Side Effects of Prostate Cancer Treatment

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Clinician Nurse, Velindre Cancer Centre

Survivorship – what is the unmet need?

- 85% reported that they had experienced side effects from treatment
- 31% said they received ‘too little’ aftercare for the treatment of side effects
- 19% said the care and support they received for the side effects they experienced were ‘bad’ or ‘very bad’ after treatment completion

PCUK 2012

Patient concerns – local survey

- 28% wanted more information on treatments
- 20% felt they were not equipped for living well after cancer diagnosis

Concerns at 6 months post treatment
- Passing urine
- Hot flushes
- Anxiety of living with cancer
- Bowel changes

The Recovery Package - More than just a PSA test

- Living with and beyond cancer
- Holistic needs assessment (HNA)
- Post treatment seminar
- Treatment Summaries
- Self–Management
**Surgery-Urinary Side effects**

- Urinary incontinence - temporary or permanent (3-30%)
- Stricture (14%)

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**Urinary function post prostatectomy**

- Continence improves over 1-24 months post surgery
- Pads and urinary sheaths offer practical reassurance
- Pelvic floor exercises
- Bladder retraining can help with frequency and urgency

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**Radical prostatectomy: Practical advice**

- Expectation management
- Constipation and straining stretch / weaken pelvic floor muscles, post op laxatives can help.
- Weight loss
- After dribble can be helped with urethral milking post micturition
- Advise reduction in alcohol and caffeine and encourage extra fluids in the form of water, squash or milk

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**Table: Urinary Function Before and After Radical Prostatectomy**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before</th>
<th>1 mo</th>
<th>3 mo</th>
<th>24 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary incontinence (%)</td>
<td>15.0</td>
<td>10.9</td>
<td>10.0</td>
<td>7.6</td>
</tr>
<tr>
<td>Bladder Strictures (%)</td>
<td>14.0</td>
<td>14.0</td>
<td>12.0</td>
<td>9.4</td>
</tr>
<tr>
<td>Total pads (%)</td>
<td>26.0</td>
<td>26.0</td>
<td>24.0</td>
<td>22.6</td>
</tr>
<tr>
<td>Thrice a day (%)</td>
<td>3.4</td>
<td>4.1</td>
<td>4.8</td>
<td>5.0</td>
</tr>
<tr>
<td>Twice a day (%)</td>
<td>3.4</td>
<td>2.9</td>
<td>1.8</td>
<td>1.6</td>
</tr>
</tbody>
</table>

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**Reference**

Surgical interventions

**IPSS – International prostate symptom score - useful assessments**

<table>
<thead>
<tr>
<th>Question</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How often do you need to get up to urinate during the night?</td>
<td>1 – 2 times</td>
</tr>
<tr>
<td>2. How often do you need to get up to urinate during the day?</td>
<td>1 – 2 times</td>
</tr>
<tr>
<td>3. How often do you feel the need to urinate but are unable to get to a toilet in time?</td>
<td>1 – 2 times</td>
</tr>
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</tr>
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</table>

**Useful assessments**

- Fluid intake diary
- Uroflowmetry & Bladder scanning
External Beam Radiotherapy

Fractionated treatment over 4-7 weeks (60-74gy)

Acute radiation induced toxicity

- Caused by inflammation and damage to epithelial lining of rectum/ bowel/ bladder.
- Starts 2 weeks into treatment and peaks at 4-5 weeks.
- Usually self limiting and requires supportive medication.
- Often settles 3-6 months post treatment

External beam radiotherapy

Acute urinary symptoms

- Radiation cystitis
- Frequency, urgency, dysuria
- Haematuria
- Urinary retention

Acute urinary symptoms management

- Avoid caffeine / alcohol
- Drink plenty but define plenty !
- Cranberry juice
- Tamsulosin
- Potassium citrate
- Buscopan
- Analgesia
- Normally transient and settles 3-6 months post RT
Long term
- Greater risk of incontinence in men who have also had trans urethral resection of the prostate
- Lack of stats on incontinence however 1% incontinence rates quoted
- Reduced bladder capacity
- Urethral stricture
- Pelvic floor exercises can be useful

Radiotherapy

Acute bowel toxicity
Most commonly rectal problems following EBRT
Men receiving RT to lymph nodes may experience small bowel problems
- Diarrhoea/constipation
- Faecal urgency/incontinence
- Tenesmus
- Bleeding
- Rectal pain
- Mucus discharge

Acute bowel toxicity
- Dietary changes: Low fibre diet, avoid milk and dairy products
- Anti-diarrhoeal drugs
- Proctosedyl suppositories
- Analgesia
- Buscopan

Pelvic Radiotherapy disease
90% of patients develop permanent change in bowel habit after RT: 20-40% moderate – severe affecting QoL.
Radiotherapy initially causes mucosal changes characterised by inflammation or cell death. Subsequently persistent cytokine activation in the submucosa leads to progressive ischaemia, fibrosis and loss of stem cells.


