Side Effects of Prostate Cancer Treatment
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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

Radical prostatectomy

Complications of radical open prostatectomy

<table>
<thead>
<tr>
<th>Complication</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peri-operative death</td>
<td>0.0-2.1</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>1.0-11.5</td>
</tr>
<tr>
<td>Rectal injury</td>
<td>0.0-5.4</td>
</tr>
<tr>
<td>Deep venous thrombosis</td>
<td>0.0-8.3</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>0.8-7.7</td>
</tr>
<tr>
<td>Lymphocele</td>
<td>1.0-3.0</td>
</tr>
<tr>
<td>Urine leak, fistula</td>
<td>0.3-15.4</td>
</tr>
<tr>
<td>Slight stress incontinence</td>
<td>4.0-50.0</td>
</tr>
<tr>
<td>Severe stress incontinence</td>
<td>0.0-15.4</td>
</tr>
<tr>
<td>Impotence</td>
<td>79.0-100.0</td>
</tr>
<tr>
<td>Bladder neck obstruction</td>
<td>0.5-14.6</td>
</tr>
<tr>
<td>Urinary obstruction</td>
<td>0.0-0.7</td>
</tr>
<tr>
<td>Urethral stricture</td>
<td>0.0-0.1</td>
</tr>
</tbody>
</table>
Radical prostatectomy
Urinary problems

- Urinary incontinence could be just the occasional leakage or severe leakage
- Stress incontinence occurs from the removal of smooth muscle (prostate and bladder neck)
- There is a definite reduction if the patient is taught pelvic floor exercises to do before surgery as well as post-operatively

Radical prostatectomy
Urinary problems

- Advise reduction in alcohol and caffeine and encourage extra fluids in the form of water, squash or milk
- Constipation and straining stretch / weaken pelvic floor muscles, post op laxatives can help.
- Less than 5% may have long term urinary problems which may require further surgery

Expectations and support

- Good understanding of pelvic floor exercises
- Incontinence can range from a few drops to no control
- Continence can take anything from day-weeks-months to return
- Close fitting underpants for pads, dark coloured trousers
- Support and supplies varies enormously across the country
- When to ask for support or referral
- Referral to specialist surgeon to discuss options internal male slings, artificial sphincters

External Beam Radiotherapy

Fractionated treatment over 4-7 weeks (60-74gy)
External beam radiotherapy (EBRT)

- UK standard was 3D conformal radiotherapy
- Metal blocks (collimators) are put in the path of the radiation beam so that it 'conforms' more closely to the shape of the tumour
- Allows a higher dose of radiation to be used
- Less normal tissue is included in the radiotherapy - fewer long term side effects

Intensity-modulated radiotherapy (IMRT)

- Ultraconformal radiotherapy
- Uses powerful planning computers and multiple fields
- Can treat irregular concave volumes
- Allows for higher doses to be prescribed

VMAT

- In IMRT, 5 to 9 beams are targeted on the prostate, one beam at a time
- VMAT method delivers radiation in a single 360° arc while the beam aperture shape continuously changes
- Compared to IMRT, VMAT results in:
  - Shorter treatment times
  - Reduced patient exposure to radiation leakage
Radiotherapy _ short term urinary Effects

- Radiation cystitis
  - Frequency, urgency, dysuria
- Haematuria
- Urinary retention
- Slow build up and peaks 2-4 weeks post RT

Radiation cystitis

- Avoid caffeine / alcohol
- Drink plenty but define plenty !
- Cranberry juice / extract (1 study showed reduced LUTI 8.7 vs 24.2 % )
- Tamsulosin
- 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

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Bowel Side Effects

Radiotherapy Bowel Side Effects

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

Early bowel toxicity

- Dietary changes: Low fibre diet,
- Fybogel
- Anti-diarrhoeal drugs
- Proctosedyl suppositories
- ?Bio drinks (Actemel etc)
- Avoid milk and dairy products

