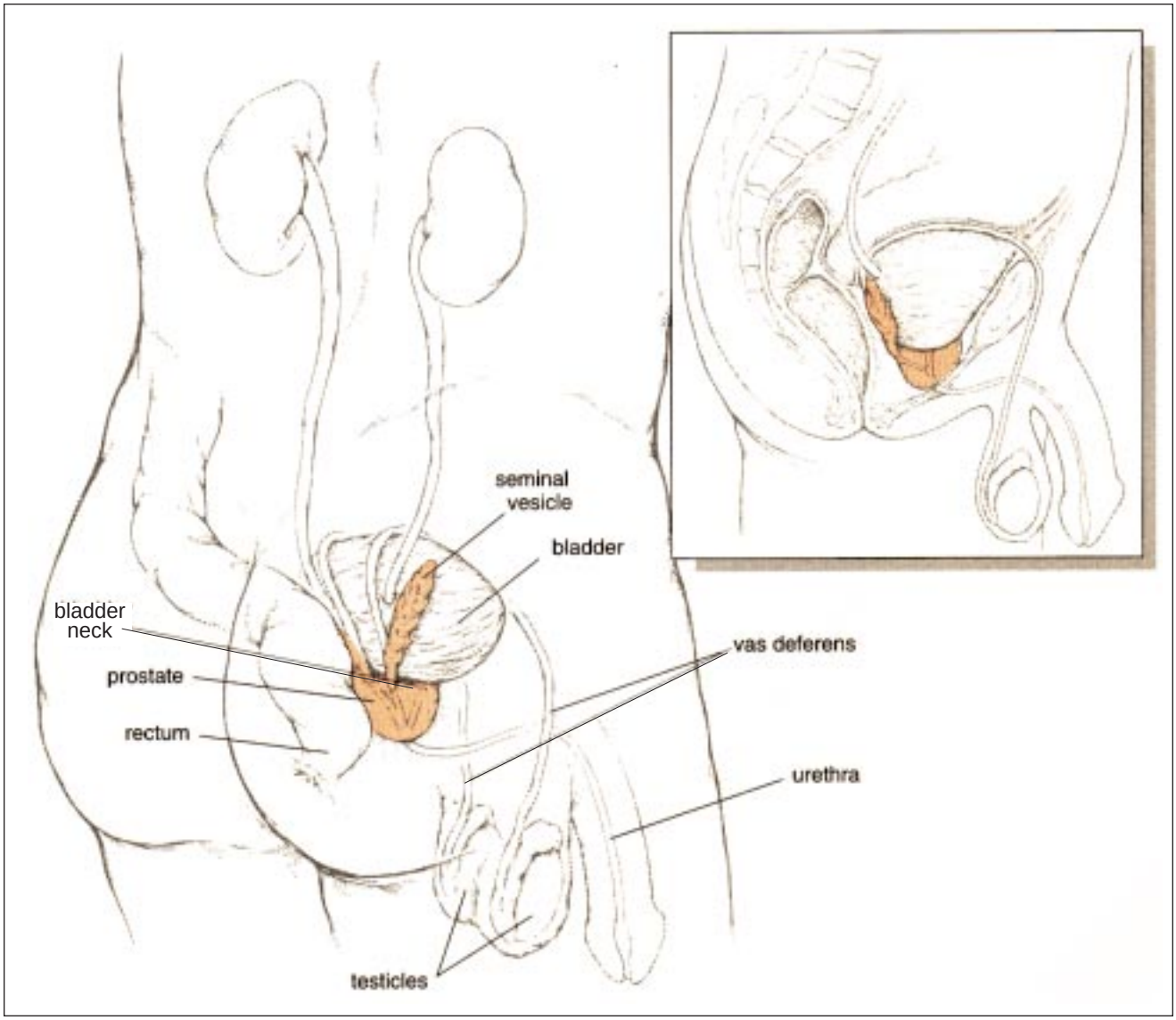
What is the prostate?

The prostate is a walnut-sized gland located just below the bladder. It surrounds the bladder neck and urethra as shown in Figure 1. Also shown in Figure 1 are the testicles, seminal vesicles and each vas deferens.

The prostate's main purpose is to produce fluid for semen. During a man's orgasm, the fluid from the prostate is squeezed into the urethra. At the same time, sperm and other substances enter the urethra from the seminal vesicles and vasa deferentia. The resulting mix is semen, which carries the sperm through the urethra and out the penis during ejaculation.

