

Research Project

Treatment Options and Health Related Quality of Life Concerns for Men with Prostate
Cancer: A Systematic Review of the Literature

Submitted by

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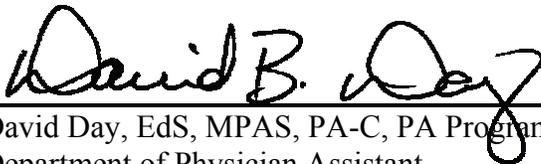
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We hereby recommend that the Research project prepared under our supervision by Shanna Armbrister entitled, Treatment Options and Health Related Quality of Life Concerns for Men with Prostate Cancer: A Systematic Review of the Literature, will be accepted as partial fulfillment for the degree of Master of Physician Assistant.

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Abstract

Introduction: Prostate cancer is the second leading cause of cancer death for American men. The treatment of prostate cancer has changed dramatically with the widespread availability of prostate specific antigen screening (PSA). With this widespread PSA screening, early detection of prostate cancer is forcing more men to weigh the difficult treatment options. Men may live many years with the disadvantages of the treatments they receive; therefore it is vital they are well informed about the treatment and management options as well as the associated side effects.

Methodology: The purpose of this systematic literature review is to evaluate the treatment options for men diagnosed with prostate cancer and determine if there is a significant difference in mortality and morbidity between each treatment option.

Results Twenty articles were reviewed using evidence based methods. Little difference was noted in mortality between treatments, except following external beam radiation. Erectile dysfunction was most significant following radical prostatectomy. Urinary symptoms and bother was mostly associated with cryotherapy, external beam radiation and brachytherapy. Complications with bowel function were identified following radiation therapies and cryotherapy.

Conclusions: It is clear that no one treatment is best for every patient. Treatments chosen should be based on age, stage of disease, and co-morbidities. The health related quality of life concerns vary with each treatment, although urinary and bowel function typically improves over time. Erectile dysfunction is common following radical prostatectomy, but nerve sparing improvements in procedures are being developed.

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Introduction

Prostate cancer is the second leading cause of cancer death to American men.¹ With the widespread availability of prostate specific antigen (PSA) screening, early detection of prostate cancer is forcing more men to weigh the difficult treatment options. The primary management options include radical prostatectomy, hormone therapy, radiation therapy, or watchful waiting. The treatment recommended for early prostate cancer is still controversial.² There is continued debate and doubt about the efficacy of various treatments because of the insufficient number of direct comparative studies.³ In view of the fact that there is no current consensus on the best treatment, knowledge about prostate cancer and the treatment options are invaluable. Men may live many years with the sequelae of the treatments they receive; therefore it is imperative the treatment and management options are known as well as the associated side effects.

Prostate Specific Antigen (PSA) is an enzyme produced by the prostate and can be measured by a simple blood test. As a man ages his prostate will enlarge, causing his PSA levels to increase. Other non-cancerous conditions such as infection or inflammation of the prostate can also cause PSA levels to rise. For this reason the PSA testing has been controversial. Studies have proven that age and race can cause a variation in PSA levels; therefore it is important to establish a baseline PSA level for each patient.⁴

Table 1- Age specific PSA Reference Ranges for Asians, Blacks, and Whites⁴

PSA Reference Ranges			
Age Range	Asians	Blacks	Whites
40-49	0-2.0	0-2.0	0-2.5
50-59	0-3.0	0-4.0	0-3.5 ⁴
60-69	0-4.0	0-4.5	0-4.5
70-79	0-5.0	0-5.5	0-6.5

If the PSA level is elevated outside the reference range a biopsy can be performed to then determine a Gleason Score. The Gleason score is used to clarify the aggressiveness of the cancer as well as the prognosis. A pathologist will analyze two biopsies of the tumor and assign a score between 1 and 5, the larger the number the more aggressive the cancer. The pathologist then takes the two most common occurring scores in the samples and combines them for a final score between 2 and 10. Therefore a score of 2-4 represents a slow growing cancer, 8-10 rapid growing cancer, and 5-7 or the 'gray zone' can either be fast or slow growing.

