

Prostate cancer: palliative care and pain relief

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Introduction: Metastatic prostate cancer is incurable and causes significant morbidity. The focus of treatment should be on improving quality of life through appropriate oncological treatment and palliative care. The National Institute for Clinical Excellence guidelines for urological cancer recommends palliative care for all patients with prostate cancer, according to need. This paper outlines the principles of modern palliative care in patients with metastatic prostate cancer within the UK.

Discussion: We highlight the main physical symptoms encountered in metastatic prostate cancer and their management. We also introduce the UK Department of Health's 'End-of-Life Care Programme'. This initiative intends to improve the lives *and deaths* of *all* patients with incurable disease and should be a priority for all health care professionals, within any setting.

Conclusion: Clearly, we have addressed the management of metastatic prostate cancer within the UK setting, though any of these government initiatives may provide a resource and framework in other countries.

Keywords: palliative care/pain relief/symptom control

Introduction

Palliative care in prostate cancer is extremely important and with an aging population is likely to become more so. In 2002, the National Institute for Clinical Excellence (NICE) outlined its guidance for urological cancers.¹ It stressed the importance of palliative care in prostate cancer at all stages and the importance of multidisciplinary team working. In this paper, we review the current evidence and guidelines as well as drawing on personal experience.

Epidemiology

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Prostate cancer is the most common cause of cancer in men and the second most common cause of cancer death after lung cancer.² It accounts for around 13% of male deaths due to cancer in the UK. The incidence is increasing and this is especially apparent in the 85+ age group, which saw a 73% increase between 1971 and 2004.²

Prostate cancer is far more common in older men, with 80% of cases being diagnosed in the over 65s. Although incidence is increasing, this apparent increase is probably secondary to the introduction of prostatic specific antigen testing. Unfortunately, mortality remains fairly stable and country specific mortalities are also similar despite incidence variation. There is variance in incidence among different ethnic groups, with African Americans having the highest risk. There is a relatively low risk among the Asian population, but this disappears in migration.

Risk factors

There is an increased risk of developing prostate cancer if one or more first degree relatives have it. If it is just one then the risk is doubled. However, if two or more are affected then the risk is increased by five to 11 times. There is some evidence that vitamins E and D may be protective and there is possibly an association with increased animal fat intake and obesity.

Pathology

The majority of prostate cancers occur in the peripheral zone of the prostate (70%) and are adenocarcinomas. The Gleason system³ is widely used as a method of classifying the glandular differentiation and can give useful information about prognosis.¹ The Gleason score is made up of two numbers, each 1–5 and they correspond to the differentiation of the cells and then the pattern in which they arrange themselves. Once these numbers are added together, the NICE guidance divides the score into well (2–4), moderately (5–7) and poorly (8–10) differentiated. A score of above 4 is associated with increased risk of metastasis and decreased survival.¹

Prostate cancer can be divided into local disease, locally invasive disease and metastatic disease. The site of disease determines presentation, treatment, symptoms and prognosis.

Local and locally invasive disease

There are several treatment options for localized prostate cancer, including watchful waiting, radical prostatectomy, external beam radiotherapy, brachytherapy, high-intensity focused ultrasound and cryotherapy. The treatments available for the disease at this potentially curative stage are associated with a variable degree of morbidity.⁴

The mainstay of oncological treatment for patients not amenable to radical curative intervention is androgen manipulation, radiotherapy

and chemotherapy. However, these options also have morbidity, including loss of potency and libido, accelerated bone loss, hot flushes and psychological effects.

Metastatic disease

Despite an increase in early detection, a large number of patients will have advanced disease at presentation. Average survival at this point is approximately 3 years, but may be considerably longer. Patients should be reviewed by an appropriate specialist and may be offered androgen manipulation, chemotherapy, radiotherapy and/or radioisotopes, but any treatment at this stage is palliative.^{1,5}

Palliative care

Palliative care is a multi-professional, holistic approach to managing advanced disease with a limited prognosis. It encompasses controlling symptoms that are physical, psychological, spiritual and social and involves those close to the patient.

