Please note that all face-to-face meetings have been cancelled until further notice. Please check your email regularly for updates from the PHSCG Committee.

Prostate Heidelberg

September 20 Issue 198

For Education, Information and Support

Meeting Hall: Ivanhoe Uniting Church 19 Seddon Street, Ivanhoe
POB 241 Ivanhoe Victoria 3079
Email: prostateheidelberg@gmail.com
Website: www.prostateheidelberg.info

Next PHCSG Meeting – Tues 15 Sept (via Zoom)

10am – 12:30pm

Join Zoom Meeting

https://us02web.zoom.us/j/85979616898?pwd=M1Btb3p5Y1h5ZUwzR1FhRlV3aHU4UT09

Meeting ID: 859 7961 6898

Passcode: 261767

Prostate Heidelberg Cancer Support Group

PHCSG provides information, education and support for those affected by Prostate Cancer. At our meetings we are committed to:

- showing respect to members, speakers and guests
- allowing members to speak without interruption
- respecting confidentiality

Our August Zoom meeting was well attended with 21 members listening to Mr David Dangerfield explaining the techniques used to restore erectile function in PC patients. As a result of his talk, this month's newletter is covering several allied articles on ED.

In this month's newsletter:

- ProtecT Trial showing patient outcomes after AM, RP & EBRT
- Changes in Penile Length after RP
- Active Surveillance – is it right for you?
- The final part of The Perils and Pitfalls of "Treating PSA" in Advanced Prostate Cancer
- Managing Erectile Dysfunction – A Patient Guide

We want to ensure that everyone stays physically and mentally as well as possible at this difficult time. So please don't hesitate to contact us if there is anything you want to talk through in relation to your treatment or wellbeing.

Max Shub	0413 777 342
Mike Waller	0438 616 240
Michael Meszaros	0407 837 538

ProtecT Randomized Clinical Trial:

Patient outcomes by treatment received - active monitoring, prostatectomy, or radiation

Source:
This article from Prostatecancer. news dated 22 Feb 2020 reports on the patient outcomes of a randomized trial according to the treatment they received. (https://www.europeanurology.com/article/S0302-2838(19)30837-1/pdf)

This is the first clinical trial where patients were randomly assigned to active monitoring (AM), radical prostatectomy (RP) or external beam radiotherapy (EBRT). They started signing up men in the UK in 1999 and continued recruitment for 10 years. By 2009, they screened over 82,000 men for prostate cancer and found 1,643 men with newly diagnosed localised prostate cancer who were willing to be randomized to initial treatment with AS, RP or EBRT, about a third in each. They then followed them for a median of ten years to see how well they did with each therapy. Imagine the effort involved! Sounds good so far -- what could go wrong?

1. Treatment choice/ oncological outcomes

In the first year, 78% of patients received the treatment they were randomly assigned. Higher risk men chose radical treatment rather than AM. Conversely, men with low-risk PC were less likely to opt for EBRT.

In the ten years of follow-up, there were only 17 prostate cancer deaths out of 1643 men randomized in the trial. The pooled, adjusted risks and the percent of the AM group that suffered each oncological outcome after 10 years of follow-up were:

- 69% lower risk of prostate cancer death for radical therapy (RP or EBRT) vs AM
  - 1.8% PC deaths among AM
- 64% lower risk of metastases or death for radical therapy (RP or EBRT) vs AM
  - 6.0% metastases or death among AM
- 77% lower risk of progression for radical therapy (RP or EBRT) vs AM
  - 24% progression among AM
- 47% lower risk of salvage ADT for radical therapy (RP or EBRT) vs AM
  - 8.8% salvage ADT among AM
- No statistically significant differences between RP and EBRT

The inferior performance of their AM protocol was predictable. Their AM protocol did not include mpMRI confirmation, biopsy follow-up, and allowed some higher-risk patients.

2. Urinary Adverse Outcomes
a. Incontinence

This was a big issue for RP, of course, but not for AM or EBRT. The percent using one or more pads per day is one commonly used measure. As one can see in the following table, incontinence was highest at the 6-month time point, but had gotten somewhat better by the end of the first year. 24% were incontinent by the end of two years, with little improvement from that point. Incontinence increased slowly in the AM group as they elected to have radical treatment.

Table 1. Incontinence: The percent who used one or more pads per day

Time point	AM	RP	EBRT
Baseline	0%	1%	0%
6 months	0%	55%	1%
1 year	1%	32%	2%
2 years	3%	24%	2%
3 years	3%	23%	2%
4 years	5%	20%	2%
5 years	5%	20%	2%
6 years	7%	21%	2%

(continued)

b. Nocturia

The researchers examined the question of whether nighttime urination was more frequent after therapy. On this dimension, only EBRT had a clinically detectable effect, and it was only at the 6 month mark. After that, it returned quickly to AM levels. RP returned to baseline level.

Table 2. Nocturia - Twice or more per night

Time point	AM	RP	EBRT
Baseline	20%	22%	20%
6 months	24%	35%	65%
1 year	23%	26%	36%
2 years	28%	23%	32%
3 years	31%	25%	32%
4 years	33%	25%	33%
5 years	35%	23%	36%
6 years	38%	25%	34%

3. Rectal Adverse Outcomes

The researchers asked the trial participants whether they had blood in their stools half the time or more. There were no discernable effects of AM or RP. Blood in stools peaked at a low level (8%) of those who had EBRT.

Table 3. Blood in stools more than half the time

Time point	AM	RP	EBRT
Baseline	1%	1%	1%
6 months	1%	1%	4%
1 year	1%	0%	4%
2 years	0%	1%	7%
3 years	1%	1%	8%
4 years	1%	1%	8%
5 years	2%	1%	8%
6 years	1%	2%	6%

4. Sexual Adverse Outcomes

This is one of the few trials that asked men detailed questions about their sexual function at baseline and for 6 years thereafter. One of the key measures of sexual function is the ability to have erections firm enough for intercourse. At baseline, about two-thirds of these 62 year old men (range 50-69), some with other comorbidities like diabetes, cardiovascular disease, and smoking, had suitable erectile function.

