

Counseling the Patient with Prostate Cancer: 2016 Update

Abbreviations: PSA: Prostate Specific Antigen; DRE: Digital Rectal Exam; SHIM: Sexual Health Inventory For Men; ICQ: International Continence Society; CIC: Clean Intermittent Cauterization

Opinion

Prostate cancer is the most common cancer in American men [1-12]. The ever-expanding, seemingly conflicting literature on prostate cancer makes counseling patients with prostate cancer a difficult but often necessary part of clinical practice. The myriad of information that can be supplied to the patient can be overwhelming and may contribute to increased anxiety about making the “best decision” [3]. It is important, then, to give the information in a current, simple, compassionate and accurate manner that empowers the patient and allows him to understand and act on the known facts about prostate cancer. As a pathological entity, prostate cancer occurs in almost all men as they age. Autopsy studies indicate that some men start to show evidence of cancer in their prostates as early as their third decade with increasing incidence over the subsequent decades. Once diagnosed, the patient needs to understand these facts as well as the modern management modalities and their application to his particular condition.

As technology advances, screening and treatment of prostate cancer and the counseling of our patients are indeed a dynamic practice related task that requires not only evidence based medicine through continuous review of the literature with the addition of experience drawn from actual day to day practice of counseling. In addition to urology, the participation of other providers from different disciplines including medical oncology, internal and family medicine, urgent care, emergency medicine, ambulatory care, and nephrology should be encouraged when needed for safe distribution of the burden of following the non-surgical cases. Most patients with localized prostate cancer can be cured of their cancer [3]. However, not all patients require a curative treatment with its attendant morbidity. Many patients have cancer that would not affect their life expectancy. This is because many patients has a life expectancy that is relatively limited especially when the patient has a low risk prostate cancer with fairly good to moderate characteristics, (low volume, and low or moderate grade). These patients do well with Expectant Management.

There are two scenarios for expectant management. The first is used for patients with life expectancy over 10 years and generally younger than 75 years old who elect expectant management. These patients are followed by Active Surveillance that includes: close follow up with PSA every 3-6 months, a repeat biopsy within 12-24 months, then periodically as determined by the physician, DRE visits at 6 or 12 months, MRI as determined by the physician. The second scenario for Expectant Management is Watchful

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Waiting. Watchful waiting means monitoring the cancer with the intent to offer only palliative treatment if progression occurs. This approach is used for patients with life expectancy under 10 years and or most patients older than 75 years in whom curative treatment is not intended.

It is important in counseling the patient in the first group who elects active surveillance to understand that he will have to adhere to monitoring the cancer with the intent to offer curative treatment (radical surgery, radiotherapy or cryotherapy) if progression occurs. Though there is no general consensus on a protocol for active surveillance, most authorities would agree on evaluating the patient about every 4 to 6 months for prostate specific antigen (PSA) testing and annual digital rectal exam (DRE). The patient can also fill a sexual health inventory for men (SHIM) and international continence society (ICQ) questionnaires in these clinic visits. Patients on expectant management on active surveillance are advised to have repeated trans-rectal ultrasound guided prostate biopsies every 12 months till age 75. On this protocol the reported “risk of progression” which is defined as the “need to undergo definitive treatment” whether radical surgery, radiotherapy or cryotherapy is 30% and the 10- year prostate cancer actuarial survival was 97.2% [1]. This also means that even with this arbitrary generous definition of progression, 70% of this group of patients did not need any treatment.

On the other hand, young and middle-age healthy patients who have a long life expectancy and moderately or highly aggressive localized prostate cancer eventually develop disease progression to cause significant morbidity and possible death. Consequently, definitive treatment with curative intent is offered to these patients. Contemporary series show that the reported complication rate with radical surgery or radiotherapy is still significant. In one report at 5 years following radical surgery or radiotherapy the erectile dysfunction rate is 79.3% and 63.5% respectively. In the

same report the risk of long term urinary incontinence is 14.4% for the radical surgery group and 4.9% for the radiotherapy group. Patients choosing radiotherapy should understand that the risk of uncomfortable bowel urgency and painful hemorrhoids are more prevalent with radiation than surgery [2]. The authors reminded us that in patients who choose radiation over surgery, performing radical prostatectomy after failure of radiotherapy is difficult and associated with more complications. We evaluated the effects of radical prostatectomy or radiotherapy on the quality of life and demonstrated that these effects can be substantial. We further demonstrated that overall general well being measures were better for those who had radical prostatectomy while cancer specific quality of life measures were similar among men treated with either of these 2 modalities [3].