As a man ages, cancer may develop in his prostate. Men over age 50 are at the greatest risk, but prostate cancer can develop in younger men as well. It is the most common type of malignant tumor in the male population overall. There is no known way to prevent prostate cancer, but treatment may be effective when the cancer is detected early.

Figure 1.



What is localized prostate cancer?

Localized prostate cancer is a tumor that has not spread beyond the prostate. This is important. If the cancer spreads beyond the prostate, it is more difficult to manage, and the risk of dying from the cancer increases.

About 67 percent of newly diagnosed prostate tumors are localized. Given enough time and left untreated, these localized tumors can be expected to grow in size and spread. Certainly they will not disappear. Prostate cancer does not cure itself.

However, growth rates for this type of cancer vary widely. Some tumors advance rapidly. Yet, in many cases of newly diagnosed localized prostate cancer, the tumors grow quite slowly over many years. For example, an 80-year-old man diagnosed with localized prostate cancer will very likely die of some other cause before his cancer grows enough to become lethal.

What are the symptoms of localized prostate cancer?

In the early stages of prostate cancer, when a tumor is small and localized, there are no symptoms. Not until a tumor grows large enough to press on the urethra and cause urinary problems do symptoms occur. By that time, the cancer may have spread beyond the prostate. Treatment is then less effective.

How is prostate cancer diagnosed?

Several tests may be needed to identify the presence of prostate cancer and to determine if it has spread. Some localized cancers may be detected by a **digital rectal exam (DRE**). This is a simple test in which the doctor inserts a lubricated, gloved finger into the rectum and feels the prostate for signs of cancer.

A **PSA test**, used in addition to DRE, increases the likelihood of cancer detection. PSA is the abbreviation for *prostate-specific antigen*, a substance produced only by the prostate. A PSA test measures the level of PSA in the bloodstream. Very little PSA escapes from a healthy prostate into the bloodstream, but certain prostatic conditions can cause larger amounts of PSA to leak into the blood. One possible cause of a high PSA level is benign (noncancerous) enlargement of the prostate. This common condition presents no serious problems in most cases. Among the other possible causes, however, is cancer.

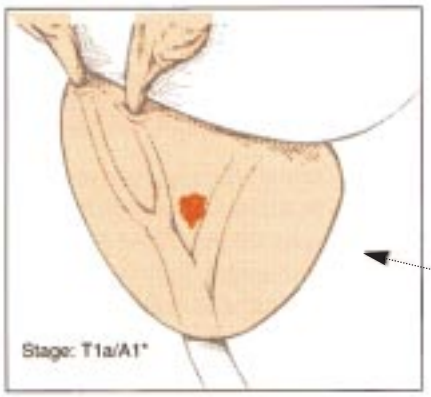
Thus, a high level of PSA in the bloodstream is a warning sign that prostate cancer may be present. This can be a useful signal. PSA testing has helped detect hundreds of thousands of prostate cancers that otherwise might not have been found. Yet, because other kinds of prostatic disease can also cause high PSA levels, PSA testing by itself cannot confirm the presence of cancer. A high PSA level only indicates the possibility of prostate cancer and the need for additional evaluation.

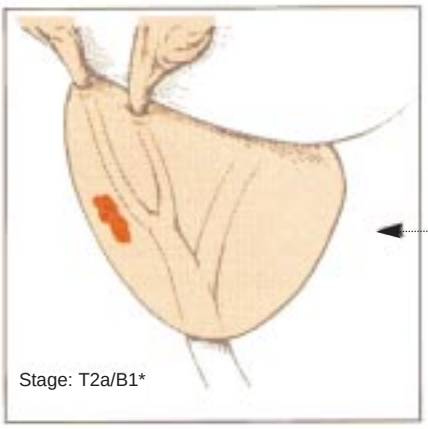
Moreover, a low PSA level does not always mean that prostate cancer is not present. An early-stage cancer may be present that has not yet caused PSA to increase in the bloodstream.