The modern hospice movement was founded by Dame Cicely Saunders in 1967 to try to improve the lives of those with terminal cancer. It is now recognized that palliative care should be extended to all patients with life-limiting illness, regardless of the diagnosis. Traditionally, palliative care has been concentrated in the last few weeks and months of life, taking over when active treatment has failed. However, the mantra 'prevention is better than cure' should apply here, as with other areas of medicine. The Policy Framework for Commissioning Cancer Services⁶ recommends the formation of palliative care within cancer centres and their coordination with community palliative care. It states that 'the palliative care team should integrate in a seamless way with all cancer treatment services to provide the best possible quality of life for the patient and their family.'

Symptoms

Advanced prostate cancer can be debilitating. Bone pain, fatigue and weight loss are common and increasing dependence and a feeling of losing control can contribute to anxiety and depression. Other symptoms include urinary outflow obstruction, weakness secondary to spinal cord compression, lymphoedema and anaemia.^{7,8}

Pain

Pain is an extremely common symptom in advanced cancer, present in approximately 70–90% of patients. This can significantly impact on quality of life, interfering with eating, sleeping and interaction with others.⁹ Treatment of pain in cancer can be difficult and complex and the term ‘Total Pain’ was used by Dame Cicely Saunders to describe intense suffering physically, psychologically, spiritually and socially.¹⁰ (Fig. 1) Not all patients will experience all of these problems, but where they are present treating one without the other will inevitably be unsuccessful. For example, attempting to treat physical pain when there is psychological pain will be suboptimal. Equally, attempting to treat psychological symptoms without addressing physical suffering will be fraught with difficulty. Somatic and psychological management should take place simultaneously via multidisciplinary approach to control pain in the terminally ill.¹¹

Bone disease is present in 90% of patients with metastatic prostate cancer and consequently bone pain is very common. The mainstay of treatment is oral analgesia and should be started in accordance with the WHO analgesic ladder.¹² (Fig. 2) The principles are to aim for simplicity, both in choice and route of analgesics,¹³ and to titrate appropriately to maximize pain control and minimize adverse effects.

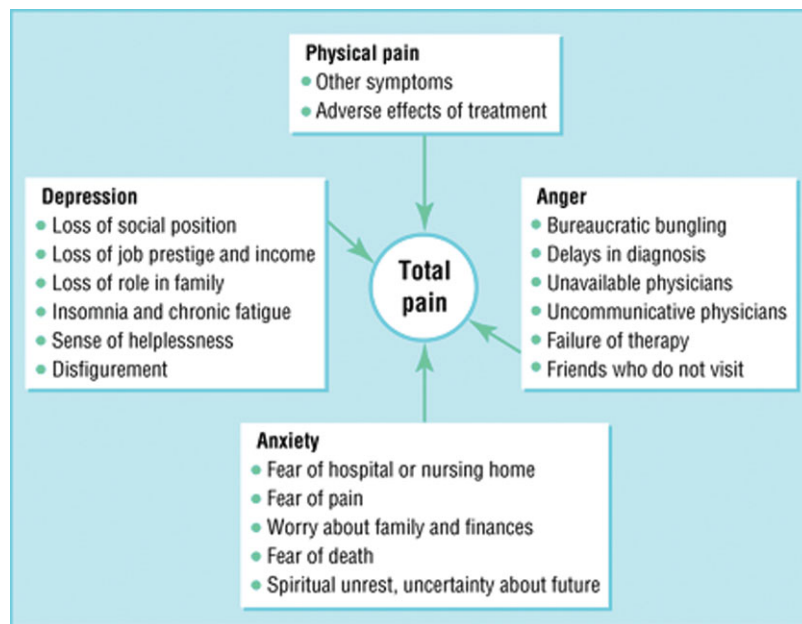


Fig. 1 Factors affecting patients' perception of pain. O'Neill B, Fallon M, *BMJ* 1997, **315**, 801–804, reproduced with permission from the BMJ Publishing Group.

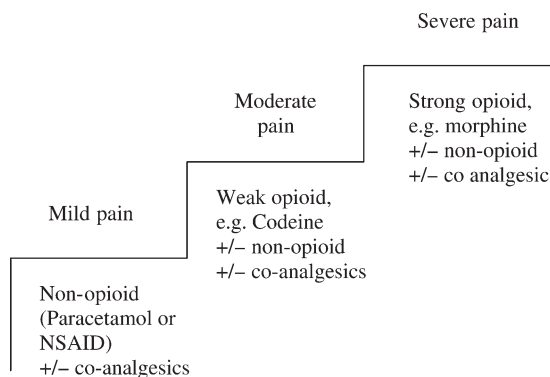


Fig. 2 Analgesic ladder.