Symptoms develop when: Apoptotic, inflammatory, ischemic or fibrotic changes affect GI physiological processes.
Pelvic radiotherapy disease

- Damage to the gastrointestinal tract can cause
  - Malabsorption
  - Bile salt malabsorption
  - Small intestinal bacterial overgrowth
  - Dysmotility
  - Reduction in digestive enzymes

Over 20 GI symptoms of PRD have been identified.

- Up to 15% of patients referred to gastroenterologists with diarrhoea were diagnosed with small intestinal bacterial overgrowth (SIBO) - improves with antibiotics

Late toxicity often not associated with inflammation so steroids often not useful

PRD rectal bleeding

- Bleeding occurs in 5% of patients after pelvic radiotherapy but impacts quality of life requiring intervention in fewer than 5%.

- 25-60% of cases not related to RT.
  - Check FBC, medication - anticoagulation ?

Patients with PR bleeding should be referred for investigations by the gastroenterologist team

- Treatment
  - Optimise bowel function and consistency
  - If cause identified and not affecting QOL then reassurance may be all that’s needed
  - Sacral formulae +/- metronidazole &/or for 4/5/6
  - Hypoxic oxygen (stimulates angiogenesis in ischaemic tissue)
  - Intra rectal formalin (chemical cauterisation)
  - Argon plasma coagulation (cauterisation) 
  - Argon plasma coagulation 1% risk of serious complications (fistula, perforation)

Bowel Management late toxicity

- Diet
- Drugs, Movicol +/- loperamide
- Pelvic Floor exercises
- Argon plasma coagulation with caution
- Referral to gastroenterology

- Endoscopy
- Tests for bile acid malabsorption & small bowel bacterial overgrowth
- More specific bowel advice
- Suppositories
- Biofeedback
Low FODMAP diet

FODMAPs attract water into the intestine during digestion—may be slowly or incompletely digested or be fermented by bacteria. This can cause bloating, constipation, gas, diarrhea, or cramping. For people with irritable bowel syndrome (IBS) or other function gastrointestinal problems.

Involves dieticians.

Prostate Brachytherapy

The insertion of radioactive (Iodine 131) seeds into the prostate. Seeds remain in place permanently.

Prostate Brachytherapy Criteria

- Stage T1c – T2a
- Gleason 6-7
- PSA ≤ 10
- Prostate Volume <40 - 50cc
- IPSS < 8
- Flow rate > 17mls/sec
- No previous prostatic surgery
- Able to ‘assume the position’
Brachytherapy – Urinary Effects

- Difficulty passing urine
- Frequency and Urgency
- Nocturia
- Retention (10% risk)
- Urethral stricture

Commenced on tamsulosin
Manage as per radiation cystitis

Side Effects of Hormone Therapy

- Neo adjuvant – adjuvant with RT
- Metastatic disease
- On biochemical relapse

Androgen Deprivation Therapy

**The Benefits of Optimal Testosterone**

- Sharp mind
- Energy
- Confident
- Happy
- Mature
- Personal
- Confident
- Healthy heart
- Higher energy
- Strong tissues & healthy skin
- Strong bones
- Plenty of energy
- Increased muscle
- Increased bone density
- Increased risk of osteoporosis

**Side effects of Hormone Therapy**

- Hot flushes
- Tiredness and fatigue
- Loss of sex drive (libido) and impotence
- Mood swings and depression
- Breast swelling & nipple tenderness
- Weight gain around the middle
- Loss of muscle mass
- Increased risk of cardiovascular disease and diabetes
- Osteoporosis.
Hot Flushes- self management

- 80% of men
- 27% - most troublesome side effect
- Stop smoking
- Drink plenty of fluid, cut down alcohol and caffeine
- Reduce amount of spicy food
- Keep room temperature cool and use a fan
- Wear cotton clothes, especially at night
- Use cotton bed sheets
- Use a cotton towel on top of sheets that you can change easily
- Have lukewarm baths and showers