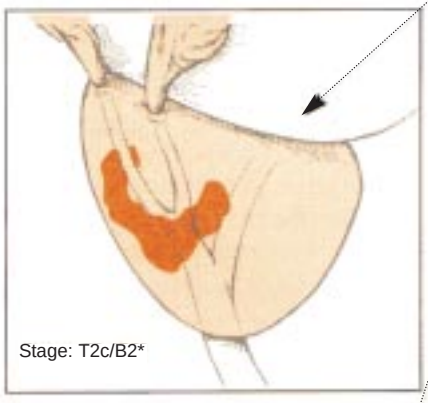
Finally, the results of either or both tests (DRE and PSA) may suggest the need for a **biopsy**. In a biopsy, a small amount of tissue is removed from the prostate with a needle. This tissue is then examined under a microscope for cancer cells. **Transrectal ultrasonography (TRUS)** is often used to guide the needle during a biopsy. TRUS employs high-frequency sound waves (ultrasound) to create a visual image of the prostate.

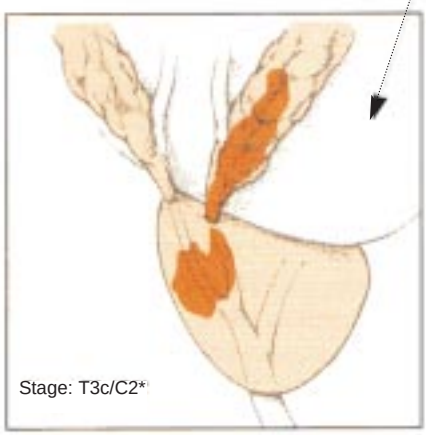
Biopsies are invasive procedures. Short-term side effects such as infection and minor rectal bleeding can occur, but serious complications are quite unusual. Only a biopsy can definitely confirm the presence of prostate cancer.

Figure 2.









TNM and ABCD Staging Systems

Stage		
TNM	**ABCD**	**Description**
T0		No evidence of tumor
T1a	A1	Clinically inapparent tumor found incidentally in tissue resected from prostate for other reasons, tumor involving **5% or less** of tissue resected
T1b	A2	Clinically inapparent tumor found incidentally in tissue resected from prostate for other reasons, tumor involving **more than 5%** of tissue resected
T1c	B0	Tumor that cannot be felt with DRE, identified because of high PSA level in bloodstream
T2a	B1	Tumor involving half or less of one prostate lobe
T2b	B1	Tumor involving more than half of one lobe, but not both lobes
T2c	B2	Tumor involving both lobes
T3a	C1	Unilateral extension of tumor outside prostate
T3b	C1	Bilateral extension of tumor outside prostate
T3c	C2	Tumor invading one or both seminal vesicles
T4a	C2	Tumor invading bladder neck and/or external sphincter and/or rectum
T4b	C2	Tumor invading additional areas adjacent to prostate
N0		No regional lymph node metastasis
N1	D1	Metastasis in a single lymph node, 2 cm or less at greatest dimension
N2	D1	Metastasis in a single lymph node more than 2 cm, but not more than 5 cm at greatest dimension, or in multiple lymph nodes none more than 5 cm at greatest dimension *(see diagram on facing page)*
N3	D1	Metastasis in a lymph node more than 5 cm at greatest dimension
M0		No distant metastasis
M1	D2	Distant metastasis, such as spinal column *(see diagram on facing page)*

*Cancer indicated by dark shading in figures.

What is tumor grade?

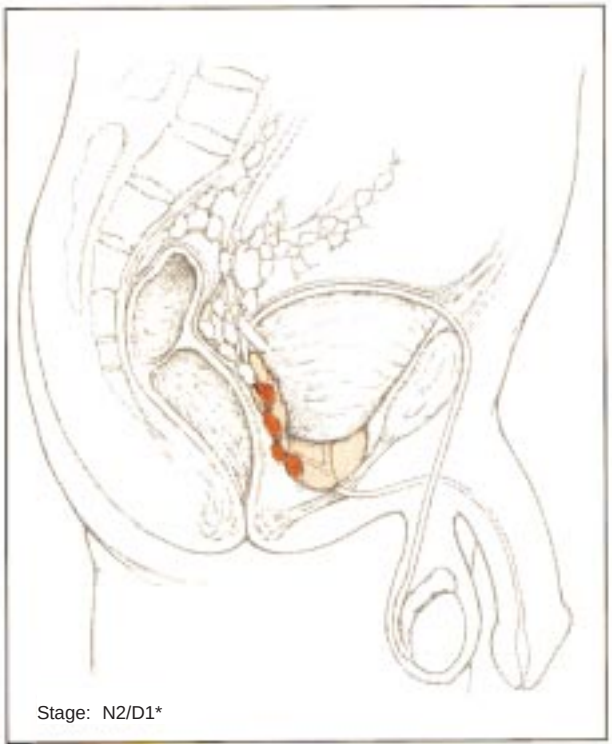
If a biopsy is taken, and prostate cancer is found, the pathologist who examines the tissue will grade the tumor. The grade indicates the tumor's "aggression level"—how quickly it is likely to grow and spread. Pathologists are specialists who interpret changes in body tissues caused by disease. The pathologist will grade the tumor based on its appearance under the microscope.

