

Surgery for Prostate Cancer

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Prostate cancer is common and the management is highly controversial. In 2014, it was the most common cancer (other than skin cancer) in the United States and the third leading cause of cancer death among men. It represents 14% of all new cancer cases in the United States (1).

Screening for prostate cancer is controversial. However, since widespread screening was instituted in the early 1990s, the 5-year survival rate improved, from 75% in 1985 to 99.8% in the early 2000s (2).

Once diagnosed, not all men need treatment (3). New genetic testing is available and approved by the FDA that can help decide which men need treatment and which can undergo active surveillance (4).

Screening has led the over-diagnosis of painless, slow-growing cancers that don't need treatment (5). Therefore, once diagnosed, it's important to seek different opinions from different specialists – the urologist, radiation oncologist and medical oncologist. These doctors specialize in prostate cancer treatment and each will have a slightly different perspective on each individual case.

It is extremely rare for a newly diagnosed prostate cancer to require "emergency "or immediate treatment. For those men that decide to have treatment or where treatment is recommended it is generally acceptable to begin therapy within 6 months of diagnosis. The bottom line is that men with newly diagnosed prostate cancer have time to make a decision about which treatment that is right for them.

For example, even for men that qualify for active surveillance, a significant number will demand treatment for a variety of reasons: daily anxiety over a cancer diagnosis, troublesome urination caused by a large prostate or the cost, risk and discomfort of necessary future biopsies, to name a few. In 2015, personalization of prostate cancer treatment has become the standard of care.

Surgery has several advantages over radiation therapies and other non-surgical options, such as cryosurgery, HIFU and laser focal therapy. The primary advantages are listed below:

- 1. Accurate staging.
- 2. Relief of obstructive voiding symptoms (like getting up at night and slow stream).
- 3. It has the best cure rate.
- 4. PSA becomes truly meaningful.
- 5. It allows us to make rational decisions regarding immediate treatment after surgery.
- 6. Salvage therapy (for recurrence) is well tolerated and relatively easy to do.
- 7. Hormone therapy (and therefore the side effects) prior to surgery is not necessary.

Accurate Staging

Though the tools we have for assessing extent and aggressiveness of prostate cancer after initial diagnosis are good, they are far from perfect. Removing the entire prostate, seminal vesicles (which are sometimes involved with cancer) and lymph nodes from specific areas allow us the best possible way to remove as much cancer as possible and know the most we can about the extent of it. The pathologist examines all of the tissue that is removed, reassesses the Gleason Score (because he now has the entire prostate to look at) and can tell us the margin status (positive or negative), if there is invasion of the seminal vesicles and if and how many lymph nodes are involved. Knowing this information then allows the urologist to use a nomogram (a prediction tool) to assess the likelihood of cure. In addition, the slides can be assessed for genetic markers in a test recently approved by the FDA know as Decipher (see below). This test can help decide if a patient will benefit from early (beginning 3 to 4 months after surgery) radiation therapy.

Relief of Obstructive Voiding Symptoms

As men age, they frequently develop obstruction to the urinary stream from the prostate. This process results primarily from large prostates but can also be caused by the shape of the prostate as well, regardless of prostate size. This results in slow stream, poor emptying of the bladder, retention of urine, predisposition to urinary tract infections, urinary bladder stones, getting up at night to urinate and urgency of urination. These obstructive voiding symptoms from bladder outlet obstruction are generally worsened by radiation – which causes swelling of the prostate and irritation to the bladder (and rectum). However, these symptoms are relieved by surgery, because surgery gets the prostate out of the way of the bladder.

Urologists often have men fill out questionnaires about their voiding and sexual function to better understand these functions. When measure urinary function with a device known as a Uroflow machine, we see that men routinely improve after surgery but stay the same or worsen after any kind of radiation.