The Gleason score directly correlates with the PSA. A score of 2-4 represents a slow growing cancer whose tissue acts similar to normal prostate tissue therefore the cancer tissue can dramatically increase PSA levels. Conversely a score of 8-10 (known as non-differentiated) does not increase the PSA level dramatically because the cells do not behave the same as normal tissue thus not increasing PSA secretion. The 'gray zone' 5-7 obviously can increase the PSA or not for the same reasons above. The Gleason score tells a great deal about how the cancer will progress over time or more specifically whether or not the cancer will metastasize. This means

that there is a 25% chance of metastasis with a score of 2-4, 50% chance with 5-7, and 75% with 8-10.⁴

Once the PSA and Gleason score are determined the next step is treatment. The primary treatment options are radical prostatectomy, hormone therapy, radiation therapy or watchful waiting. Watchful waiting (WW) is an option most chosen by older men with slow growing cancers confined to the prostate. The best candidates for this option are: men with a life expectancy of less than 10 years due to age (men over 75), men over the age of 70 with a Gleason score of 2-4, and men whose cancer is confined to the prostate and need time to decide what type of treatment is best for them.⁴

The surgical option is called radical prostatectomy (RP) where men undergo complete excision of the prostate. There are two approaches to this surgery. The first and more common approach is a retropubic procedure.⁴ The surgeon goes in through an incision from the navel to just above the penis. The approach gives clear access to the prostate, making it easier to save the nerve bundles that control erection. A man can remain potent if even one nerve bundle is spared.

The second approach is a perineal procedure. The surgeon goes in between the legs with an incision between the anus and scrotum. Generally less bleeding occurs, and heavier men can recover sooner. Unfortunately, saving the nerve bundles that control erection is more difficult.

There are two types of radiation treatments: external beam radiation and radiation seed implants. External radiation involves a large machine that very accurately delivers high doses of radiation while minimizing damage to other tissue. It does this by aiming the radiation from many angles through the pelvis to the prostate.

Brachytherapy is a radiation treatment where seed implants are introduced into the prostate by needles which are guided by ultrasound. The needles inject about 70 to 150 rice-size radioactive seeds into the prostate. These seeds deliver twice the dose of radiation as external beam radiation delivers and causes less damage to the healthy tissue.

Hormonal therapy can help if the cancer has spread beyond the prostate. Male hormones (androgens) can speed the growth of prostate cancer. Removing these hormones from the body can slow the growth of the cancer. Options include bilateral orchiectomy (surgical castration), Luteinizing-hormone-releasing-hormone (LHRH) agonists, estrogen therapy, and antiandrogens combined with LHRH agonists. Each therapy has its own unique mechanism of action which halts hormone production.

Cryotherapy is an option for men in their 70s who don't want surgery, can't afford the procedure, or have failed radiation therapy. Cryotherapy literally freezes the prostate. It is a non-invasive procedure where about five 6 inch metal rods are placed into the perineum and liquid nitrogen is delivered via the rods to the prostate. Eventually the prostate thaws and the cancer cells should break apart. The disadvantages are impotence, short-term urinary dysfunction, and rectourethral fistula. About nine out of ten patients (90 percent) experience long-term difficulties in having erections.⁴

In addition to treating the cancer, the possibility of long-term effects on urinary, bowel and sexual function may be of significant concern particularly in men with early stage disease.³ Erectile dysfunction is one of the more common and persistent health problems following surgery.⁵ Many men report negative emotional and behavioral effects because of the sexual dysfunction. The extent of sexual dysfunction depends largely on what mode of treatment is chosen.²

Stress urinary incontinence is also a common complication of various treatments. Rates of incontinence are reported between 2.5% and 87% after surgery, but a majority of men regain function within 24 months of surgery.⁶

Evaluating the consequences of bowel dysfunction is a secondary concern to most patients when choosing a treatment. Bowel dysfunction includes loose stools, bowel urgency, rectal bleeding and crampy pelvic pain.⁷ Overall there seems to be little change to bowel function following surgery and watchful waiting.^{2, 1} It does however have a large impact on men who choose radiation therapy.