None of the questionnaires asked about perceptions of penile shrinkage in length and girth, climacturia (urination at orgasm), or Peyronie's (abnormal penile curvature), which are often symptoms that affect sexual function post-prostatectomy. Nor do they ask about how the loss of ejaculate has affected sex. That is a certainty with surgery, a near-certainty after radiation, and is not affected by AM. Their definition of erectile function includes the effect of any erectile function aids (e.g. ED meds, injections, pumps, or implants) they may have been using.

For those randomized to RP, erectile function was possible for 5% at 6 months (remember: they *all* had nerve-sparing surgery). It recovered somewhat to as much as 13% at 2 years but did not recover appreciably beyond that. At every time point, their erectile function was significantly worse than the other treatment cohorts.

For the AM cohort, erectile function declined by 6 months and continued to deteriorate thereafter as they aged and elected to have radical therapies, predominantly surgery.

For the EBRT cohort, erectile function had dropped to a minimum value of 18% at 6 months. This may be largely attributable to the fact that all of the men in the EBRT cohort had 3-6 months of ADT. It is unknown how much, if any, of their testosterone came back after that and how long it took to recover. Erectile function snapped back a bit post-ADT, getting as high as 34% at 3 years. At 6 years, potency was twice as high as those who had RP. Again, this was based on the 3D-CRT technology, and is below the rates usually seen for this age group with IMRT, brachytherapy, or SBRT.

Table 4. Erectile function - the percent who had erections firm enough for intercourse

Time point	AM	RP	EBRT
Baseline	68%	66%	63%
6 months	59%	5%	18%
1 year	60%	6%	34%
2 years	54%	13%	32%
3 years	49%	14%	34%
4 years	43%	15%	31%
5 years	40%	16%	28%
6 years	35%	15%	29%

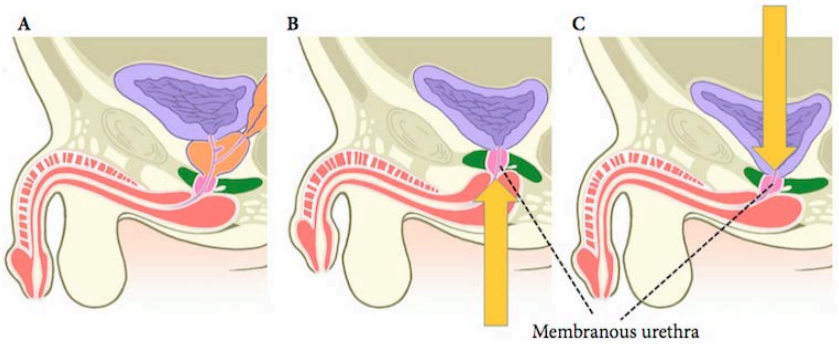

Fig. 2 Illustration of chronological changes in pelvic anatomy after radical prostatectomy. Membranous urethra is pushed proximally at 10 days post- radical prostatectomy (RP), and tends to be repositioned at 12 months after RP. (A) preoperative; (B) 10 days after RP; and (C) 12 months after RP.

Discussion

This study is the first to focus on pelvic anatomical changes after RP, which cause chronological changes in PL. Measurement of SPL provides the closest approximation of the erect PL; therefore, several studies have used SPL as a measure of PL. To maintain measurement quality, only one author (Y.K.) measured SPLs and was blinded to previous results. Further, only patients who completed the entire 2-year study were included in the analysis.

In the present study, SPL was shortest 10 days after RP and then gradually recovered to pre-RP values after 12 months. Similarly to the present study, SPL measurements taken 1week after RP in previous studies were reportedly the shortest; however, the reported changes over time in SPL have tended to differ; some reports state the SPL 2SPL to preoperative levels 3– 5 years later. Another report mentioned that postoperative SPL recovered to the preoperative level 6–12 months after surgery, which is consistent with the present results. Long-term follow-up studies have been affected by substantial drop-out rates, but in the present study we were able to obtain SPL measurements from >100 cases at different time points over the 2-year study period.

Because the bladder is thought to be loosely fixed by vascular pedicles and connective tissues, it can be moved down towards the bottom of the pelvis after removal of the prostate, albeit with some resistance. Moreover, the proximal side of urethra can retract towards the bladder after urethrovesical anastomosis (Fig. 2B).

Indeed, we observed intrapelvic retraction of the urethral stump during urethrovesical anastomosis in surgery. Because the urethra pierces the urogenital diaphragm but is thought to be loosely connected, it is liable to be pulled down slightly into the pelvis. A previous report posited the membranous urethra as being fixed to the urogenital diaphragm and not easily retractable into the pelvis. Although the urogenital diaphragm is fixed to the pelvic bone, it is a membrano- muscular structure and not very firm; therefore, the urogenital diaphragm itself, as well as the membranous urethra, can move vertically (Fig. 2). We usually apply perineal pressure during urethrovesical anastomosis to push the urethral stump towards the pelvis for easy observation during robot-assisted RP. According to our MRI findings, the bulb of penis appears to have retracted towards bladder 10 days after RP; this indicates that the membranous urethra and urogenital diaphragm were lifted proximally. Comparison of MRI findings at 10 days and 12 months after RP showed that the bulb of penis returned to almost the same position as before RP; therefore, we speculate that the tension of the vascular pedicles and connective tissues, which pull the bladder proximally, loosens over the course of a year (Fig. 2C). MRI showed that the bulb of the penis was lifted proximally by an average of 3.9 mm at 10 days after RP.

In conclusion, this is the first study to show that slight vertical repositioning of the membranous urethra after RP causes changes in SPL over time. Anatomically, the glans and corpus spongiosum surrounding the urethra form an integral structure, and the proximal urethra is drawn into the pelvis during urethrovesical anastomosis. Changes in PL represent one aspect of anatomical changes induced by RP and the results of the present study elucidate these changes in the short term after RP; however, further research is needed to elucidate long-term changes in PL with respect to the influence of sex hormones or changes in penile blood flow after RP. These results of the present study could help inform patients about changes in penile appearance after RP.