One common system for indicating tumor aggression levels is by Gleason score. Gleason scores range from 2 to 10. A score of 2 – 4 indicates low aggressiveness, and 5 – 6 moderate aggressiveness. A score of 7 – 10 means an aggressive tumor. This system is not perfect, but Gleason scores do provide an indication of how quickly particular prostate cancers may spread.

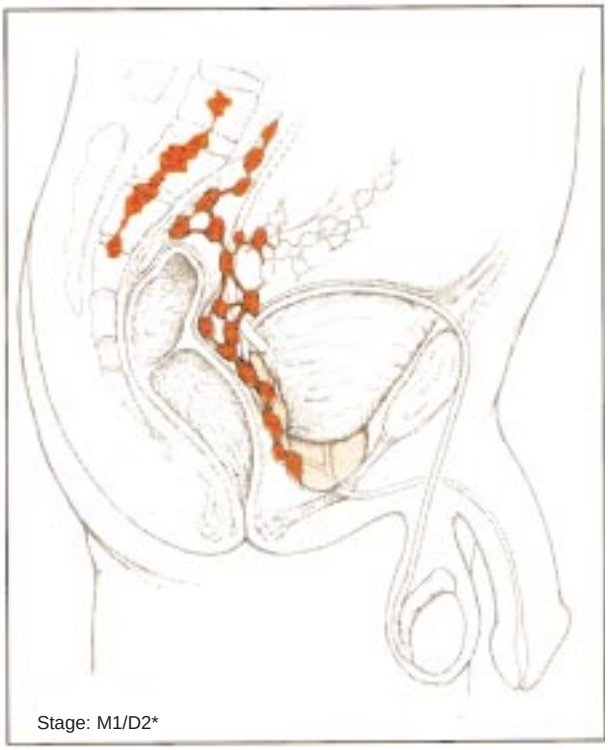
How is prostate cancer staged?

Staging of prostate cancer means estimating the size and location of the cancer (how far it has already spread). Staging is necessary to decide what type of treatment, if any, is most appropriate. There are a number of staging methods. Some of them, like DRE and PSA testing, are the same methods used to help detect prostate cancer.

Figure 2 on page 4 shows the main stages of prostate cancer. To classify the stages, one of two different systems may be used. Classification symbols from both these systems, the TNM system (T0 through M1) and the ABCD system (A through D), are shown side by side in Figure 2. Note that stages T1 – T2 in the TNM system, and A – B in the ABCD system, are clinical stages for prostate cancer that is localized.



Stage: N2/D1*



Stage: M1/D2*

What are the choices for treating localized prostate cancer?

The three generally accepted options for treating localized prostate cancer are radical prostatectomy, radiation therapy and surveillance. Other treatments are considered investigational because not enough patients have been followed and tested long enough to know how well the treatments work.

The first option, **radical prostatectomy**, is an open surgical procedure. The entire prostate and nearby tissues are removed while the patient is under anesthesia.

For the second option, **radiation therapy**, there are two types. The most widely used type, **external beam radiation therapy**, treats the prostate and other selected tissues with a carefully targeted beam of radiation from a linear accelerator. There is no surgery. In the other type, called **brachytherapy**, tiny radioactive "seeds" are implanted in the prostate. This requires a surgical procedure. Placement of the "seeds" is usually guided by transrectal ultrasound. In some cases, both brachytherapy and external beam radiation therapy may be used.

The third option, **surveillance**, or observation, means no active treatment immediately. There are regular examinations to check for cancer growth. If an examination's results at any point suggest a need for active treatment, radical prostatectomy or radiation therapy may be recommended.

What are the benefits and risks of each treatment?

Radical prostatectomy

Radical prostatectomy's chief benefit is that it may remove all of the cancer. If the tumor is truly localized, taking out the prostate takes out the tumor as well. Staging methods, however, are not always accurate. A cancer thought to be localized may turn out not to be. In such cases, removing the prostate may not remove all of the cancer. Nevertheless, for localized prostate cancer, treatment by radical prostatectomy offers the patient a very good chance he will be free of the disease for the rest of his life.