Surgery has a Better Cure Rate than Radiation

A recent study from Sweden (6) reported the overall survival and cancer-specific survival in men treated for prostate cancer between 1996 and 2010. 98% of all men treated for prostate cancers in Sweden were captured. This compared 21,533 men treated with surgery and 12,982 men treated with radiation. Median follow up was 5.37 years and men were matched based on risk groups. In all groups, except when men already had metastatic prostate cancer, surgery was significantly better in reducing death from prostate cancer and death from any cause.

This is not the only study to find this (7, 8, 9, 10). A study published in European Urology in 2011(7) reviewed 404,000 men treated for prostate cancer and found that the 10-year, cancer-specific mortality rate was 5 times worse (29.2% vs 6.1%) in men treated with radiation. Radiation therapy was better than surgery in octogenarians –but octogenarians rarely need treatment at all because prostate cancer is slow growing. Most octogenarians can be safely monitored with active surveillance.

P_{SA} Becomes Truly Meaningful

Immediately after radiation, the PSA will rise unless the patient is on hormone therapy. It then slowly begins to lower but is always detectable. In addition, somewhere between 15% and 25% of patients that receive radiation of any kind also will undergo a "PSA Bounce". This is where the PSA can spike to as high as 15ng/ml within 3 years of receiving treatment. It is thought that this phenomenon happens because of radiation prostatitis – inflammation in the prostate caused by the radiation. This is very unnerving for patients and doctors alike because we can never tell if this PSA elevation is from prostatitis or persistent cancer. Furthermore, prostate biopsies are unreliable within the first 2 years following radiation.

If a prostate biopsy shows persistent cancer within 2 years of receiving radiation, we don't know if the cancer is still dying from the treatment or if it is going to survive and continue to grow. After prostatectomy, however, the PSA should be lower and become non-detectable within about 6 weeks of surgery.

Of all men that have prostatectomy, about 25% have a subsequent rise in the PSA value. A subsequent rise of PSA doesn't always mean that cancer has returned, but sometimes it does and those patients sometimes receive external beam radiation to the previous location of the prostate known as the "prostate bed." This is referred to as "salvage radiation. The point is that after surgery the PSA should be non-detectable (we shouldn't find any PSA). If at some point the PSA rises, we know something is up and we investigate.

Rational Decisions about Follow-up Treatment after Surgery

Based on the pathology analysis that we have within a week of surgery and based on a recently FDA approved genetic test, "Decipher" (11) we will determine appropriate follow up treatment after surgery. This test allows us to assess if the patient will benefit from radiation therapy shortly after the patient recovers from surgery. Based on the pathology we can also determine if the patient my benefit from short term or permanent hormone therapy. After radiation, we just have to wait and see what happens. If the PSA is rising after radiation treatment (external beam, proton beam or seeds) then a series of scans are ordered and if these are negative, a prostate biopsy is done to see if persistent or recurrent cancer is in the prostate.

Salvage Radiation Therapy can be Effective and is Safe after Surgery

Arnold Palmer, the famous professional golfer, is the best public example of how delayed radiation after surgery is sometimes necessary to "mop up" residual cancer cells. This can happen even if the pathology indicates that the cancer was completely confined to the prostate. Presumably in these cases, cancer cells have skipped outside the prostate and were not removed with prostatectomy.

Mr. Palmer underwent a radical prostatectomy in January of 1997. Subsequently his PSA became detectable and was rising. As a result, in the fall of 1998 he was treated with radiation therapy to the prostate bed, where the prostate had originally resided (12). Mr. Palmer went on to live a long life and was cured of prostate cancer. He died of natural causes in late 2016.

The bottom line is that PSA recurrence after radical prostatectomy is a very manageable and more often than not, salvage radiation solves the problem. Salvage radiation is generally well tolerated and typically has minimal complications. Conversely, when the PSA rises after radiation it is a difficult problem to sort out what this means. It could be a "PSA bounce" (see above), a persistence or recurrence of cancer in the prostate itself or represent cancer in areas (lymph nodes, bone) other than the prostate (called metastasis).