Changes in penile length after radical prostatectomy:

investigation of the underlying anatomical mechanism

Source:
The entire article can be found on:
https://bjui-journals.onlinelibrary.wiley.com/doi/pdf/10.1111/bju.13777

Unfortunately, not all urologists are forthcoming about penile changes after RP. This article, in *BJU International*, explains the reasons for penile volume

Abbreviations:
RP Radical Prostatectomy
PL Penis Length
SPL Stretched Penis Length

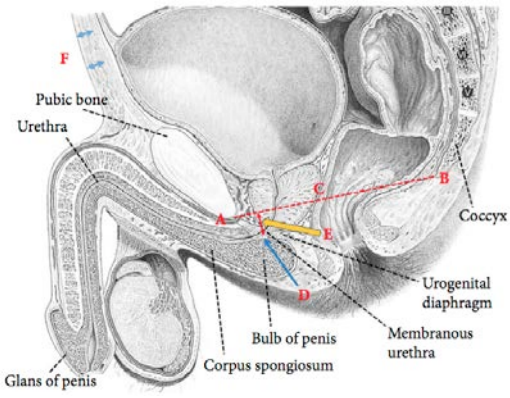

Fig. 1 Mid-sagittal view of pelvic anatomy; cited from Pernkopf Anatomy. (A) Bottom edge of pubic bone. (B) Lowest end of coccyx. (C) Midline of pelvic outlet (red dotted line). (D) Most proximal attachment point of urethra and bulb of penis. (E) Perpendicular distance from 'D point' to 'C line' (red line with bidirectional arrowheads = distal end of membranous urethra to pelvic outlet [DMU-PO] distance). (F) Thickness of subcutaneous fat at lower abdomen.

Active Surveillance for Prostate Cancer

Source: https://www.prostate.org.au/news-media/news/active-surveillance-for-prostate-cancer-is-it-right-for-you/

If you have low risk prostate cancer, Active Surveillance is increasingly being recommended as a management option for your disease, in order to avoid unnecessary and invasive treatments when it is clinically safe to do so. Estimates suggest about 60% of low risk prostate cancers in Australia are managed with Active Surveillance.

If you decide on Active Surveillance to manage your prostate cancer, it's important to follow your surveillance protocol, in consultation with your doctor and specialists. This ensures that if your cancer starts to grow, it can be caught and treated before it spreads beyond the prostate. If you miss any tests on Active Surveillance, you increase your risks of unchecked disease progression, which could be harmful.

So, what is Active Surveillance, and is it a good treatment option for you?

How are prostate cancer treatment decisions made?

In deciding how best to treat your prostate cancer, your doctor needs to determine the type of cancer you have and how likely it is to progress to advanced disease.

Cancers that are not likely to grow and spread are considered low-risk prostate cancer, while those that are more likely to progress to advanced disease are considered high-risk prostate cancer. The grade and stage of the cancer helps determine the risk level.

Grade: the aggressiveness of the cancer cells and how quickly they are expected to grow. This is based on the biopsy results and is determined by a pathologist. Low-grade cancers usually grow slowly and are less likely to spread. Higher grade cancers are more likely to grow quicker and spread to other body parts.

Stage: describes the cancer's size and whether it has spread beyond the prostate. This is based on the digital rectal examination and imaging tests. Imaging tests include CT, MRI, bone scan and PMSA PET scans. The amount the cancer has spread gives an indication of how extensive the cancer is.

Your doctor will consider the level of risk from your cancer and other factors including your age, general health and your personal preferences before recommending the best treatment for you. If you have low risk localised prostate cancer you might be offered Active Surveillance. Occasionally, Active Surveillance is offered to men with intermediate risk (medium risk) prostate cancer.

Active Surveillance is not recommended for men with high risk or aggressive prostate cancer. Instead, active treatment like surgery or radiation therapy will be offered.

To learn more about prostate cancer grading visit PCFA's website here.

What is Active Surveillance?

Active Surveillance is a treatment option for men with low risk prostate cancer. There is now strong evidence that it is safe for men with low risk prostate cancer to be regularly and carefully monitored. Occasionally, Active Surveillance is recommended for men with intermediate risk prostate cancer. In Australia most men with low risk prostate cancer choose Active Surveillance as their preferred treatment.

The aim of Active Surveillance is to closely monitor or survey the cancer for any signs or symptoms of disease progression that could cause harm. These signs may be an increase in the stage of the cancer determined by MRI or repeat biopsy, an increase in the grade of the cancer or a significant rise in the PSA level. Most cancers never progress and do not need any further treatment. If the cancer is seen to be progressing, treatment like surgery or radiotherapy will be recommended. It is quite acceptable for a man to start Active Surveillance but then change his mind and have active treatment later even if his cancer hasn't changed.

Active Surveillance can delay the need for treatment for several years in some men and for others they may avoid ever needing to have active treatment for their prostate cancer.

Who can have Active Surveillance?

Active Surveillance may be suitable for you if you have low risk prostate cancer defined by:

- PSA levels less than or equal to 10ng/ml and
- low grade cancer – Grade Group 1 (Gleason score of less than or equal to 3+3=6) and
- early stage cancer that is localised within the prostate – TNM Stage 1 or 2.

Occasionally men with intermediate risk prostate cancer choose Active Surveillance. These men are often highly motivated to delay treatment or may have other health problems.

Why choose Active Surveillance?

Low risk prostate cancers are often slow growing and less likely to spread to other parts of the body.

Active treatments like surgery and radiotherapy can come with significant side-effects that will affect your daily life.

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Research shows that many men who choose Active Surveillance never need active treatment. For others on Active Surveillance, treatment can be safely delayed for several years.

What does Active Surveillance involve?

Active Surveillance can be different for different men. Your doctor will advise you on your specific Active Surveillance monitoring protocol. It is very important that you keep track of your appointments and do not miss regular tests that have been scheduled for you.