Purpose of Study

The objective of this study is to evaluate the treatment options for men of all ages diagnosed with localized prostate cancer and determine if there is a dramatic difference in mortality and health related quality of life between each treatment option. Health related quality of life concerns are primarily related to sexual, urinary, and bowel functioning.

Literature Review

Watchful waiting

Arredondo examined the health related quality of life of men who selected watchful waiting.¹ A group of men who chose watchful waiting were compared to a group of men without prostate cancer. The group's sexual and urinary functioning was equal at the beginning of the study. The study examined physical and mental capabilities; mental health had no change from beginning to the end of the study. Urinary and bowel functioning decreased due to the aging process and sexual functioning was affected most significantly due also to the aging process. According to this study, the men who chose watchful waiting were older, had more co-morbidities, and had low risk cancer.

Klotz et al., suggested that most men with favorable to low risk cancer will likely die of unrelated causes. The study consisted of 299 patients over 70 years of age with low to intermediate cancer risk. Their PSA doubling time was followed for eight years. If the doubling time was two years or less or grade progression of cancer on re-biopsy was found, radical prostatectomy was offered. Results of this study indicate most men with low to intermediate risk cancer could be followed with palliative care (with intervention as necessary) and tend to die of unrelated causes.⁸

Radical prostatectomy

A five-year outcomes study following the effects of prostatectomy and radiotherapy was reviewed.² Urinary incontinence was noted to be worse following surgery when compared to external beam radiotherapy. Men who underwent surgery reported problems with urinary frequency and nocturia. Two years after surgery, declining erectile function was observed in over 80% of men and following five years, more than 50% of men had declining erectile dysfunction. Function progressively increased as years following surgery increased. There was little change in bowel function from two years to five years.² Litwin identified significant outcomes regarding bowel functioning after treatment. Patients who underwent radical prostatectomy reported some bowel impairment following surgery. The level of impairment improved dramatically around three months after surgery and then leveled off with no further improvement. Despite bowel dysfunction patients seldom expressed regret about the treatment chosen.

Lepor et al., performed a study on the impact of radical retropubic prostatectomy on continence and found urinary incontinence to be a time dependent process.⁶ The majority of men in the study eventually regained urinary function within 24 months. The examiners were unable

to identify any predicting factors leading to early return of continence status. The study suggests that radical retropubic prostatectomy has a significant impact on improving urinary tract symptoms such as emptying bladder, urinary frequency, interrupted stream, straining, and nocturia.⁶

A longitudinal study using patient surveys pre and post surgery evaluated the health related quality of life following radical perineal prostatectomy (RPP).⁹ The study revealed a more than favorable outcome for urinary, bowel and erectile functioning. The study is the first to provide a longitudinal assessment of quality of life following RPP.⁹ Patients recovered normal urinary function after the median time of 5.8 months. This study indicates the benefit of bilateral nerve sparing RPP and recommends further studies of this approach.

Watchful waiting vs. Radical prostatectomy

A significant study comparing prostatectomy and watchful waiting was evaluated.² No significant difference in mortality was found between watchful waiting and radical prostatectomy.² The length of time for the survival benefit to surface requires a longer longitudinal study to evaluate the benefits of radical prostatectomy 10 years post surgical. Another study evaluating active surveillance with delayed intervention concluded that most men will die of unrelated causes and that a compromise between surveillance and therapy would be a practical solution.⁸ Prostate specific antigen (PSA) doubling time (DT) was used to qualify patients to surveillance or active therapy. A DT of three years or less was the threshold for active therapy and approximately 20% of patients fell into this group. The remaining patients if selected appropriately and monitored carefully will likely die of unrelated causes. A comparative trial needs to be done to evaluate this approach.