Men will need multiple X-rays and a biopsy of the prostate to sort out what the source of the PSA is. Treatment options will include hormone therapy and local therapy such as cryosurgery (freezing the prostate) and "salvage" radical prostatectomy. "Salvage" prostatectomy can be done safely and robotically by expert surgeons but healing afterwards is dramatically affected in a negative way by surrounding radiation damage to local tissues caused by the original radiation – including external beam, proton beam and seed radiation. This causes problems with recovery of bladder control and sexual function. In essence, if a patient is destined to need two major treatments like surgery and radiation, it is best to have surgery first.

Pre-Treatment (neo-adjuvant) Hormone Therapy Not Needed Before Surgery

It has now been known for many years that intermediate and high-risk patients with prostate cancer (PSA> 10ng/ml, Gleason Score >6 or palpable disease) are best treated with hormone therapy before, during and after radiation (15). Hormone therapy helps the radiation be more effective and increases the cure rate. However, it also causes erectile dysfunction, hot flashes and decreased energy – to name the most common side effects.

Several randomized trials were conducted in the 1990s where men received three to four months of hormone therapy prior to radical prostatectomy. Although the initial results of these studies showed that hormone therapy decreased positive margins a subsequent meta-analysis showed no benefit in terms of biochemical (PSA) recurrence rate or ultimate cancer cure (16). Furthermore, there was no significant benefit to administering hormone therapy prior to surgery even in the highest risk patient. In this study, where high risk men received surgery as the primary treatment, the disease specific survival at 10 years was 84%

$S_{ide \ \text{Effects of Surgery Are Not Worse Than Radiation}}$

Radiation oncologists often use the argument that surgery has a worse complication rate than radiation treatment. Although it is true that if we measure quality of life scores (quantitative scores of bladder function, bowel function, sexual function and overall well-being) surgery patients take a bigger hit initially. However, quality of life scores are essentially identical at one year whether men have brachytherapy, external beam radiation or surgery (17).

With surgery, the majority of men typically lose their continence and erections but the vast majority of men recover these functions over the first year. If we take into account that most men today that need treatment are intermediate and high-risk and will need hormone therapy in addition to radiation, but not surgery, the argument in favor of surgery is even stronger. Furthermore, radiation oncologists are reluctant to talk about other important and significant side effects of radiation.

A recent study from Ontario, Canada (18) compared men without prostate cancer (the control group) to men receiving either surgery or radiation for prostate cancer. Men that had surgery had no higher risk of requiring a subsequent readmission to the hospital, a subsequent anal or rectal procedure, development of a secondary cancer or an additional open surgical procedure. The rates of these problems increased from 2 to 10.8 times for men that received radiation (see chart below).

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Compared to patients without treatment for prostate cance		
	Surgery	Radiation
Number	15,870	16,595
Age	61.5	69.4
Hosp admission Within Five years: HR	1	10.8
Rectal/Anal Procedure: HR	1	2.72
Second Cancer: HR	1	2.08
Open Surgical Procedure Within Five years: HR	1	3.68
HR = Hazard Ratio		

Complications After Treatment

State of the Art Robotic Surgery for Prostate Cancer

Robotic surgery was approved by the FDA for prostate cancer treatment (Robot Assisted Radical Prostatectomy – RARP) in 2001. Initially, there were concerns that this technique of surgery may lead to higher cancer recurrence rates or higher complications. Significant experience with this technique in many different countries has now been accumulated (19). This data show conclusively that robotic surgery does not compromise cancer control rates. In addition, these control rates are applicable to all risk groups. Furthermore, blood loss is less, hospitalization time is less and men tend to recover physically more quickly – allowing them to resume their normal activities in just a few weeks. In addition, they tend to recover their bladder control and sexual function more quickly and to a better degree.

In my opinion, RARP allows the surgeon to do a more accurate, reliable and reproducible surgery. However, experience makes a big difference. For men who are considering surgery make sure that the surgeon you hire is the most experienced in your geographical area. If you can afford to travel it may be worth it. Make sure you ask the surgeon his (her) personal results and how many procedures they do per year. Like anything else in life; "The more you do of something, the better you get at it."