Gynacomastia and breast pain

- Occurs in around 50% of patients on antiandrogen
- Breast bud radiotherapy
- Tamoxifen
- Surgery

Hot Flushes

Complementary Therapies

- Acupuncture
- Hypnotherapy
- Herbal remedies
  - Red clover
  - Evening Primrose
  - Sage

Medical Management

- Medroxyprogesterone 20mg od for 10 weeks (NICE)
- Low dose Anti-androgen - cyproterone acetate
- SSRI's
- Consider intermittent hormone therapy

Metabolic Syndrome

- Abdominal Obesity
- High Triglycerides
- Low HDL
- HT
- High fasting glucose

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- HT
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ADT & Cardiometabolic Syndrome

Regular monitoring is recommended of:
- Weight/BMI
- Blood pressure
- Serum lipids
- Fasting blood glucose

Changes occur early, often within 3 to 6 months of starting treatment.

First assessment for risk factors should occur at 3 months and at 3 monthly intervals.
- Dietary advice
- Prescribe physical activity where possible

Management

ADT & Cardiometabolic Syndrome

ADT results in increased bone resorption through:
- Increased osteoclast formation
- Increased osteoblast apoptosis
- Increased osteoclast activation leads to a decrease in bone mineral density
- Overall, ADT results in more bone resorption than formation, placing prostate cancer patients at greater risk of osteoporosis and fractures

ADT & Cardiovascular Risk

Androgen deprivation therapy increases the risk of cardiovascular toxicity.
**NICE Prostate Cancer Guidelines 2014**

- Consider assessing fracture risk in men with prostate cancer who are having androgen deprivation therapy, in line with Osteoporosis (NICE clinical guideline 146).
- Do not routinely offer bisphosphonates to prevent osteoporosis in men with prostate cancer having androgen deprivation therapy.
- Offer bisphosphonates to men who are having androgen deprivation therapy and have osteoporosis.
- Consider denosumab for men who are having androgen deprivation therapy and have osteoporosis if bisphosphonates are contraindicated or not tolerated.

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**Lifestyle Education!!!!!!**

<table>
<thead>
<tr>
<th>Metabolic Risk</th>
<th>Osteoporotic Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet</td>
<td>Low fat, high fibre</td>
</tr>
<tr>
<td>Exercise</td>
<td>Aerobic</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Moderation</td>
</tr>
<tr>
<td>Smoking</td>
<td>Smoking cessation</td>
</tr>
<tr>
<td>Weight</td>
<td>Healthy BMI</td>
</tr>
<tr>
<td>Treatment</td>
<td>Statin etc</td>
</tr>
</tbody>
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**Psychological morbidity of cancer**

- In a 2006 survey of people with a cancer diagnosis:
  - 26% of respondents said cancer had affected their relationships.
  - 25% of that number said that their relationship had broken down as a result.
  - 32% of respondents said that their relationships were put under ‘enormous strain’.
  - 43% said that their sex life suffered.
  - 42% of men diagnosed with cancer suffer some form of depression as a result.
Summary

- Men live a long time with prostate cancer
- Men live a long time with the consequences of prostate cancer treatment
- We should be managing men holistically rather than concentrating solely on the PSA test... though this is still important!
- Men should be supported to self-manage wherever possible
- Benefits of healthy lifestyle should not be overlooked and should be strongly encouraged or 'prescribed'

Metastatic prostate cancer – a new paradigm

**STAMPEDE TRIAL**

- 2962 locally advanced / metastatic prostate cancer patients
- LHRH alone
- LHRH + Zometa
- LHRH + Docetaxol
- LHRH + Docetaxol + Zometa

<table>
<thead>
<tr>
<th>Treatment</th>
<th>OS 67 months</th>
<th>OS 77 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>LHRH only</td>
<td>67 months</td>
<td>77 months</td>
</tr>
<tr>
<td>LHRH + Docetaxol</td>
<td></td>
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**Metastatic disease subset**

- OS 23 months (43-65)

Treatment algorithm for metastatic prostate cancer

- LHRH agonists +/- docetaxol
- Add antiandrogen
- Antiandrogen withdrawal
- Castrate resistant disease
- Docetaxel Chemotherapy
- Abiraterone
- Enzalutamide
- Radium-223
- Cabazitaxel

Thank you for listening.

With thanks to Helen Johnson, from whom slides were appropriated with wild abandon