Other drug treatments that are useful include bisphosphonates.¹⁴ It has been found that zoledronic acid decreases the incidence of skeletal related events in patients with prostate cancer and bony metastases.¹⁵ There is also a role for bisphosphonates in the management of bone pain refractory to analgesia (and as an adjunct) and radiotherapy.^{16,17} Incident pain can be a significant problem for these patients. Incident pain refers to pain that is only present or much worse with a particular activity. This can often present a problem with analgesic management. For example, increasing background opioids can increase drowsiness and other side effects without significantly impacting on the incident pain. Often the most effective way of managing this is to anticipate the activity and take breakthrough analgesia to try to prevent the pain.

Bone lesions in the spine can lead to nerve root compression and neuropathic pain. This pain typically radiates along a nerve root and is sharp, burning or tingling in nature. Simple analgesics are useful here as are opioid analgesics.¹⁸ However, it is often necessary to add in adjuvant analgesics, such as gabapentin, amitriptylline and steroids. In patients with refractory pain, anaesthetic approaches can be considered and are often very useful when systemic treatment is suboptimal.¹⁹

For all the usefulness of analgesics, it is important to utilize other treatment modalities. Disease modifying treatments can be very useful in the management of pain and other symptoms in advanced cancer. Radiotherapy, chemotherapy, hormone therapy and surgery (especially in long bones) can all play a part in reducing morbidity and increasing patient autonomy. The prophylactic pinning of long bones should be considered when there is impending fracture. Impending fracture is more likely if bone lesions are peritrochanteric, large or causing enough pain to affect function. Recently, minimally invasive surgical procedures such as kyphoplasty and vertebroplasty have been shown to be useful.²⁰ Radioisotopes can partially or completely control pain in

70% of patients,²¹ but this can increase the risk of myelosuppression if chemotherapy is to be considered later.²² Local radiotherapy can be particularly helpful if there are painful areas corresponding to known bony lesions and can be important for trying to decrease risk of fracture. It can achieve pain control in the majority of patients.²³ With a short predicted survival time, the most appropriate treatment for the majority of situations is a single treatment and not daily attendances to hospital over a week or two.²⁴ Non-drug measures are equally important and include heat pads, TENS and immobilization of the painful area. Psychological treatments can be useful such as relaxation or cognitive behavioural therapy and learning to avoid precipitating activities, perhaps by providing helpful equipment.¹³

Cord compression

Spinal cord compression affects 1–12% of patients with metastatic prostate cancer and is an oncological emergency.²⁵ Prevention of cord compression is important and clinicians should have a high index of suspicion. Disability arising from delay is associated with decreased survival²⁶ and any function lost before treatment is rarely regained. For this reason, speed is of the essence and investigation and management should not wait for classical signs to develop. Treatment should initially be with high dose steroids followed by early radiotherapy or surgery depending on performance status and prognosis.²⁷ Decompressive surgery plus postoperative radiotherapy has been shown to be more effective than radiotherapy alone.²⁸ Although, many patients will not be suitable for this treatment.

Gastrointestinal symptoms

Anorexia and weight loss are commonly seen in advanced cancer and contribute not only to tiredness and lethargy, but also family concern. Drugs are often prescribed to treat these symptoms and include megesterol acetate and corticosteroids. Megesterol acetate is usually effective after 1–2 weeks and can increase food intake and improve well being. Corticosteroids, when used can also have antiemetic and analgesic properties, but are short lived as appetite stimulants²⁹ and have unpleasant medium-to-long-term side effects.

Nausea is a very common problem in advanced cancer and the cause is multifactorial, including autonomic failure, gastroparesis, constipation and the use of strong opioids. It is important to treat the

underlying cause as much as possible and use an antiemetic that is appropriate to the most likely cause.