Jenkins surveyed African-American and White men regarding sexual quality of life after prostate cancer treatment and found that sexual functioning is important to a majority of men regardless of ethnicity. The study concluded that it is vital that men receive an accurate depiction of how likely dysfunction will be and the chances of recovering after various treatments.⁵

Cryotherapy

Touma et al., searched the literature about the current status of salvage therapies following radiation failure for prostate cancer. Salvage cryotherapy is a valid option in patients with preoperative PSA less than 10ng/ml, Gleason score less than 8, a clinical stage less than T3 who are hormonally naïve.¹⁰ Salvage cryotherapy is an especially good option for older men with some co-morbidities who are considered to be an anesthetic risk.¹⁰ Major complications are urinary incontinence, impotence, pelvic pain and urinary retention.^{10, 11} Rectourethral fistula is a serious complication with a reported rate of 0%-3%.¹⁰ This complication is due to inaccurate probe placement. Onik et al., also reported 2.9% (2 out of 55 patients) of patients with rectourethral fistulas.¹² No cases of fistulas were reported by two separate randomized controlled studies performing cryotherapy.^{11, 13} Erectile dysfunction was the most severe and bothersome complication of cryosurgery followed by urinary symptoms.^{10, 11} Complication rates and severity correlate closely with the duration and area of freezing.¹⁰

Brachytherapy

Down et al., analyzed data from CaPSURE (Cancer of the Prostate Strategic Urological Research Endeavor) on brachytherapy as monotherapy (BMT) and radical prostatectomy. It was found that patients treated with BMT had higher urinary function from 0-6 months after treatment than those who had radical prostatectomy. Both treatment groups had decreases in

sexual function that never returned to pretreatment baselines.¹⁴ At one year after treatment patients treated with brachytherapy had more irritative urinary symptoms while patients treated with RP had more problems with urinary incontinence.¹⁴ While rectourethral fistulas are an uncommon side effect following radiation, they have been reported in approximately 0.3% to 3% of patients after brachytherapy.¹⁵ Flam et al., studied brachytherapy as a monotherapy and found that only 19 out of 600 patients needed to undergo transurethral resection of the prostate because of inability to relieve urinary symptoms.¹⁶

Litwin et al., completed a longitudinal study on bowel function and bother following brachytherapy, radical prostatectomy and external beam radiation (EBR). Bowel function differs greatly in men treated with surgery, brachytherapy, and external beam radiation. Compared with RP, patients treated with EBR or brachytherapy experience more impairment in bowel functioning.⁷ Patients treated with radiation compared to RP made a marked improvement during the first 3 months but do not reach a steady state until a year after therapy.⁷

Brachytherapy was found to be a viable treatment option with the majority of side effects to be self-limiting. A 12-year outcomes study provides support that brachytherapy is a successful treatment option in men presenting with clinically localized prostate cancer.¹⁷

External Beam Radiation

Rosser et al., reviewed the medical records of 964 patients who received radiotherapy as their only treatment.¹⁸ Of the 98 men 60 years or younger 47% had biochemical failure or presenting persistent cancer on subsequent biopsies. Of the 866 men aged 60 or older 30% had biochemical failure. Men with prostate cancer who are 60 years or younger and treated with radiotherapy may be at significant risk for long-term biochemical failure.¹⁸

Bladder cancer risk following EBR was studied retrospectively by Chrouser et al on 1,743 patients. The retrospective review suggests there is not evidence of increased risk of bladder cancer after radiation therapy.¹⁹ In the study by Litwin et al., patients who underwent EBR had more problems with bowel function and bother following treatment compared to brachytherapy and RP.⁷ Those patients also did not regain an improved steady state until 1-2 years following therapy.⁷