Active Surveillance involves regular testing. Some of the tests you will have include:

- PSA testing - PSA will be checked at regular intervals. PSA levels fluctuate over time, even if the cancer isn't growing. Your doctor will decide whether you need further tests by looking at the pattern of your PSA changes.
- Digital Rectal Examination (DRE) - This is where the doctor feels the prostate through the wall of the back passage (rectum) to check the size of the prostate and if there are any abnormalities or changes.
- MRI scan – An MRI scan is done before you start Active Surveillance to make sure the cancer hasn't spread outside the prostate. It may also be done as part of your Active Surveillance plan, especially if your PSA test or DRE have changed.
- Biopsy - All men need a biopsy at diagnosis to determine the grade of the cancer before being offered Active Surveillance. During Active Surveillance, you will need further biopsies.

If your test results suggest that your cancer could be growing, you may be offered further tests to check on the cancer. If any changes are found, you could be advised to have active treatment that aims to cure the cancer.

Active Surveillance is continuing to be studied and protocols might change as new evidence becomes available. This could affect which tests are required and how often they need to be repeated. As they are developed, new tests may be offered to help predict whether treatment is needed or not.

Some questions to help you make your decision.

When deciding whether to undergo Active Surveillance, here are some things to ask your doctor:

- What do the tests tell us about my cancer?
- How do you know it hasn't spread?
- What would happen if I don't start treatment straight away?
- What are my options for treatment?
- What are the pros and cons of each option in my case?
- Are there other factors I need to consider before deciding?
- What are the risks from delaying treatment?
- What lifestyle changes should I be making?
- How often will I need to have repeat investigations such as MRI and/or biopsy
- If I start on Active Surveillance, what is the likelihood I will need to have active treatment in the future

Taking your partner or another support person with you to medical appointments can help you to make treatment decisions.

Who should move from Active Surveillance to treatment?

Active Surveillance has been shown to be a safe option for men with low risk prostate cancer to either avoid or delay the need for treatment. Men who remain on Active Surveillance have the same chance of living for 10 years as they would if they had chosen to have surgery or radiation therapy.

The length of time men remain on Active Surveillance is variable and many men may never need treatment. Some reasons men move from Active Surveillance to treatment include:

- Increase in cancer grade - the biopsy results show that the tumour is becoming more aggressive.
- Increase in cancer size – the tumour has become bigger and may have started to spread. This is determined by a PSA level increase, results from a biopsy and/or MRI scan.
- Anxiety - some men can feel very anxious because they are afraid their cancer will grow.

If you are on Active Surveillance and are thinking about starting treatment, understanding as much as you can about prostate cancer and the different treatment options can help you decide which option is best for you. Ask your doctor and/or Prostate Cancer Specialist Nurse for as much information as you need. It can also be helpful to discuss your options with your partner, family and/or close friends. Speaking to people at your local prostate cancer support group or through PCFA's Online Community can also help you decide.

Compliance is essential for a good result with Active Surveillance.

Research has found that many Australian men with low risk prostate cancer do not fully comply with prescribed Active Surveillance protocols.

While the reasons for non-compliance require further research, possible barriers include individual factors, social and cultural demographics, lack of support, gaps in the health care system, and the need for improved patient-clinician communications.

It's vital to keep up with routine monitoring of your prostate cancer. If you don't, you increase the risk that changes to your prostate cancer may not be detected, leading to advanced disease and lower prospects for long-term survival.

PCFA is actively looking at ways to address awareness and action in order to improve outcomes for Australian men impacted by prostate cancer, consistent with the seven priority actions identified in our recently released Survivorship Essentials Framework

Visit PCFA for information and support at www.prostate.org.au/support/ or call on 1800 22 00 99.

The Perils and Pitfalls of "Treating PSA" in Advanced Prostate Cancer Part 2

https://www.prostatecancer.news/2020/07/the-perils-and-pitfalls-of-treating-psa.html

Friday, July 10, 2020

This is the second and final part of an article giving an explanation of PCa progression detailing:

PSA-based Endpoints

Danger of Withholding Early ADT

2. PSA-based Endpoints

What we really want to know is this: will the treatment enable patients to live longer? Overall survival is the gold standard of success of randomized clinical trials. The "problem" for clinical trials is that prostate cancer is such a slow killer, that it may take 15 years or more to discern a difference (https://www.prostatecancer.news/2016/08/how-long-is-long-enough-length-of.html) if patients have localized or recurrent prostate cancer at the start. (For most other types of cancer, 5-year overall survival is more than adequate.) Clinical trials are often ended when half of the control group dies (median survival). But, depending on patient characteristics at the start, median survival may never be reached within the duration of the clinical trial.

Prostate cancer-specific survival (how long before patients succumbed to their prostate cancer) is little better. It is also hampered by the fact that patients with prostate cancer may die of something else sooner, possibly because their cancer was debilitating. It is often unclear to the doctor who signs the death certificate whether the cancer was the end cause, a contributing cause, or a non-contributing factor. To get clinical trial results before new medical science and technology renders the results irrelevant, we want to use surrogate endpoints that are highly correlated with and predict overall survival.

The earliest endpoints that can be used to measure the success of a prostate cancer therapy are PSA based. All of the following surrogate/secondary endpoints are PSA based:

- PSA50 - the percent who had a reduction in PSA by 50% or more
- Nadir PSA - the lowest PSA reached after therapy (https://www.prostatecancer.news/2017/01/nadir-psa-predicts-survival-after.html)
- PSA doubling time (PSADT) - whether the therapy slowed PSA growth
- Biochemical recurrence (BCR) - depending on initial treatment, and there may be multiple salvage therapies, each with a PSA failure defined for it (https://www.prostatecancer.news/2019/08/the-definition-of-second-biochemical.html)
- Biochemical Recurrence-Free Survival (bRFS)
- Biochemical failure (BF)- rise in PSA by a pre-specified amount post-therapy
- Biochemical No Evidence of Disease (bNED)
- Time to BCR/ BF
- Time to start of lifelong ADT (based primarily on a pre-defined PSA failure benchmark)
- Failure-free survival (FFS) or Progression-free survival (PFS) or Event-free survival (EFS) - defined as BF or radiological progression or clinical progression or death.