Radical prostatectomy's chief disadvantage is the risk of complications resulting from the operation. **Figure 3** illustrates this risk graphically. The graph is based on complications reported in the medical literature for patients who had radical prostatectomies. Selected complications are listed across the bottom of the graph. Each circle in the column above a listing represents a group of patients for whom the listed complication was reported.

Percentages are listed up the left edge of the graph. How high a circle appears on the graph indicates how large a percentage of that patient group experienced the complication.

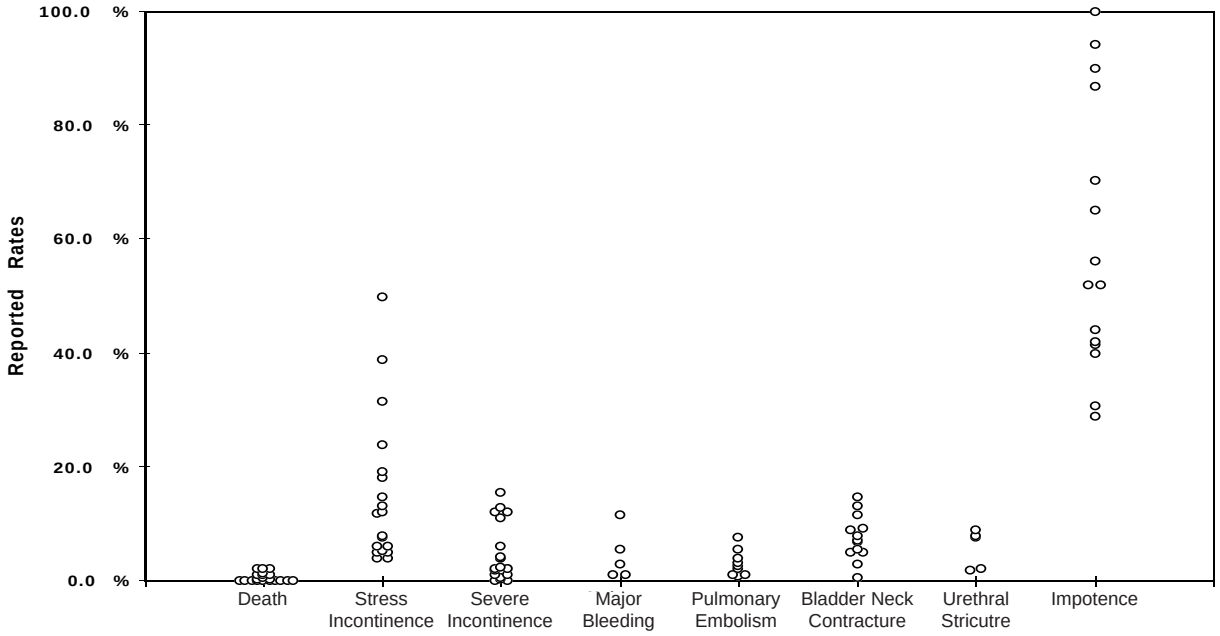
Death is the first listing. Note that although the graph does show some risk of death following surgery, the risk is very low. This can be seen from the number of circles clustered on or close to the 0-percent level.

By contrast, Figure 3 shows a high risk of impotence following radical prostatectomy. Impotence is the inability to achieve or maintain an erect penis. Most circles for the impotence listing on the graph are above the 50-percent level. In those groups, more than half the patients experienced impotence as a complication following radical prostatectomy.

The risk of impotence varies with individual patients. It often depends on a patient's age and health, on the stage of his cancer and on the skill of the surgeon. If impotence does occur following surgery, a number of options are now available to treat the problem. How impotence and other complications might be treated are questions to ask the doctor. *(See page 10.)*

The graph also shows a risk of urinary incontinence after radical prostatectomy, especially stress incontinence. Urinary incontinence is the involuntary loss of urine. In stress incontinence, the leakage occurs with some kind of physical activity,

Figure 3. Complications: Radical prostatectomy



such as during coughing, sneezing, a sudden change of position or physical exertion. Severe incontinence means a nearly continuous leakage that requires several pads a day.

The most recent articles in the medical literature report a rate of less than 5 percent for severe incontinence after radical prostatectomy. Up to 30 percent of patients, however, may have occasional dripping for a while. In most patients, the dripping eventually stops without need for special treatment.