General Information and Recovery after Surgery

In experienced hands, RARP generally takes between 1.5 and 3.5 hours. Differences in time will vary depending on the size and shape of the prostate and the size and shape of the patient. If a bilateral lymph node dissection (lymphadenectomy) is recommended – based on the Briganti nomogram – this will account for 30 to 60 minutes of the operative time. Men will wake up with a catheter in the urethra that has been placed during anesthesia. This is placed to help healing of the new connection between the urinary bladder and the urethra (known as the anastomosis) and will drain urine. This will only cause mild discomfort.

In addition, sometimes a drain (small plastic tube) will be placed during surgery. This exits through the skin into a small bulb and collects serum from the surgical site. It will collect urine if there is a leak where the surgeon has connected the bladder to the urethra after prostate removal. Usually the drain is removed the day following surgery. In my practice, I do not routinely place a drain.

The majority of men will be discharged the day following surgery and return one week later to have the catheter removed, review the details of the pathology report and check on their recovery. Most will return to work within 2 to 3 weeks but I advise no heavy lifting above 15 pounds for six weeks. About 25% of my patients have immediate return of complete bladder control. About 50% are essentially dry and not needing pads by 6 weeks, 85% are dry by 3 months and 90 to 98% by one year.

Variation in recovery of bladder control depends on patient age, preoperative bladder control, prostate size, nerve sparing technique and surgeon experience. Men under the age of 65 that have good erections prior to surgery have about an 85% chance of having satisfactory erections that are good enough for intercourse within a year.

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Most urologists will have men take regular doses of drugs like Viagra after surgery to help erection recovery. This practice is perfectly safe; the biggest problem is the expense of the drugs. We don't believe that one drug (Viagra, Cialis, Levitra or Stendra) is better than the others. In addition, I often have men take at least one dose of Viagra 100mg on the third day prior to surgery. There is some laboratory evidence in animals that this practice helps decrease the shock of surgery to the nerves.

Usually we wait until the first visit after catheter removal (approximately 6 weeks following surgery) to assess sexual and erection function. If men are getting at least partial erections (elongation and engorgement of the penis) then just continuing on "Viagra like" drugs is probably fine.

For men that want to be proactive and for men that are having zero erections at the first visit starting a program of intra-cavernosal injections (ICI therapy) is recommended. This is a treatment where the patient learns how to inject a small amount of medicine with a tiny needle directly into the penis. It is analogous to a diabetic giving themselves insulin. With the correct dose, a full erection will result within about ten to fifteen minutes and last about an hour. This practice is then performed two to three times per week and will keep the penis healthy while the nerves are waking up. It will also allow the patient to have intercourse.

Men will follow up with the surgeon usually every 3 months for the first year following surgery and every 6 months after the first year. At each follow up visit a PSA blood test is performed and the urologist will assess overall health, bladder function and sexual function. In the few men that do not regain satisfactory bladder control (urinary continence) medical therapy can sometimes be successful. If this fails then a small surgical procedure can be performed to resolve urinary incontinence.

For men that are slow to have erections return or that never recover erections that are satisfactory for intercourse, several options like ICI therapy and a penile prosthesis can be used to successfully address this problem. It is important to know that surgery for prostate cancer does not have an effect on sex drive, sensation of the penis (the way it feels to touch) or the ability to achieve orgasm. Approximately 95% of my patients are able to achieve an orgasm (climax) within the first month of surgery – though this may be without an erection. This will seem odd to most men because we typically associate the two things (erection and climax) together. In fact, they involve two different nerve systems. During surgery we are moving the nerves that affect erections. In addition, it is important to know that the climax after surgery is a dry climax because we have removed the organs (prostate and seminal vesicles) that make the semen.

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Timothy G. Wilson, MD

Professor and Chair of Urology – Urologic Oncology

Director of Urologic Oncology Research

John Wayne Cancer Institute

Santa Monica, California