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- The following surrogate endpoints are *not* PSA-based:
- Radiographic Progression-free Survival (rPFS) or Disease-free survival (DFS)- progression on scans or death
- Objective Response Rate (ORR) - tumor size or number reduction using RECIST criteria
- Change in Bone Scan Index
- Time to radiographic progression or failure
- Metastasis-free survival
- Clinical progression - pain, bone fracture, spinal compression

As an example of circular reasoning, we can see in the ORIOLE trial that 6-month Progression Free Survival (PFS) was chosen as the primary endpoint. PFS was defined as PSA progression (by >25% over nadir and by > 2 ng/ml) *or* radiographic progression *or* death. As we can readily see in the exponential growth curve, the odds of a new metastasis on a bone scan/CT are very low and there are not likely to be any deaths. Therefore, PFS was almost entirely PSA progression. But the protocol "treated PSA." It is therefore illogical to conclude, even for a Phase II trial, that oligometastatic treatment slowed progression.

3. Danger of Withholding Early ADT

While ORIOLE, STOMP, and SABR-COMET were Phase 2 clinical trials whose results were not meant to change practice, many patients and their doctors (often under pressure from patients) would like to believe they do. If the metastases are in places that are safe to irradiate (e.g., away from the mediastinum), there is little risk in doing so. However, if they do not understand the circular reasoning evident in the ORIOLE trial, they may put off therapies that are known to increase survival. There is also a risk of unreasonable expectations.

Some patients (and doctors) believe that by delaying ADT, they can increase their quality of life, and delay castration resistance. Neither is true.

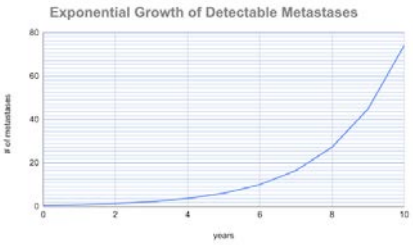
Contrary to popular belief, *decreasing* the intensity of hormone therapy and *delaying* its use brings *earlier* castration resistance and death. The strongest evidence for this comes from the STAMPEDE (on Zytiga and Xtandi), LATITUDE, and SPARTAN trials. Among men who were *newly diagnosed* with metastatic prostate cancer:

- Overall survival was longer if men used Zytiga + ADT.
  - No difference based on the number of metastases
  - Failure-free survival was longer if they used Zytiga + ADT
- Overall survival was longer if men used Xtandi+ADT
  - Survival was especially lengthened if there were fewer metastases
  - PSA progression-free survival was longer if they used Xtandi+ADT
- Overall survival was longer if men used Erleada+ADT
  - PSA progression-free survival was longer if they used Erleada+ADT

A clear pattern emerges: early use of intensive hormone therapy prolongs survival and prolongs the time to castration resistance. Men who were oligometastatic benefited from early, intense hormone therapy.

The TROG 03.04 RADAR trial examined the duration of hormone therapy in high-risk men treated with radiation. They found that, after 10 years of follow-up, men treated with 18 months of ADT survived *longer*, and reached castration resistance *later* compared to men treated with 6 months of ADT.

The TOAD trial looked at starting ADT at the first sign of recurrence vs. waiting for metastases to be detected. Men treated *earlier* reached castration resistance *later*. It also showed there was no major detriment to global health-related quality of life by starting ADT earlier (htpps://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(17)30426-6/fulltext)



Maha Hussain reported the results of a randomized clinical trial comparing intermittent vs continuous ADT in recurrent men with metastases. She found that:

- Time to castration resistance was not different for the two protocols (Figure S5)
- For men with minimal disease, overall survival was 6.9 years for those on continuous therapy vs 5.4 years for those on intermittent therapy. The trial was underpowered for this difference to reach statistical significance.
- It took 4-5 years for the survival curves to start separating - long follow-up is needed to detect survival differences.

Taken together, all these major randomized clinical trials show that the best way to use ADT in the oligometastatic setting is to use it early and heavily. Reducing the number of cancer cells as quickly and effectively as possible, even reducing those cells that haven't begun to measurably contribute to PSA, extends survival. The effect of evolutionary selection pressure allowing castration-resistant cells to survive is dwarfed by the reduction in sheer numbers. Circular reasoning may harm patients.

PLEASE NOTE: The prognoses and treatments in this article are standard of care [SOC] in the US. Treatments may vary in Australia. Please ensure you discuss your diagnosis and treatment options with your consulting specialist.

Managing Erectile Dysfunction – A Patient Guide

Source:
www.ucsfhealth.org/education
SDURO0095 • Revised 3/18

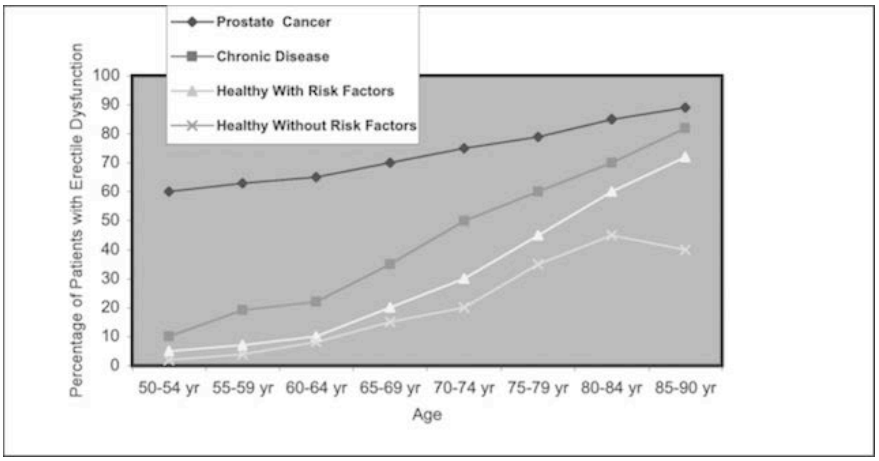


Figure 1: Prevalence of Erectile Dysfunction with Age in Different Patient

What is ED

Normal male sexual function is often thought of as a linear process: sexual interest or desire is the first phase which often leads to penile erection, during which the penis becomes firm by filling with blood. After a period of sexual excitement/activity most men experience ejaculation (release of semen from the penis) which is accompanied by orgasm, a sensation of intense pleasure and/or contentment. It is important to note that orgasm and ejaculation are separate processes that may occur independently. It is also possible to experience ejaculation and/or orgasm in the absence of penile erection.