Other complications shown on the graph in Figure 3 are major bleeding, pulmonary embolism, bladder neck contracture and urethral stricture. Major bleeding simply means more bleeding than usual. (This may be treated with a blood transfusion.) Pulmonary embolism means that a blood clot (called an embolus) travels through the bloodstream and lodges in an artery of the lung. Most clots dissolve within a short time after injection of an anticoagulant drug.

Bladder neck contracture and urethral stricture involve scarring and scar tissue formation that could obstruct the flow of urine. If the urine flow is obstructed, another operation may be needed.

A radical prostatectomy, even with no complications, requires a patient to spend a certain number of days in the hospital. This number has been decreasing in recent years. At present, it is about three to six days. When the patient leaves the hospital, he will still have a tube called a catheter in his bladder. The catheter is there temporarily to drain urine from the bladder. Usually it can be removed after 10 to 21 days.

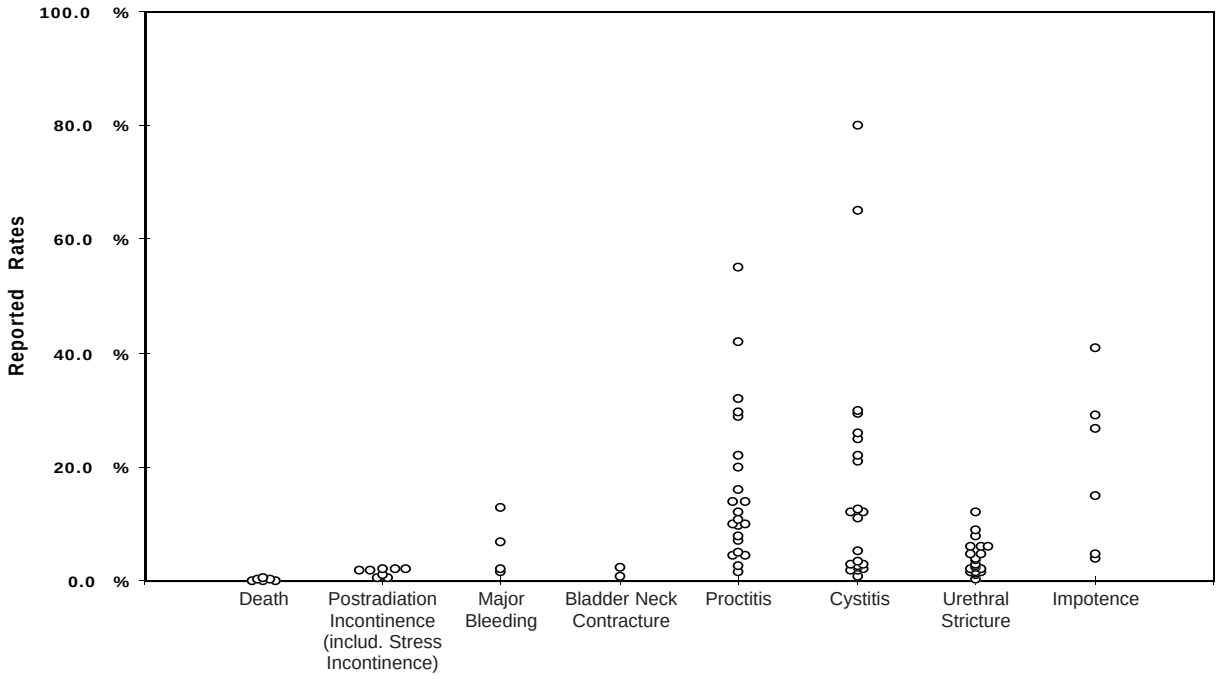
Radiation therapy

External beam radiation is the major type of radiation therapy used for localized prostate cancer. Results reported in the medical literature show it to be an effective therapy. The results are especially favorable for the first 10 years after treatment. Some recent reports indicate good results for 20 years or more after treatment.

In addition, external beam radiation has the advantage of being well tolerated by most patients. Modern techniques enable the radiation beam to be aimed with great precision at target areas. This precise targeting kills cancer cells while minimizing the effects of radiation on normal tissues.

One disadvantage of external beam or of any type of radiation therapy is that it leaves the prostate in place. Consequently, the possibility exists that some cancer may remain and recur in future years. Also, even though modern techniques

Figure 4. Complications: External beam radiation



lessen the effects of radiation on normal tissues, there are potential complications.

Figure 4 indicates graphically the risks of complications from external beam radiation. As in the graph for complications following radical prostatectomy (Figure 3), each circle represents a group of patients for whom a particular complication was reported in the medical literature.