Gray et al., followed 145 patients in a 20 year outcomes study finding patients treated with EBR can survive for many years after treatment, although many eventually require adjuvant therapy and die of recurrent disease.²⁰

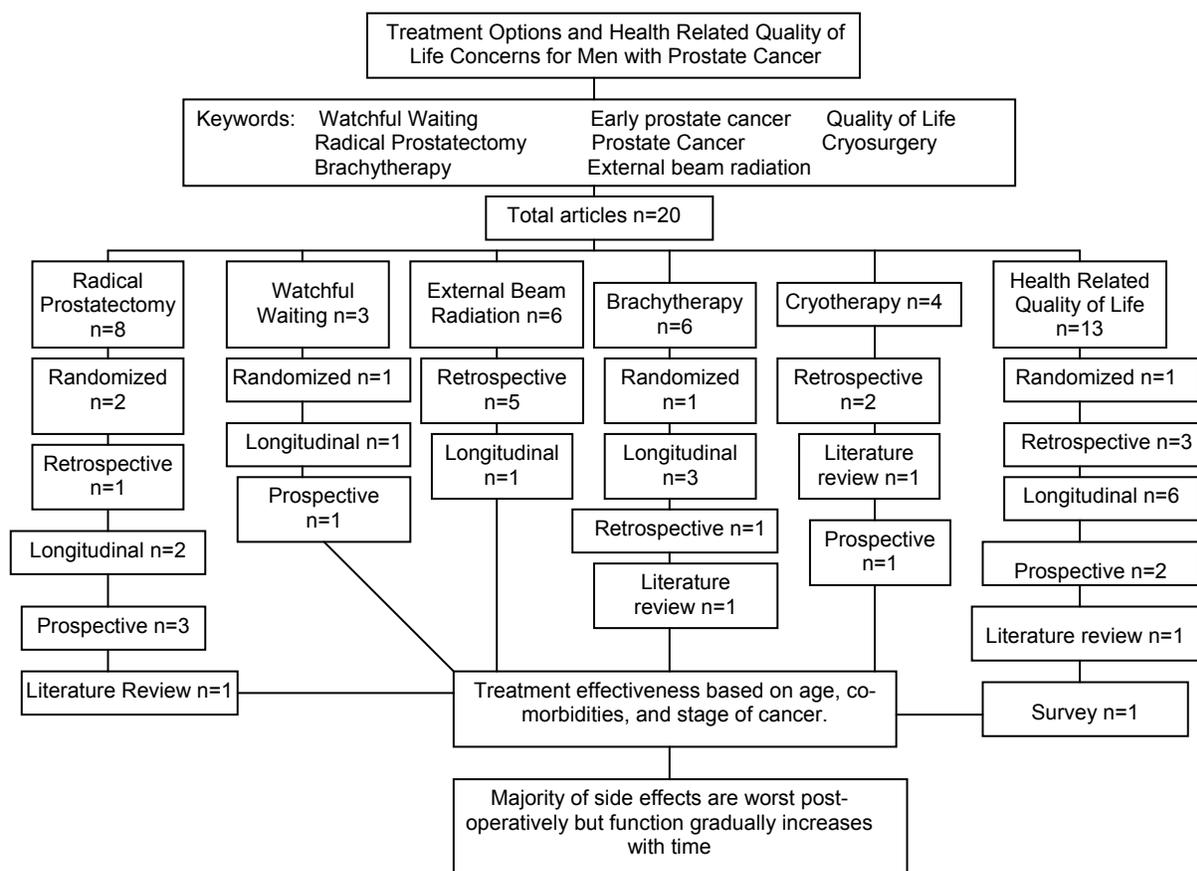
Methodology

Systematic review of literature was done utilizing the Medline First Search database. The keywords used for the search include watchful waiting, early prostate cancer, quality of life, radical prostatectomy, prostate cancer, cryosurgery, brachytherapy, external beam radiation. The mortality and health related quality of life outcomes of men who chose watchful waiting, radical prostatectomy, cryotherapy, brachytherapy, and external beam radiation were analyzed. The systematic review was limited to men with localized prostate cancer.