Decreased sexual desire or libido is common and may occur in the setting of psychological distress (depression/anxiety), stress, and relationship conflict. Some health problems are associated with decreased desire. Decreased sexual desire has also been associated with low blood levels of testosterone, the "male hormone."

Erectile dysfunction – commonly known as ED – is defined as the inability to achieve or maintain an erection that is sufficient for satisfactory sexual activity. Ejaculation, the release of semen during sexual activity, relies on coordinated action of the muscles of the lower urinary tract and prostate. The prostate and the seminal vesicles produce most seminal fluid. Medications, surgeries, and radiation treatments for prostate problems often cause changes in ejaculation. Ejaculation changes are also common with increasing age.

Orgasm occurs as an experience of intense physical and emotional pleasure at the climax of sexual activity. Our current scientific understanding of the experience of orgasm is limited. Many factors, including emotional, psychological, and health considerations, contribute to the experience of orgasm. Changes in ejaculation may also influence a man's perceptions of orgasm. Some men may also experience ejaculation but have a mild or even no sensation or orgasm.

It is important to realize that male sexual function is not simply the ability to have a rigid erection and/or an ejaculation. A careful assessment of sexual life and the quality of a man's sexual relationship are important to produce the best outcomes when addressing sexual problems. Mutually satisfactory sexual relationships can be maintained in the presence of ED or other sexual problems. For more information about this, refer to the books listed at the end of this guide.

Chronic disease includes other cancer, hypertension, cardiac disease, diabetes or stroke.

Risk factors include antidepressant use, consumption of more than two alcoholic drinks per day, smoking, obesity, lack of exercise and watching television for more than 8.5 hours per week. ED and Cancer Surgery or Radiation ED is very common after major pelvic surgery or radiation, including treatments for prostate or bladder diseases. The nerves that drive erection, called cavernous nerve bundles, are located immediately next to the prostate gland. During a radical prostatectomy (RP, an operation for prostate cancer) these nerves may be injured by being cut or separated from the prostate. This may cause temporary or permanent ED. Because the prostate makes most of the fluid in semen, men who have had RP do not experience ejaculation. Radiation to the prostate, the bladder or rectum can also damage the cavernous nerves and lead to problems with erections and ejaculation. Although ED and absence of ejaculation are common after RP or prostate radiation, sexual desire and the ability to achieve orgasm are still possible.

A "nerve-sparing" RP or radical cysto-prostatectomy (RC, an operation for bladder cancer) is a procedure designed to remove cancer while preserving the cavernous nerve bundles. The theoretical advantage is that erectile function may be at least partially preserved. In the hands of an experienced surgeon and if both nerve bundles are spared, 50 to 90 percent of patients have a return of at least some erectile function over 2 years post-surgery. When only one nerve bundle is spared, the percentage of patients that have return of erections over 2 years is closer 25 to 50 percent. If a non-nerve sparing technique is necessary, the proportion of patients able to achieve erections without using one of the several available aids, is about 16 percent or less. Nerve sparing surgery offers a number of advantages in terms of erectile function. However, in some cases the patient's tumor may make nerve sparing approaches inadvisable. Patients with large and/or high grade tumors may not be candidates for nerve sparing surgery.

Nerve sparing surgery is superior to non-nerve sparing surgery in terms of preserving erectile function. However, a number of other factors are also important. Patients with medical problems (e.g. high blood pressure, high cholesterol, diabetes, tobacco use), men who have ED prior to surgery/radiation, and older men are more likely to have difficulty obtaining a rigid erection after surgery/radiation. Most men under the age of 50 treated for prostate cancer recover erectile function; only about 20% of men over the age of 70 have return of erections without medical therapy. Depression, psychological

(continued)

stress, and relationship conflict may also make recovery more difficult by affecting both sexual desire and penile erection.

Even in nerve sparing surgery there is typically some trauma to the cavernous nerves during RP/RC based on their closeness to the prostate. Men should expect several months of difficulty attaining natural erections even after nerve sparing operations. The process of recovery may take up to 2 or 3 years.

For men undergoing radiation, the amount and extent of radiation as well as whether or not they are treated with hormone therapy correlates with the likelihood of ED, either temporary or permanent. Men may not experience immediate ED while under treatment with radiation but over time ED symptoms become more prevalent after radiation treatment. Reductions in libido and difficulties with erections may also result from the use of hormone therapy; this is generally reversible when the therapy is discontinued. The likelihood of irreversible effects is related to patient age, pre-treatment sexual function and the length of time hormone therapy is given.

Penile rehabilitation is a strategy for optimizing erectile function outcomes after treatment of prostate or bladder cancer with surgery and/or radiation. This approach is based on the theory that lack of blood flow and erections after cancer treatment will lead to scarring and shrinkage of the penis; thus, even if the nerves recover over time changes to the penis itself may make erections difficult. Theoretically, if blood flow to the penis can be maintained the tissue may be less prone to scarring and shrinkage.

The most common form of penile rehabilitation involves use of oral medications and/or devices to help stimulate blood flow and erection. The evidence is mixed on how well these interventions work but there is little risk of harm from using treatments to help erections after surgery. Staying engaged in a program of rehabilitation can help men stay committed to recovery of their sexual quality of life, and use of the medications can help to facilitate sexual activity during the recovery process. Attention to vascular health (e.g. exercising, eating a sensible diet) and maintaining intimacy with one's sexual partner is also a critical component of penile rehabilitation.