A comparison of Figures 3 and 4 shows several similar complications for both types of treatment. The risks of incontinence and impotence appear somewhat lower following external beam radiation therapy. However, Figure 4 shows high risks for proctitis and cystitis. Proctitis is the inflammation of the rectum, and cystitis is the inflammation of the bladder. In some cases following radiation therapy, these complications may be severe and long lasting. In most cases, they are mild and short-lived side effects that disappear without further treatment.

A patient does not need to be hospitalized to receive his doses of radiation. Each external beam radiation treatment lasts only a few minutes. The whole course of treatments, however, takes six to eight weeks. Over that period of time, the patient goes for a treatment once a day, five days a week.

The second type of radiation therapy is **brachytherapy** (in which radioactive "seeds" are implanted in the prostate). Use of brachytherapy has been increasing. However, few long-term results have been reported for the techniques currently used to place the "seeds." Therefore, it is still not possible to reach general conclusions about the benefits and risks of modern brachytherapy techniques.

Surveillance

Management of localized prostate cancer by surveillance, or regular examinations with no active treatment, has two chief advantages. These are low initial cost and no immediate side effects or complications. Surveillance may be a reasonable choice for a patient diagnosed with localized prostate cancer that is at an early stage with a low grade (Gleason score, 2–4). Evidence from the medical literature indicates that such a patient has a reasonably strong possibility of surviving the cancer for at least 10 years.

The chief disadvantage of surveillance is that, with time, the cancer could advance and become incurable. If it spreads beyond the prostate during the period between checkups, there is a good chance the eventual results will be deadly. Moreover, when prostate cancer spreads, it often spreads into the bones. A patient's quality of life could be painfully restricted before he dies.

What should be considered in choosing a treatment option?

Four considerations are especially important in choosing a treatment option: the stage of the cancer (how far it has spread), its grade (Gleason score), the age of the patient and the patient's values—what he thinks is most important.

Cancer stage

The lower the stage of prostate cancer, the better the results are likely to be from any form of treatment—including surveillance. Patients with stage T2a tumors can be considered to have low-stage prostate cancer. However, patients whose tumors have advanced to stage T2c may be in danger of having the cancer spread beyond the prostate. Surveillance may be less of an option for these patients. *(See Figure 2 on page 4.)*

Cancer grade (Gleason score)

Similar to patients with low-stage prostate cancer, patients with low-grade tumors (low Gleason scores) will generally have better treatment results than patients with high-grade tumors regardless of the type of treatment. *(See page 5 for discussion of Gleason scores.)*

Gleason scores for most newly diagnosed tumors are in the 4 – 6 range. Long-term cure rates from active treatment of patients with high-grade tumors (Gleason score of 7 – 10) are much less favorable than cure rates from treating patients with a Gleason score of 2 – 6. If prostate cancer patients with high-grade tumors choose no treatment, the majority will die of their disease.

Patient's age

Low-stage, low-grade, localized prostate cancer left untreated often grows slowly. It may cause no problems for 5 to 10 years. For this reason, older men—particularly older men with other medical problems—may have a low risk of ever experiencing problems from their prostate cancer. However, a man with a life expectancy of more than 10 years may live long enough to develop problems. Reports in the medical literature indicate that patients who choose surveillance tend to be older than patients who choose an active treatment such as radical prostatectomy.

Patient's values

Because individual patients differ in what they consider important, they choose different trade-offs (often in consultation with their families). Some men, no matter what their age or the stage and grade of their tumor, simply do not want to walk around knowing they have prostate cancer if they can do something about it. They will risk the chance of impotence or incontinence for a chance to cure their disease.

Other men are more concerned about how the potential complications of a particular treatment could affect the quality of their lives. They may choose a treatment with less chance of cure rather than risk a complication such as incontinence or impotence. The patient's personal values are often the most important factor of all in choosing a treatment.

Questions to ask the doctor

❑ How advanced is my prostate cancer?
What is its stage? (How far is it estimated to have spread?)

❑ What is my cancer's grade? (How quickly is it likely to spread?)

❑ Do I need further tests? Why or why not?

❑ Do I need a second opinion?

❑ What are my treatment choices (including surveillance)?
What are the advantages and disadvantages of each?

❑ What are the chances for each active treatment to cure my cancer?

❑ What are the risks of complications from each treatment?
What kinds of complications are likely from each?
How are the complications themselves treated—for example, impotence or incontinence?