Constipation affects a large majority of patients with advanced prostate cancer and can exacerbate other symptoms such as nausea, urinary retention, lethargy, abdominal pain and anorexia.²⁹

General debility

There are many things that contribute to a feeling of generalized weakness and debility in patients with metastatic prostate cancer. Anaemia is common problem that can leave men feeling tired and breathless. The anaemia may be due to chronic disease, poor nutrition, treatment with chemotherapy or radiotherapy, haematuria or bone marrow failure secondary to metastatic invasion. However, it is often a combination of these causes. Treatment options include symptomatic treatment such as blood transfusion and also attempting to treat the underlying cause. Iron tablets should generally be avoided, unless there is proven iron deficiency as they contribute to constipation and are largely ineffective.

Lower limb weakness contributes to decreased mobility and an increase in dependency. Again it has many different causes and management should be aimed at treating the underlying cause, of which spinal cord compression, lymphoedema, steroid induced proximal myopathy are among the most common.

Lymphoedema

Lymphoedema can be painful, prone to infection and can affect relationships with family and friends and cause feelings of isolation and exclusion.³⁰ Penile and scrotal oedema can be particularly distressing, characterized by extreme discomfort for patients, with limitation of ambulation and voiding in the standing position. Sexual intercourse is often impossible, and with impairment of proper hygiene of the perineal region, the patient's quality of life and self-esteem are often severely affected.³¹ Lower limb lymphoedema can be caused by lymph node enlargement, inferior vena caval (IVC) obstruction or large tumour load in the pelvis and management is difficult. Treatment can include bandaging, manual lymphatic drainage, skin care,³⁰ prompt treatment of cellulitis, IVC stenting if appropriate, scrotal support and emotional support. Drug therapy is unfortunately largely ineffective and diuretics do little to reduce swelling.³² One should always be aware of the possibility of co-existent deep vein thrombosis (DVT),

especially if unilateral, unequal or painful. If this is suspected, it should be investigated using ultrasound Doppler and is usually treated with regular low molecular weight heparin at treatment dose in this group of patients, rather than warfarin.

Delirium

More than 85% of patients with cancer will experience confusion when nearing the end-of-life.³³ They are often elderly with many different reasons for confusion such as progressive renal impairment, sepsis or dehydration and drug therapy can contribute. In a survey of confused cancer patients, 69% had multiple causes and 64% were associated with drugs, especially opioids.³⁴ Often confusion associated with opioids responds to 'Opioid rotation', where a patient's drug is changed to an alternative opioid, to allow better titration with fewer side effects. This however, should only be done with specialist advice.

Approaching death

'Most doctors have witnessed patients die undignified, soulless, high tech deaths and hoped for something better for themselves and their patients'.³⁵ Unfortunately, despite excellent care of dying patients in hospices, this care is often not transferred to the hospital setting.³⁶ Improving this should be a priority for all and the End-of-Life Care Programme goes some way towards addressing this.

NHS cancer plan

The NHS Cancer Plan was a strategy document published by the Department of Health in September 2000. It was a 10-year plan which set out actions needed to improve the prevention and treatment of patients with cancer. One of the key elements of the plan was enhancement of palliative care services, so that patients could receive high quality symptom control at physical, psychological and spiritual levels. It placed emphasis on the provision of high quality information and good communication between patients, staff and their carers. The plan stressed that all patients should have access to specialist palliative care advice and services, irrespective of where they lived.

'The NHS Cancer Plan and the New NHS: Providing a Patient-Centred Service' was a document published to mark the fourth anniversary of the NHS Cancer Plan. It detailed the progress that had been

made, and with respect to palliative care service provision described the two main advances that had been made. The publication of the NICE guidance on Supportive and Palliative Care for Adults with Cancer and the development of the End-of-Life Care Programme.

Supportive and palliative care for adults with cancer (NICE guidance)

The guidance on supportive and palliative care for adults with cancer was published by NICE in March 2004. It placed importance on the holistic approach to managing patients, their carers and relatives following a diagnosis of cancer. In particular, the multidisciplinary team (MDT) was recognized as key in the process of providing continuity of total care. The importance of working as a multidisciplinary team cannot be stressed enough. To believe that the suffering experienced by patients with a terminal diagnosis can be solely managed by one professional body is foolish. Within the context of the Palliative Care Team, members of the MDT should include those who can deal with physical, spiritual, psychological and social needs. Rehabilitative and nutritional needs should also be recognized and addressed along with the provision of access to complementary therapies.