Type of Therapy	Advantages	Disadvantages
Oral Medication (Viagra®, Levitra®, Cialis®, Stendra®)	• Pills taken by mouth • Effective in many men	• Not always effective in patients who have prostatectomy, particularly when a non nerve-sparing approach is used • May take 30-120 minutes for full effect • Requires sexual stimulation to be effective • Potential side effects include headache, flushing, stomach upset, muscle pain • Cannot be taken with some medications, especially any sort of nitrate medication for heart problems
Medicated-Urethral Suppository for Erections (MUSE™)	• Small pellet placed in the urethra • Few systemic side effects	• Can cause pain and/or burning sensation • Requires training • Refrigeration required • Side effects include (rarely) painful and prolonged erection of more than six hours, fainting, dizziness, pain or burning for the sexual partner
Penile Injections	• Highly effective • Few systemic side effects • Works in three to five minutes	• Some medications require refrigeration • Requires injection into the penis • Requires office training • Can cause penile pain • Can cause prolonged erection • Theoretical risk of penile scaring
Vacuum Device	• No systemic side effects • Potentially low cost	• Can cause numbness or bruising • Erection sometimes described as "less natural" • requires the use of a tight ring at the base of the penis • Some men find the device awkward to use
Penile Prosthesis	• Highly effective • Can be activated and deactivated in seconds	• Requires anesthesia and surgery • Small risk of infection which requires removal • Mechanical device which may break and require replacement

FOOT NOTE:

A new procedure, pioneered in Melbourne by microsurgeon Professor Christopher Coombs and urologist Dr David Dangerfield, has been found to achieve success in restoring potency after prostate surgery. A study published in the prestigious urology journal European Urology found erectile function was restored within 12 months of surgery for 71 per cent of men left impotent by prostate surgery. Overall, 94 per cent of men in the early study reported "significant improvements in sexual function".

The minimally invasive operation works by using nerves taken from the lower limbs to re-establish neural pathways to the penis providing the chemicals that initiate erectile activity. First, a 30cm section of the sural nerve - taken from the calf - is transplanted into the groin. One end of this nerve is grafted onto the main nerve in the upper thigh - the femoral nerve - and the other end is inserted into the penis. This process is performed twice; once on each side of the body.

Over the following months, nerve fibres regenerate on both sides - from the femoral nerves travelling down via the graft into the penis - gradually restoring erectile function.

The novel nerve grafting technique is minimally invasive. It achieves the best rates of restored erectile function after prostate surgery of any surgical procedures currently available, dramatically improving the quality of life of most patients. Seven out of 10 men who undergo this procedure are able to sustain erections for satisfactory sexual intercourse, and the majority enjoy significant improvements in sexual function.

It is important to note that all surgery involves some level of risk and outcomes may vary. This information is not intended as personal advice nor recommendation. You should seek independent medical advice to determine whether the procedure is right for your individual circumstances.

Learn to be your own researcher to make the best treatment decisions, by being proactive and an advocate for your own health

Prostate Cancer Trials

Efficacy and Safety of Pembrolizumab (MK-3475) Plus Enzalutamide Plus Androgen Deprivation Therapy (ADT) Versus Placebo Plus Enzalutamide Plus ADT in Participants With Metastatic Hormone-Sensitive Prostate Cancer (mHSPC)

(MK-3475-991/KEYNOTE-991)

Status:Recruiting | Trial ID:NCT04191096 Phase 3
Recruitment date:12/02/2020

Monash Health (Site 0305)
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Study Coordinator
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Peter MacCallum Cancer Centre (Site 0306)
Melbourne, 3000 VIC, Australia
Study Coordinator

Navigate: An online treatment decision aid for men diagnosed with prostate cancer and their partners

An NHMRC funded trial 'Navigate' to evaluate the impact of an online resource for men with low-risk prostate cancer when making a treatment decision, and to assess the uptake of Active Surveillance; satisfaction with treatment decision, decisional conflict and regret.

Principle Investigator/s
Professor Penelope Schofield

Professor of Health Psychology, Swinburne University of Technology.

Head of Behavioural Science, Peter MacCallum Cancer Centre.

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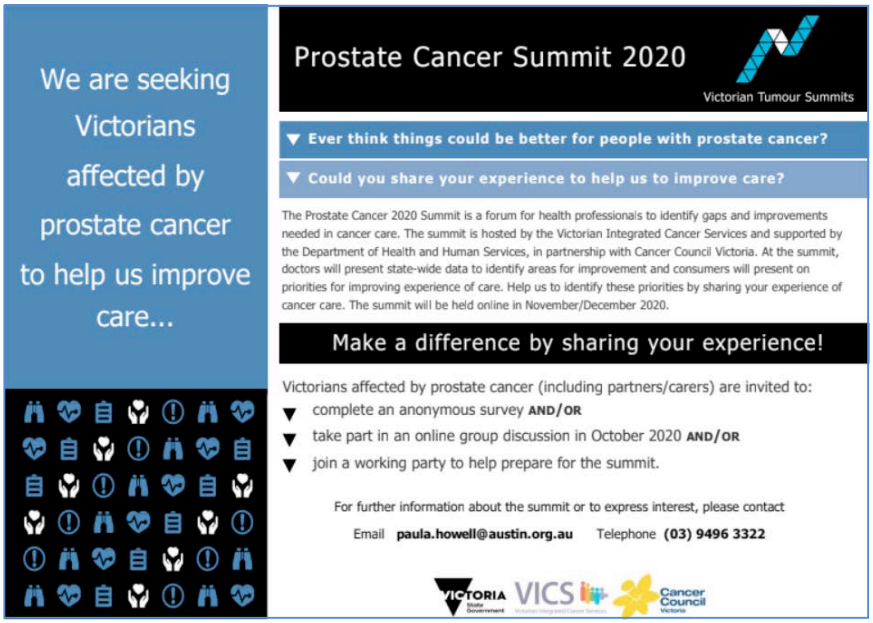

Prostate Heidelberg Cancer Support Group Meetings

While we are having to distance ourselves and are unable to hold face-to-face group meetings we are engaging speakers via video conferencing

Guest Speaker

Tuesday 15 December 2020

Dr Cleola Anderiesz is an experienced senior executive with 18 years of experience in health across the research, not-for-profit, and government public sector.

Committed to quality in healthcare, Dr Anderiesz holds a PhD in Medicine and a Senior Executive MBA. She is skilled in policy, strategy, innovation, program development and implementation, stakeholder engagement, and evidence-based decision making.

