Treatment modalities in localised prostate cancer

It is clear that prostate cancer is an important neoplastic disease for the NHS to manage. It has been well studied that prostate cancer will affect almost all males if they live for a sufficient duration, which is an important consideration in line with the demographic changes occurring within the developed world. In the first of a two-part series, this article will review screening, clinical presentation and diagnosis of prostate cancer.

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This article will focus upon reviewing the current evidence base for recommended treatment modalities for patients with a confirmed diagnosis of prostatic carcinoma, a common tumour in males in the UK. In addition, the general background of this neoplastic disease including epidemiology, the controversy of screening for prostate cancer, usual clinical presentation and how a diagnosis is confirmed will also be reviewed.

Background and epidemiology

The prostate is a male accessory sex organ that secretes alkaline fluid to help form semen. Prostate cancer is an enigmatic neoplasm in men. Research suggests that almost all men would die with histological evidence of the disease being present if they lived into their 80s. Furthermore, prostate cancer shows very different rates of progression and metastasis in different patients. Unfortunately, prostate cancer is the most common cancer in men and now comprises nearly a quarter of the new diagnoses of malignant cancer in men in England and Wales. Furthermore, the Chief Medical Officer of Scotland predicts that over 3,000 men will be diagnosed with the condition between 2016 and 2020. The condition is a significant cause of cancer-related death with over 10,000 deaths in the UK as a result of the cancer in 2008, accounting for 12% of annual male deaths from cancer. Mortality is related to metastasis, most commonly to the vertebrae and local lymph nodes.

Screening

Screening for prostate cancer is currently a controversial practice. The most common method of screening for prostate cancer is using prostate specific antigen (PSA) as there is an association between prostate cancer and a raised PSA. PSA can be easily measured as a blood test, which is an acceptable testing method for patients compared to other invasive screening procedures. However, the test has a number of limitations. Firstly, the normal PSA level increases in other prostate pathologies including benign prostatic hyperplasia, a recent urinary tract infection or prostatitis. Furthermore, PSA increases slightly as we age from 2.5ug/L between 40–50 years old rising to 7.5ug/L in 80–89-year-old men. Secondly, there is recent evidence to suggest that the PSA test has low sensitivity, as men who test positive for prostate cancer can often have a normal PSA (ie. false negatives). The PSA test has a low specificity with two out of three men with raised PSA not having cancer who would then be referred for more unnecessary screening tests.
Clinical presentation

The clinical presentation depends upon a number of factors including size, exact anatomical location and the presence of metastasis. Patients with local disease generally present with urinary symptoms that include hesitancy, frequency, poor flow, incomplete bladder emptying and urge incontinence. Patients with locally invasive disease may develop haematuria, rectal symptoms (tenesmus), perineal or suprapubic pain. Metastatic disease has a varied presentation and depends on the secondary tumour location. Presentation can include bone pain, sciatica, anuria (secondary to bladder obstruction) and paraplegia secondary to spinal cord compression. Patients with metastatic disease will also generally have signs of systemic disease that include weight loss, anaemia and lethargy.

Confirming the diagnosis

A patient may be suspected of having prostate cancer as a result of symptoms or as a result of a raised PSA test, with an abnormal prostate on digital rectal examination (DRE). In this patient cohort it is important to confirm a diagnosis before proceeding to treatment.

The gold standard diagnostic test is a biopsy and pathological review of the tissue looking for cytological and histological abnormalities. This procedure is an outpatient procedure that is completed under a local anaesthetic. Biopsy access is achieved transrectally with ultrasound guidance (TRUS). Recommended best practice from the European Association of Urology states that local anaesthetic should be given to

Box 1: Prostate Cancer TNM Staging

<table>
<thead>
<tr>
<th>Tumour</th>
<th>Node</th>
<th>Metastasis</th>
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<tbody>
<tr>
<td>T1: Tumour in the prostate gland that cannot be detected by PR exam</td>
<td>N0: No evidence of spread to lymph nodes</td>
<td>M0: No evidence of spread to distant body sites</td>
</tr>
<tr>
<td>T2: Tumour in the prostate gland that can be detected by PR exam</td>
<td>N1: Evidence of spread to local lymph nodes (eg. pelvic nodes)</td>
<td>M1: Evidence of spread to distant body sites</td>
</tr>
<tr>
<td>T3/T4: Tumour in the prostate gland has invaded local tissues</td>
<td>N2: Evidence of spread to distant lymph nodes</td>
<td>-</td>
</tr>
<tr>
<td>T4: Tumour in the prostate gland has invaded adjacent tissues (eg: bladder).</td>
<td></td>
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The PROTECT study (nine centre UK trial) assessed the feasibility of the PSA test being used as a screening tool. The report considered the issues raised above, amongst others, and concluded that there is currently insufficient evidence to introduce a wide-scale prostate screening programme.