Results

Nineteen articles were selected for review between the years 1993 and 2005 (Figure 1). Although there were 19 articles chosen most addressed more than one treatment, therefore the results section has some overlapping. Oesterling et al., was a book reference and was not included in Figure 1. This reference was utilized for background information.⁴

Figure 1: Literature Review Flow Sheet



Three studies were found addressing watchful waiting as a treatment option. Each article concluded that men who chose WW lived many years with prostate cancer and died of unrelated causes.^{1, 2, 8} Eight articles were found to have radical prostatectomy either the main topic or as an associated study. All the studies showed erectile dysfunction as the main complication of surgery. The more care taken to spare the nerves that supply erection the less severe the dysfunction.^{2, 3, 6-8, 12, 14, 21} Six articles following the efficacy and long term side effects of external beam radiation were selected.⁷ One study exclusively addressed the severity of bowel dysfunction following treatment and found it to be most prevalent following EBR compared with brachytherapy and RP.⁷ The other five studies also listed bowel dysfunction as well as urinary

dysfunction and bother.^{3, 18-21} Another study used age as a predictor of success with EBR, patients over 60 had more success with the treatment.¹⁸ Six articles addressed brachytherapy as a viable treatment option for patients who can not tolerate surgery.^{7, 11, 14-17} Four articles addressed cryotherapy as a treatment either as a salvage therapy for other failed treatments or as a monotherapy with minimal associated morbidity.^{7, 11-13} All the articles address health related quality of life (HRQoL) issues during the research, but only thirteen had HRQoL issues at the helm of the research.^{1, 3, 5-7, 9, 11, 12, 14-16, 19, 21}

Discussion

Evidence in Literature

The review was completed because of the vast amount of information available about prostate cancer treatments with no clear consensus amongst the experts. There is continued debate and doubt about the efficacy of various treatments because of the insufficient number of direct comparative studies. The purpose of this systematic review was to review and organize the information in an easily comprehensive format for patients and health care professionals.

After reviewing the nineteen selected articles the same conclusions were identified within each of the correlating studies; that no one treatment is the best for all patients. The literature shows that age, co-morbidities and the stage of the cancer dictates what treatments should be recommended. A young patient in good health with no co-morbidities whose cancer is confined to the prostate will have the greatest benefit from radical prostatectomy.^{2, 6, 7} The most significant and daunting side effect will likely be erectile dysfunction.^{2, 3, 6-8, 12, 14, 21} If surgery is not an option other viable ways to manage the cancer are radiation, cryotherapy, and watchful waiting. For older men with co-morbidities and decreased life expectancy these are all possible choices.

Weakness in Literature

There is a vast amount of research about all the facets of prostate cancer in circulation. Literature is available spanning PSA research to health-related quality of life issues. Multiple conclusions could be made from the peer-reviewed articles compiled. In regards to mortality and health related quality of life issues all questions were addressed and answered. There were no significant weaknesses in the literature identified

The study focused on localized cancer confined to the prostate as did the majority of studies in the Literature. There needs to be more information and studies on the efficacy of treatments for men whose cancer is beyond the prostate. Also few longitudinal and randomized trials were identified. The efficacy of newer treatments, such as cryotherapy, needs to be studied longitudinally.

Validity of Review

The systematic review of the literature was conducted utilizing Medline First Search with the previous mentioned keywords. Once selected, the articles were reviewed and included if peer reviewed and fell between years 1990 and 2005. The articles were evaluated and organized into a flow sheet, (See Figure 1).

Weakness in review

The review could have focused more specifically on one or two treatments options and thus provide a more direct comparison. Bias could be claimed because the authors, institutions, and journals were not blinded from the author. Although the references are listed the reader is relying on the author's interpretation of the studies results. The author could be biased due to family connection with a prostate cancer survivor. More qualifying inclusion criteria other than disease stage and date of study could have been included.