Dr Cleola Anderiesz
Deputy Chief Executive Officer at Cancer Australia

PHCSG Videos

Very many thanks to Graham Goeby who does a tremendous job of editing the videos of our guest speakers and to David Bellair for keeping the website up to date.

Please check out the new page on the PHCSG website www.prostateheidelberg.info with links to videos of recent speakers. Just click on Videos in the menu on any page.

Topics:

- The latest Scanning Techniques & Treatment for PC
- Urinary Incontinence
- Erectile Dysfunction
- PSA & the meaning of Test Results

Internet Resources

Members have found the following websites useful

PCFA ONLINE COMMUNITY

The new PCFA Online Community is now live.

Log in to contact the online community with any questions –

onlinecommunity@pcfa.org.au

The internet is a good source for research but it should not be trusted to give you answers for your personal care. Always speak to your doctor to clarify any medical advice.

Prostate Cancer Foundation of Australia for guides & help
www.PCFA.org.au

Australian Cancer Trials Information on clinical trials
www.australiancancertrials.gov.au

USA Prostate Cancer Foundation (Guide) PDF guide for men newly diagnosed with PC
www.PCF.org/guid

Us TOO International PCa Education (USA) USA PC support groups' information & newsletter
www.UsToo.org

Cancer Council Victoria for general support services
www.CancerVic.org.au

ExMed Cancer Program Melbourne based 'best practice' exercise medicine program
www.EXMedCancer.org.au

ProstMate (PCFA) A companion to record PC results

Beyond Blue for help with depression and anxiety
HELPLINE 1300 22 4636

Continence Foundation of Australia for assistance with incontinence aids
HELPLINE 1800 33 0066

Australian Advanced Prostate Cancer Support Group for men diagnosed with advanced metastatic PC
www.JimJimJimJim.com

PCRI Prostate Digest (USA) Prostate Cancer Research Institute supporting research and disseminating information to educate and empower patients, families and the medical community
www.pcri.org/insights

PAACT Newsletter (USA) Patient Advocates for Advanced Cancer Treatments
www.paact.help/newsletter/

PHCSG Correspondance

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PHCSG Correspondance

Max Shub Facilitator
Mike Waller Treasurer
Spiros Haldas Library
David Bellair Web Site
Michael Meszaros Welfare Officer
Sue Lawes Secretary/Newsletter

PHCSG Meetings 2020 10am – 12:30pm

Tues 18 Feb (guest speaker)
Tues 17 March
Tues 21 April
Tues 19 May
Tues 16 June (guest speaker)
Tues 21 July
Tues 18 August (guest speaker)
Tues 15 September
Tues 20 October
Tues 17 November
Tues 15 December (including Xmas lunch) (guest speaker)

Please note that all face-to-face meetings have been cancelled until further notice. Please check your email regularly for updates from the PHSCG Committee.

2020 PHCSG Articles

If you have any feedback or wish to include articles on specific aspects of Prostate Cancer please contact Sue at:

prostateheidelberg@gmail.com

March 2020

- PCFA Consumer Advisory- Coronavirus and Cancer

April 2020

- Telehealth & Delayed Hospital Treatments due to COVID-19
- Fexapotide Triflutate (FT) injection – a new kind of focal treatment to extend time on active surveillance

Prostate Cancer Trials

- DASL-HiCaP Trial
- Evaluation of a mainstream model of genetic testing for men with prostate cancer

May 2020

- ADT May Offer Some Protection From COVID-19 in Men with Prostate Cancer
- TULSA – Novel MRI-guided ultrasound treatment destroys prostate cancer
- Whack-a-Mole A Treatment of Oligometastasis
- Long-term adjuvant ADT improves results of brachy boost therapy in unfavorable-risk prostate cancer patients
- Harnessing the immune system to control prostate cancer spread to the bone

Prostate Cancer Trials

- A study to see whether PET scans using a chemical called Exendin can detect metastatic prostate cancer
- Evaluation of a mainstream model of genetic testing for men with prostate cancer

June 2020

- Evaluating the Outcomes of AS in Gleason Grade 2 Prostate Cancer
- Advancing precision medicine for metastatic prostate cancer
- Impact of Primary Prostate Cancer Treatment with Subsequent Metastatic Disease
- Comparative Analysis & Survival Outcomes in a Real-World Practice Setting
- Fexapotide Triflutate (FT) injection – a new kind of focal treatment to extend time on AS

Prostate Cancer Trials

- Impact of 18F-DCFPyL PET scanning in patients undergoing post-prostatectomy Radiotherapy

July 2020

- Testosterone Therapy does not Increase the Risks of PCR or Death after Definitive Treatment for Localised Disease
- Association of Pre-Salvage Radiotherapy PSA Levels after Prostatectomy with Outcomes of Long-term Antiandrogen Therapy in Men with Prostate Cancer
- Testosterone Replacement in the treatment of Advanced Prostate Cancer
- Memorial Sloan Kettering Cancer Center PCa nomograms Prediction Tools

August 2020

- Advanced Prostate Cancer Algorithm
- Blood Test Predicts Response to PC Treatment (liquid biopsy)
- The Perils and Pitfalls of Treating PSA in PCa
- Reprogramming Immune Cells could Switch Defence into Attack in PCa
- Maintenance of Sexual Activity Following ADT

September 2020

- ProtecT Trial showing patient outcomes after AM, RP & EBRT
- Changes in Penile Length after RP
- Active Surveillance for PC – is it right for you?
- The final part of The Perils and Pitfalls of "Treating PSA" in Advanced Prostate Cancer
- Managing Erectile Dysfunction – A Patient Guide

Prostate Cancer Trials

- Efficacy and Safety of Pembrolizumab (MK-3475) Plus Enzalutamide Plus Androgen Deprivation Therapy (ADT) Versus Placebo Plus Enzalutamide Plus ADT in Participants With Metastatic Hormone-Sensitive Prostate Cancer (mHSPC)
- Navigate: An online treatment decision aid for men diagnosed with prostate cancer and their partners