Management of locally-advanced prostate cancer: Update on surgery

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Prescribing Information and Adverse Event reporting for Janssen medications can be accessed here.
Disclosures

• Honorarium – Janssen
• UK CI – PROTEUS study (NCT03767244)
• Intuitive Surgical Proctor
Learning objectives

• Understand the implications for clinical practice of recently released from studies investigating the use of surgery in men with localised disease
Urology Surgery Present

Pre-diagnosis counselling

Diagnosis

Risk stratification

Treatment

Holistic Patient Management
Pre-diagnostic Counselling

Promises and perils of using genetic tests to predict risk of disease

Jan Scott and colleagues argue there is little value, and a risk of harm, in testing asymptomatic people with no family history of polygenic conditions.

Increasing numbers of patients and clinicians are undertaking low cost genetic testing in asymptomatic people to identify genetic variants that might predict risk of developing diseases. Tests for approximately 75,000 genetic variants are now commercially available, such as lifestyle counselling, closer surveillance, more intense screening, and pharmacological prophylaxis. But the proliferation of genetic variants and related risk scores might cause clinicians and consumers to misinterpret their results. People at low risk may be overdiagnosed.

BMJ Feb 2020
Pre-diagnostic Counselling


• Prospective cohort study of n=376 BRCA1 and n=447 BRCA2

• Method – commenced in 1998 (EMBRACE) – end of follow up – June 2016

• Outcome
  • 16/376 BRCA1 and 26/447 BRCA2
  • SIR BRCA1 - 2.35 (95% CI 1.43-3.88), SIR BRCA2 – 4.45 (95% CI 2.99-6.61)
  • 2/376 BRCA1 and 4/447 BRCA2 died from their disease

• Conclusion
  • BRCA2 carriers at higher risk of developing prostate cancer + more aggressive prostate cancer
  • Family history and mutation location influence

BRCA1, breast cancer gene 1; BRCA2, breast cancer gene 2; SIR, standardised incidence ratio

http://ccge.medschl.cam.ac.uk/embrace/
Pre-diagnostic Counselling

Interim results from the IMPACT study: evidence for prostate-specific antigen screening in BRCA 2 Mutation Carriers. Eur Urol 76(2019) 831-842

• Study evaluating targeted PSA screening of men with BRCA 1/2 Mutations
• Men 40-69yr were included. *A control population was included*
• 65 centres, 20 countries, over 3000 men, median age 54yrs
  • 919 BRCA1 carriers, 709 BRCA1 non carriers, 902 BRCA2 carriers, 497 BRCA2 non carriers

• Method – Annual PSA testing for 5 years, biopsy if PSA >3ng/ml, if BRCA offer end of screen biopsy

• Outcomes
  • Cancer incidence rate per 1000 person years in BRCA 2 vs non carriers were 19.4 vs 12.0;p=0.03
  • Clinically significant disease in BRCA 2 vs non carriers 77% vs 40%; p=0.01

• Conclusions
More higher risk prostate cancers are found in BRCA2 carriers than non-carriers
More cancers picked up at an earlier age

PSA, prostate-specific antigen
Prostate cancer: diagnosis and management

NICE guideline [NG131]  Published date: May 2019  Uptake of this guidance

1.2 Assessment and diagnosis

Magnetic resonance imaging and biopsy

1.2.1 Do not routinely offer multiparametric MRI to people with prostate cancer who are not going to be able to have radical treatment. [2019]

1.2.2 Offer multiparametric MRI as the first-line investigation for people with suspected clinically localised prostate cancer. Report the results using a 5-point Likert scale. [2019]

1.2.3 Offer multiparametric MRI-influenced prostate biopsy to people whose Likert score is 3 or more. [2019]

1.2.4 Consider omitting a prostate biopsy for people whose multiparametric MRI Likert score is 1 or 2, but only after discussing the risks and benefits with the person and reaching a shared decision (see table 1). If a person opts to have a biopsy, offer systematic prostate biopsy. [2019]
Diagnosis

THERE IS AN AREA OF NEED: - to refine who does not need a biopsy / MRI

- **GU ASCO 2020**
  - Klotz L et al. Analysis of small non-coding RNAs in urinary exosomes to classify prostate cancer into low grade (GG1) and higher grade (GG2-5)
  - Pye H et al. Evaluation of Proclarix, a prostate cancer risk score, used together with magnetic resonance imaging for the diagnosis of clinically significant prostate cancer
  - Fasulo V et al. TMPRSS2: ERG expression in prostate cancer- Imaging and clinicopathological correlations

- **Upcoming EAU 2020**
  - Screening of asymptomatic prostate cancer Fri 20 March
  - Expert guided poster tour – How to improve MRI based biopsy for finding relevant prostate cancer Fri 20 March
  - Serum and urinary markers for prostate cancer diagnosis Sat 21 March

RNA, ribonucleic acid; TMPRSS2; transmembrane protease, serine 2; ERG, ETS-related gene; MRI, magnetic resonance imaging
Risk stratification

Life expectancies

How long, on average, people can expect to live using estimates of the population and the number of deaths.