Conclusion

With the increasing advances in medicine, patients need to be informed of the treatment options available. Being well informed about the benefits and risks of various treatments will facilitate a patient's ability to make an informed decision. Understanding the differences between the treatment options may help health care providers educate their patients in making an informed decision.

After reviewing the literature, it is clear that no one treatment is the best for all patients. The literature clearly shows that age, co-morbidities and the stage of the cancer dictates what treatments should be recommended.

A young patient in good health with no co-morbidities whose cancer is confined to the prostate will have the greatest benefit from radical prostatectomy.^{2, 6, 7} The most significant and daunting side effect will likely be erectile dysfunction. It was found in the review that although men may never regain the exact sexual performance they had prior to surgery, their erectile function will often steadily improve over time after nerve sparing procedures. The literature indicated that as medical procedures are advancing more efforts/techniques are being developed to spare the nerve bundles that control erection.

If surgery is not an option, other viable ways to manage the cancer are available including radiation, cryotherapy, or watchful waiting. For older men with co-morbidities and decreased life expectancy watchful waiting is always an option. Studies suggest men with localized disease lived many years with the cancer and died of unrelated causes.^{1, 8} The only morbidity associated with waiting was urinary symptoms that were also found to be as equally bothersome in men without cancer of the same age. Complications such as hypertrophy can cause urinary obstruction, frequency, straining, and a weak stream. Improved urinary function can be

anticipated for men who choose surgery that may result in urinary incontinence. Studies show that urinary incontinence typically resolves within 24 months of surgery.

Brachytherapy seems to be a more superior form of radiation delivery than external beam radiation.^{7, 16, 17} There are fewer side effects and these resolve with time and also are less likely to be a failed mode of therapy. The option is good for men who either do not want surgery or can not have surgery. The side effect profile was found to be somewhat self-limiting. Bowel and urinary bother were worst in the first three months following treatment and eventually returned to baseline within one year. The risk for rectourethral fistula is uncommon but was reported in less than 3% of cases.¹⁵

Cryotherapy is an especially good option for older men with some co-morbidities who are considered to be an anesthetic risk.¹⁰ The side effect profile is similar to radiation therapy. Impotence and declining urinary function are the major side effects. Major complications are urinary incontinence, impotence, pelvic pain and urinary retention. Rectourethral fistula is also an uncommon problem but still was reported in less than 3% of cases and attributed to the poor probe placement.¹⁰

One study reported external beam radiation an option for older men with a failure rate of 47%.¹⁸ The bowel bother associated with this treatment was worse than all of the other treatment options. There was also a risk for bladder cancer following this treatment which was not found with brachytherapy. Men may live many years following treatment but may eventually need adjunctive therapy.

Ultimately, the treatment decisions reside with the patient; it is the responsibility of health care providers to make sure all the facts are presented and the patient is aware of all the risks and benefits associated with treating prostate cancer.

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Appendices

Study Year	Research Address 1.Radical Prostatectomy 1a. RRP 1b. RPP 2. WW 3.Radiotherapy 4.Quality of Life 5.Background 6.Brachytherapy 7. Cryotherapy 8. EBR	Level of Evidence 1. Random Control 2.Retrospective 3. Background 4. Prospective 5. Longitudinal 6. Literature Review	Demographics Main data	Findings	Supportive of Research
Holmberg et al 2002	1,2	1	Watchful Waiting n=348 Radical Prostatectomy n=347	31 of 348 WW patients died from cancer; 16 of 347 RP patients died from cancer; 31 of 348 WW pts died from other causes; 37 of 347 RP pts died from other causes	No difference between surgery and waiting for overall survival
Potosky et al 2004	1,3,4	2	RP n=901 EBR n=286	79.3% ED following RP; 63.5% ED following EBR 15% incontinence following RP; 4% incontinence after EBR	Quality of Life after ERB better for ED and urinary incontinence. Bowel function better after RP