The key reasons for this were the paucity of understanding of the natural course of prostate cancer, issues with the accuracy of the diagnostic test and questions over the effectiveness of treatment and side effect profiles. Therefore, the suggested practice is to measure PSA in patients with symptoms associated with prostate cancer (urinary symptoms, weight loss, back pain). In line with the issues raised above it has been suggested that the tendency to test asymptomatic patients, thus using PSA as a screening tool, should be stopped.
patients undergoing a TRUS biopsy.\textsuperscript{13} Patients commonly report discomfort during the procedure and may have symptoms of haematuria and/or a small amount of rectal bleeding.\textsuperscript{12} Prognostic information from the needle biopsy is then reviewed in a multidisciplinary team meeting using internationally recognised scoring systems and a management plan is formulated.

**Review of treatment modalities**

**Scoring systems**

There are two major scoring systems that clinicians use when considering management options for patients with prostate cancer, one relating to tumour grading and one relating to tumour staging.

Firstly, in the 1960s Donald Gleason, an American pathologist, developed a tumour grading system that is now the most commonly used prostate cancer grading protocol worldwide.\textsuperscript{11,14} Pathologists review aspects of cancer growth including the degree of differentiation, appearance of normal tissue structure, nuclear to cytoplasm ratio and the number of mitotic figures.\textsuperscript{14-15} Pathologists who review prostate biopsy tissue samples will assess the two commonest patterns (Gleason 1–5) to give a combined Gleason score between 2 and 10. A higher score is associated with rapidly growing tumours that are likely to spread.\textsuperscript{2,12,14}

Secondly, patients with confirmed cancer will have local staging of their cancer by DRE, CT looking at lymph node status and by using MRI scan imaging to assess the extent of disease ahead of radical treatment. In addition, an isotope bone scan is routinely recommended for all except low risk patients (Gleason 6 or less and PSA <10ug/l and T1 stage).\textsuperscript{5,16}

Most centres use the Tumour Node Metastasis [TNM] staging tool that is of great importance for clinicians to make clinical management decisions. The method by which the score is calculated is shown in Box 1.\textsuperscript{11,12}

Scoring systems and pre-treatment PSA levels are known to be very important factors in predicting treatment response and outcome. There is consistent evidence from observational studies that a high Gleason score, high T-stage score or high pre-treatment PSA levels is associated with a greater risk for lymph node involvement, and death from prostate cancer.\textsuperscript{4-5,16-17} These factors are used to classify localised prostate cancer into risk categories. These are: Low Risk (Clinical Stage T1–T2a and Gleason score <6 and PSA at diagnosis <10ug/l); Intermediate Risk (Clinical Stage T2b or T2c or Gleason score 7 or PSA at diagnosis 10–20ug/l); and High Risk (Clinical Stage T3–T4 or Gleason score 8–10 or PSA at diagnosis >20ug/l).\textsuperscript{11-12,16}

**General treatment considerations**

Regardless of the severity of the prostatic neoplasm there some important general considerations that are essential for optimal patient care. It is recommended that all patients with prostate cancer, or indeed any urological cancer, are managed in a multidisciplinary team (MDT).\textsuperscript{16} This team should include a wide range of healthcare professionals including urologists, oncologists,
radiologists, pathologists and specialist nurses. In addition, there are a number of patient factors that will impact the treatment modalities offered by medical staff or requested by the patient.

Firstly, the patient’s general medical condition is a major consideration for a clinician to advocate a surgical or pharmaceutical treatment. An assessment of general medical condition(s) should include comorbidity, the patient’s age (not to be used in isolation), cognitive function and life expectancy. Secondly, it must be stressed that the patient’s symptoms and their impact upon the patient’s life should guide treatment. This is because surgical treatment options for patients with prostate cancer are associated with undesirable side effects including impotence and incontinence. Therefore, patients may be offered treatment if their symptoms, such as lower urinary tract symptoms and bladder outflow obstruction, are affecting their quality of life. For example, a 75-year-old man with troublesome and distressing symptoms may opt for curative treatment whereas another man of the same age without severe symptoms may opt for non-radical treatments.

**Conclusion**

It is clear that prostate cancer is an important neoplastic disease for the NHS to manage. It has been well studied that prostate cancer will affect almost all males if they live for a sufficient duration, which is an important consideration in line with the demographic changes occurring within the developed world. Therefore, clinicians and nurses both require a comprehensive understanding of the background to prostate cancer, some of the controversy surrounding screening tools currently used and the major treatment options for the benefit of their patients. This paper has attempted to achieve the above objectives.

**Part two of this article in the December edition will review treatments for localised prostate cancer and locally advanced prostate cancer.**

**Conflict of interest: none declared.**

**References**