Source: Office for National Statistics

ONS December 2019
Risk stratification

Prostate cancer: diagnosis and management

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High-risk localised prostate cancer

1.3.13  Do not offer active surveillance to people with high-risk localised prostate cancer. [2019]

1.3.14  Offer radical prostatectomy or radical radiotherapy to people with high-risk localised prostate cancer when it is likely the person’s cancer can be controlled in the long term. [2019]

Locally advanced prostate cancer

1.3.28  Consider pelvic radiotherapy for people with locally advanced prostate cancer who have a higher than 15% risk of pelvic lymph node involvement and who are to receive neoadjuvant hormonal therapy and radical radiotherapy. [2008]

1.3.29  Do not offer immediate post-operative radiotherapy after radical prostatectomy, even to people with margin-positive disease, other than in the context of a clinical trial. [2008]

1.3.30  Do not offer adjuvant hormonal therapy in addition to radical prostatectomy, even to people with margin-positive disease, other than in the context of a clinical trial. [2008]

1.3.31  Do not offer high-intensity focused ultrasound and cryotherapy to people with locally advanced prostate cancer other than in the context of controlled clinical trials comparing their use with established interventions. [2008]

1.3.32  Do not offer bisphosphonates for the prevention of bone metastases in people with prostate cancer. [2008]
Treatment

- 50 year old male
- PSA - 23.9ng/mL
- MRI – cT3a
- Biopsies – Gl 4+5=9 bilaterally
- CT CAP and Bone Scan - Clear
Treatment

Overall Survival

- 88% survive at least 10 years
- 73% survive at least 15 years

Warning
You are running the tool with high risk features in which it has been less well tested.

Scroll down for potential harms
Incontinence
Defined as: ‘Wore one or more pads in the last 4 weeks’

With conservative management, fewer than 1 in 100 men have this issue after 3 years.

| Less than 1% |

With radical prostatectomy, about 20 in 100 men have this issue after 3 years.

| 20% |

With radiotherapy, about 3 in 100 men have this issue after 3 years.

| 3% |

Bowel Issues
Defined as: ‘Bloody stools about half the time or more frequently’

With conservative management, fewer than 2 in 100 men have this issue after 3 years.

| Less than 2% |

With radical prostatectomy, fewer than 2 in 100 men have this issue after 3 years.

| 2% |

With radiotherapy, about 7 in 100 men have this issue after 3 years.

| 7% |

Erectile dysfunction
Defined as: ‘Erections insufficient for intercourse’

With conservative management, about 27 in 100 men have this issue after 3 years.

| 27% |

With nerve-sparing radical prostatectomy, about 86 in 100 men have this issue after 3 years.

| 86% |

With non-nerve-sparing radical prostatectomy, about 86 in 100 men have this issue after 3 years.

| 86% |

With radiotherapy, about 39 in 100 men have this issue after 3 years.

| 39% |

Estimates for incontinence dysfunction have been taken from the UK-based Prostate Testing for Cancer and Treatment (ProtecT) found here: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5782813/

Estimates for bowel dysfunction have been taken from the UK-based Prostate Testing for Cancer https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5782813/

Estimates for erectile dysfunction have been derived from a large American study. The full research can be read here: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5782813/

PREDICT model outcome – prostate.predict.nhs.uk accessed Feb 2020
Treatment – “if not now, when?”
Treatment

- proPSMA study (ANZCTR Trial No. 12617000005358) – Hofman MS et al. BJUI 2018
  - High Risk Disease (≥ ISUP GG 3, PSA ≥ 20, stage ≥ T3)
  - Patient preference re treatment options once results known

Use of gallium-68 prostate-specific membrane antigen positron-emission tomography for detecting lymph node metastases in primary and recurrent prostate cancer and location of recurrence after radical prostatectomy: an overview of the current literature

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ISUP, International Society of Urological Pathology; GG3 Grade Group 3; PSMA, prostate-specific membrane antigen
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This meeting is initiated and funded by Janssen. An independent faculty have determined the structure and scientific content of the meeting. Prescribing Information and Adverse Event reporting for Janssen medications can be accessed here.