Late side effects bowel

- 90 % of patients have altered bowel function
- 40 % moderate to severe

- Now known as pelvic radiotherapy disease
Pelvic Radiotherapy disease

Symptoms of PRD - diarrhoea
- Check patients dietary intake
- Stop smoking
- Ant diarrhoeal +/- bulking agent
- Pelvic floor exercises
- 8-15% diagnosed with bacterial overgrowth - improves with antibiotics
- Large bowel strictures (3-15%) - stenting

PRD rectal bleeding
- Occurs 21-50% of patients.
- Often settles down over time
- Should be offered GI assessment
- 25-60% of cases not related to RT
- Treatment
  - Optimise bowel function and consistency
  - Sucralfate suppositories / enemas
  - Hypobaric oxygen (stimulates angiogenesis in ischaemic tissue)
  - Argon plasma coagulation

PRD Flatulence
- Most common probable cause is diet too healthy
- Many people assume a healthy diet after diagnosis, rich in fermentable fibre.
- Reduce complex carbohydrates (pulses, beans, lentils, spicy food bran...etc)
- Sometimes a bulking agent may help with faecal transit – reducing time for fermentation.
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

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

Hot Flushes

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

Medical Management
- Medroxyprogesterone
- Low dose Anti-androgen – cyproterone acetate
- SSRTs
- Consider intermittent hormone therapy
Gynacomastia and breast pain
- Occurs in around 50% of patients on antiandrogen
- Breast bud radiotherapy
- Tamoxifen
- Surgery

Weight gain and muscle loss
- Regular resistance exercise such as swimming
- Diet
- Dietician
- Reduced muscle and increase in body fat can affect body image of the patient.
- Metabolic syndrome

Exercise advice
- Remember a little exercise is better than no exercise
- Start with small changes
- Set yourself realistic goals
- Keep a diary to monitor your progress
- Don’t be too hard on yourself if you have an ‘off’ day
- Listen to your body
- Involve your friends and family
  
  Acceptance of a new norm

Lethargy, cognitive decline, mood changes
- Exclude other causes eg anaemia
- May improve with time
- Some exercise can increase energy levels
- Counselling
- Antidepressants
- Refer to National Exercise referral scheme
**Bone Health in Prostate cancer**

- Androgen deprivation (ADT) is associated with Osteoporosis and Bone fragility.
- DEXA scans at diagnosis and 2 yearly thereafter if found to have osteoporosis (EAU guidelines).

**Bone Loss Is Accelerated With ADT**

![Bone Loss Graph](image)

- Normal men
- Postmenopausal women
- ADT

**How to improve Bone Health with Regular exercise**

- Gentle regular exercise reduces cancer related fatigue especially when delivered as a formal programme.

**How to improve Bone Health**

- Smoking Cessation
- Reduce alcohol intake
- Healthy BMI
- Diet sufficient in Vit D and Calcium. If not supplement
- Bisphosphantes

Useful for pain relief from bone deposits
Reduce and delay skeletal complications
No survival benefit
Castrate refractory disease management

- Docetaxol chemotherapy
- Abiraterone
- Enzalutamide
- Radium 223

Metastatic prostate cancer – a new paradigm

**STAMPEDE TRIAL**

- 2962 locally advanced / metastatic prostate cancer patients

<table>
<thead>
<tr>
<th>Treatment</th>
<th>OS (months)</th>
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<tbody>
<tr>
<td>LHRH alone</td>
<td>67</td>
</tr>
<tr>
<td>LHRH + Docetaxol</td>
<td>77</td>
</tr>
<tr>
<td>LHRH + Zometa</td>
<td></td>
</tr>
<tr>
<td>LHRH + Docetaxol + Zometa</td>
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Metastatic disease subset
OS 22 months (43-65)

Conclusions

- Docetaxel improves survival for hormone-naive prostate cancer
- Zoledronic acid does not improve survival
- Adding both improves survival but offers no obvious benefit over adding just docetaxel
- Multi-arm, multi-stage trials are practicable and efficient

- **Docetaxel should be:**
  - Considered for routine practice in suitable men with newly-diagnosed metastatic disease
  - Considered for selected men with high-risk non-metastatic disease in view of substantial prolongation of failure-free survival