❑ How much will each prostate cancer treatment cost?
How much will treating possible complications cost?

❑ If I choose surgery, how many days will I be in the hospital?
How much time will I need to fully recover?

❑ If I choose radiation therapy, how much time will be required?

❑ What is likely to happen if, for now, I choose no treatment (surveillance)?
How frequently will I need examinations while under surveillance?

Additional questions to ask the doctor:

❑ _____

❑ _____

❑ _____

Glossary

Anticoagulant: A substance that hinders clotting of blood.

Bladder neck: Area of thickened muscle fiber where the bladder opens into the urethra *(See Figure 1)*. Acting on signals from the brain, bladder neck muscles can either tighten to hold urine in the bladder or relax to allow urine out and into the urethra.

Bladder neck contracture: Scarring of tissue at the bladder neck as a complication of surgery. Bladder neck contracture may lead to urinary problems that require further surgery to correct.

Cystitis: Inflammation of the bladder, often marked by painful urination. Cystitis is a possible side effect of radiation therapy but is usually short-lived.

Impotence: Inability to achieve a penile erection sufficient for sexual intercourse. Impotence is also known as "erectile dysfunction."

Invasive: Involving cutting or puncturing the skin or inserting instruments into the body.

Lymph nodes (or lymph glands): Small rounded masses of tissue distributed along the lymphatic system—most prominently in the armpit, neck and groin areas. Lymph nodes produce special cells that help fight off foreign agents invading the body. Lymph nodes also act as traps for infectious agents.

Malignant tumor (cancer): A new growth of tissue (tumor) in which the cells multiply uncontrollably, with a potential for spreading from one organ to other parts of the body and eventually resulting in death.

Metastasis: Spread of the disease from a bodily organ to other, unrelated parts of the body.

Proctitis: Inflammation of the rectum often marked by pain, diarrhea and rectal bleeding. As a side effect of radiation therapy, proctitis is short-lived in most cases.

Rectum: The lower part of the large intestine, ending in the anal opening.

Semen: Thick whitish fluid made up of substances produced by the prostate, seminal vesicles and other glands of the male reproductive system. Sperm, produced by the testicles, are carried by semen through the urethra and out the penis during ejaculation.

Seminal vesicles: Two pouch-like glands behind the bladder. They produce a thick gel, one of the substances from which semen is formed.

Sperm: Male germ cells (gametes or reproductive cells).

Sphincter: A band of muscle fibers that can relax or tighten to open or close a bodily opening or passage.

Testicles: Paired, egg-shaped glands contained in a pouch (scrotum) below the penis. They produce sperm and the male hormone testosterone.

Urethra (male): A tube extending from the bladder neck to the tip of the penis. During urination, the urine enters the urethra at the bladder neck and travels the tube's entire length. During sexual orgasm, semen enters the prostatic part of the urethra (Figure 1), goes through the penile urethra and ejaculates from the tip of the penis.

Urethral stricture: Scarring of tissue in the urethra as a complication of surgery, narrowing the channel. The resulting urinary difficulties may require corrective surgery.

Vasa deferentia (singular, vas deferens): Two tubes (Figure 1) through which sperm travel from the testicles to the seminal vesicles and urethra.

Where to find more information

American Foundation for Urologic Disease
1128 North Charles St.
Baltimore, MD 21201
410.468.1800

Cancer Information Service
National Cancer Institute
National Institutes of Health
800.4CANCER (800.422.6237)

This publication is intended for patients and lay readers. It is a summary of the Report on the Management of Clinically Localized Prostate Cancer, developed by the American Urological Association, Inc., and the Prostate Cancer Clinical Guidelines Panel.

The report is intended to furnish to the skilled practitioner a consensus of clear principles and strategies for quality patient care, based on current professional literature, clinical experience and expert opinion. It does not establish a fixed set of rules or define the legal standard of care, preempting physician judgment in individual cases.

An attempt has been made to recommend a range of generally acceptable modalities of treatment, taking into account variations in resources and in patient needs and preferences. It is recommended that the practitioner articulate and document the basis for any significant deviation from these parameters.

Finally, it is recognized that conformance with these guidelines cannot ensure a successful result. The parameters should not stifle innovation, but will, themselves, be updated and will change with both scientific knowledge and technological advances.

For additional copies, please contact:

American Urological Association
Health Policy Department
1120 N. Charles Street
Baltimore, MD 21201
410-223-4310