Cryosurgical ablation of the prostate (freezing) is another curative modality. Cryosurgery has been approved and is reimbursable by Medicare (United States government paid health insurance for citizens over 65 years). Similar to Brachytherapy, Cryotherapy is done as a day surgery procedure. This offers an advantage over external beam radiation that mandates about forty two days of consecutive radiation sessions. When counseling the patient for cryotherapy, the urologist should confirm that the patient is aware of the possible complications that can happen. The incidence of complications with the third generation cryotherapy machines is 1% for rectourethral fistula and recurrent urinary tract infections. The incidence of urethral sloughing and incontinence requiring pads is 2% and 4% respectively. The incidence of prolonged retention requiring clean intermittent cauterization (CIC) and perineal or penile pain is 6% [4,5]. Though the incidence of erectile dysfunction after cryotherapy is significant, there are reports that showed up to 39% of patients may regain their potency at 24 months follow-up [6]. Similar to post radiation therapy, radical surgery is challenging to perform should cryotherapy fails. The reported 5 years disease specific survival for cryotherapy is 94% [7].

Our goal, then, is to identify selected patients with clinically significant prostate cancer who have cancer that is curative by therapeutic intervention and in whom cure is necessary, i.e., patients with long life expectancy. Long-established treatment options in these patients include radical prostatectomy and radiation therapy [external beam or radioactive seed implantation (Brachytherapy) or combination of the 2 radiation modalities]. Our own view is that radical prostatectomy is the treatment of choice in healthy young patients with long life expectancy (15 years or more) and clinically significant cancer that is confined to the prostate. On the other hand, in older patients who have reasonably long life expectancy, radiation therapy by (external beam or by radioactive seeds) or by cryosurgery are appropriate. Radiotherapists often use adjuvant hormonal therapy for patients managed by radiotherapy.

Patients with advanced disease are best managed with hormonal manipulation, i.e., androgen (male hormone) deprivation. The major source of androgen in men is the testicles. Patients on hormonal treatment should be warned of the known side effects of decreased libido, hot flushes and gynecomastia as well as the cardiovascular side effects and hypercholesterolemia [8]. Another source that contributes a small fraction of circulating

androgens is the adrenal glands. The role of chemotherapy in many advanced prostate cancer is expanding. Our own preference for hormonal treatment with testicular androgen deprivation is simple scrotal orchiectomy (surgical removal of testicles via small scrotal incision). Compared to medical castration by LHRH agonists or antagonists, orchiectomy is simple, quick and much more economical (cost of orchiectomy is equivalent to the cost of a few months of medical therapy). In addition, patients who have a surgical orchiectomy do not need anti-androgens with their additional side effects and cost.

Patients with advanced prostate cancer who were treated by standard androgen deprivation (medical or surgical castration) eventually have disease progression. These are considered to have hormone refractory prostate cancer. Other modalities of hormonal manipulation can be added at this time (secondary hormonal therapy). These include additional or different dosage of anti-androgens, utilization of estrogenic (female hormone), or estrogen-containing combinations. Chemotherapy can also be utilized. More effective chemotherapy has been introduced for these patients and is being utilized more frequently in appropriately selected patients. Abiraterone, Enzalutamide, Radium-223, and immunotherapy by cancer vaccine or Monoclonal antibodies are newer treatment modalities for certain patients. Radiation therapy for painful bony lesions is valuable. Abiraterone (Zytiga) is a medication that blocks the production of androgens by the prostate cancer, the testes and the adrenal glands. It is shown to improve survival in men with advanced prostate cancer whether or not they have already been treated with chemotherapy. Abiraterone must be taken with steroid to avoid serious complications. Side effects include fluid retention and a drop of serum potassium level. Enzalutamide (Xtandi) blocks the effects of androgens on the cancer cell leading to retardation of its growth and delay in chemotherapy use. It is shown to increase survival in patients who did not receive chemotherapy. Radioisotopes such as Radium-223 can be utilized for generalized bone pain.

Immunotherapy is a newer approach to treating advanced prostate cancer involves empowering the body's own immune response to attack cancer by one of these two methods. The first method, cancer vaccine called simuleucel-T (Provenge). This vaccine is made by isolating dendritic cells from the patient's blood and stimulating them outside the body with various chemicals. The energized dendritic cells are re injected to the patients over two weeks in three injections. Complications are shown to be mild like fever, fatigue, and headache. The second method involves the use of monoclonal antibodies such as ipilimumab (Yervoy) that works by stimulating the actions of the Killer cell (T-cells). It has shown promise and is already being used to treat advanced melanoma but not approved for prostate cancer yet.

Nutritional recommendations for patients with prostate cancer emphasize the role of a low-fat diet. Fat intake should be less than 40 gm (and preferably less than 33 gm) daily. Consumption of adequate amounts of vegetables and fruits including tomatoes (cooked or fresh) and berries is likely beneficial. The role of nutritional supplements has not been demonstrated. Among these nutritional supplements, vitamin E, selenium, lycopenes and Ellegic acid are being studied but have not shown promise.

Investigational treatment modalities are being explored and may prove valuable in the near future. These include growth factor inhibitors, agents that promote differentiation, apoptosis (programmed cancer cell death), angiogenesis inhibitors (agents that inhibit new vessel formation by growing tumor cells thus starving them), and gene therapy (manipulating genes that promote or suppress cancer growth or spread).

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