Oesterling 1997	5	3	Na	Na	Na
Jenkins et al 2004	4, 5	Survey, 3	N=1,112 white N=118 AA	51% of WW returned survey; 28% AA returned survey	Na
Lepor et al 2004	1a	4	N=500 radical retropubic prostatectomy	98.6% pts completed the survey at 24 mo	98.5% men were continent at 24 mo after RRP
Litwin et al 2004	1, 3, 4,6	5	n=1584 RP=1276 EBR=99 BT=209	Surgery pts reached steady state by 3mo; radiation pts took >1yr	PT's treated with brachytherapy and EBR had worse bowel function than RP
Arredondo et al 2004	2, 4	5	n=310 men diagnosed between 1990-2001 who chose WW	72% of men answered survey at 1yr; 18% at 5yrs	WW better to similar HRQoL compared to men without cancer
Klotz et al 2004	1, 2, 4	4	n=299 men 70yrs or greater chose WW	At 8yrs actuarial survival was 85%; disease specific survival was 99%	Most men with favorable risk will die of unrelated causes.
Touma et al 2005	7	6	N=74 articles	Salvage cryotherapy 5yr biochemical relapse-free rate was 40%	Cryotherapy is a valid option

Han et al 2003	7	4	N=106 treated with cryosurgery median age 70	Incontinence 3%; urge incontinence 5%; retention 3.3%; rectal discomfort 2.6%; no fistulas or infections	Cryotherapy well-tolerated minimally invasive
Prepelica et al 2005	7	2	N=65 treated with cryosurgery median age 72	PSA biochemical disease-free survival in 83.3%	Cryotherapy feasible option; needs longer follow-up
Onik et al 1993	7	4	N=55 treated with cryosurgery Group 1-froze with 2 probes Group 2-froze with 5 probes	Group 1 – 3 pts had residual disease; group 2 – 1 pt had residual disease	Transrectal Ultrasound effective technique for treatment with minimal morbidity
Downs et al 2003	6	5	N=419 treated with brachytherapy as monotherapy	84.5% of EBR pts had higher function scores than 67.4% of RP pts; similar percentages with bowel function	BMT and RP well tolerated treatments with mild effects of HRQoL
Flam et al 2004	1,6	1	N=600 treated with brachytherapy	3.1% pts needed TURP	TURP is safe to perform following BMT
Potters 2005	6	2	N=1,449 treated with brachytherapy	Overall survival 81%; disease specific 93%	Brachytherapy is a definitive option for treatment

Chrouser et al 2005	7,8	2	N=51 with history of radiation with fistulas	30% received EBR; 30% received BT; 40% received both	Surgical intervention required for fistulas in EBR and BT
Rosser et al 2002	8	2	N=964 with radiation therapy	47% of the 60yrs or less group had biochemical failure; 30% of the older group had failure	EBR treatment for men 60 yrs and younger have high fail rate
Chrouser et al 2005	8	2	N=1,743 received EBR	In more than 12,353 man-years of follow-up no increase of cancer was found	No increased risk of bladder cancer following EBR
Gray et al 2001	8	2	N=145 received EBR	Actuarial survival at 15 and 20yrs was 45.9% and 24.6%, respectively; cause specific survival was 64.5% and 37.7%; of those who survived 47% were on hormonal therapy	Many pts following EBR will need hormonal therapy

Yang et al 2004	1b,4	2,5	N=109 treated with RPP	1 in 4 patients recovered the sexual summary scores by 18 mo	Future studies needed on benefit of bilateral nerve sparing RPP on sexual HRQoL
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RP=radical prostatectomy

RPP=radical perineal prostatectomy

WW=watchful waiting

BT=brachytherapy

TURP=transurethral resection of prostate

ED=erectile dysfunction

HRQoL=health related quality of life

EBR=external beam radiation

BMT=brachytherapy monotherapy

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