End-of-life care programme

The End-of-Life Care Programme was a strategy developed by the NHS, chaired jointly between the National Cancer Director and the National Director for Older People's Services. It aims to address the challenges faced when caring for a patient with a terminal diagnosis. Such challenges include allowing a patient to live and die where they wish, and provision of adequate training and support for carers and staff. It includes the use and development of three tools:

1. Gold Standards Framework
2. Preferred Place of Care Document
3. Liverpool Care Pathway

By using these tools, it is hoped that patients will be given greater choice with respect to their care, experience a reduction in the number of inappropriate transfers of care and interventions and an overall improvement in the quality of end-of-life care.

Gold standards framework

The Gold Standards Framework³⁷ was created by health professionals working in primary care to improve the management of patients in the community who are in the advanced stages of disease. The framework was created following the realization that many patients are subjected to hospital admissions at the end-of-life which perhaps could have been avoided with good forward planning. It includes concepts and tools which enable those working in the community to enable patients to die where they wish and, crucially, to die in comfort. The framework encourages those responsible for providing care at home to participate in discussions with patients and their carers at an early stage, to identify problems and wishes for future care. It forms a vital part of the NHS End-of-Life Care program and although was originally created for those patients with a diagnosis of cancer, is now being extended to any patient with a terminal diagnosis and prognosis of less than 1 year. By June 2006, all 34 cancer networks and one-third of GP practices within the UK were using the framework, affecting one-third of the population.³⁷ Patients are included if they are deemed to be in need of palliative care and have a predicted life expectancy of less than 1 year, which may be supported by clinical indicators. By fulfilling seven tasks, known as the seven 'C's, the following goals aim to be achieved: good symptom control, establishment of the patient's preferred place of care, security, support and empowerment for patients and carers and confidence for staff providing care during this challenging time. The seven 'C's are as follows:

1. Communication. Patients are entered onto a supportive care register to facilitate regular discussion between patients, carers and staff. The records are patient held to facilitate communication between members of the multi-disciplinary team.
2. Coordination. A coordinator is nominated to facilitate frequent discussion and to maintain records.
3. Control of symptoms. Assessment tools are suggested in order to address symptoms early and well.
4. Continuity. Good record keeping and the use of the supportive care register enables effective communication between professional teams, which is particularly important for out-of-hours care where regular health professionals may not be available for advice and support.
5. Continued learning. Audit and reflective practice are encouraged to improve the management of patients. Specific outcome measures include patients dying in the place they choose, evidence of advanced care planning, coordination of care and systematic thinking.

6. Carer support. Carers require separate assessment, written targeted information and bereavement support.
7. Care of the dying. The Liverpool Care Pathway has been designed to achieve good symptom control and communication in the last 48 h of life. It is also a key feature of the NHS End-of-Life Program.

Preferred place of care document

The 'Preferred Place of Care Document' (PPC)³⁸ was created by the Lancashire and South Cumbria Cancer Network following the realization and acknowledgement that patients often die in a place that they would not have chosen. Between 1996 and 1999 (Office for National Statistics 2002), 25% patients died at home in Lancashire and South Cumbria.³⁸ Previous studies have revealed that around 50% terminally ill patients wish to die at home.³⁸ Thus, it appears that there is a discrepancy between where patients die and where they would choose to die. The PPC document is a tool which facilitates advanced care planning. It is a patient held document and, therefore, follows the patient trajectory. It places importance on early discussions regarding patient's wishes for end-of-life care so that inappropriate hospital admissions and interventions can be minimized. Early involvement of professionals within the social work department facilitates consideration of patient's, family and carer's feelings and social network. Patients who may be considered appropriate for commencement of the PPC document might be those who are eligible for benefits under special rules (DS 1500), those who are receiving input from a specialist palliative care team and those who are in the terminal stages of their disease. After the death of the patient, the document is retrieved, anonymized, analysed and reflected upon so that resources can be optimized for future care of patients. A pilot study carried out following use of the tool by district nurses in the Lancashire and South Cumbria Cancer Network raised concerns regarding use of the tool. Nurses felt uneasy discussing such a sensitive topic, and discomfort at retrieving the document after death. These issues are to be explored further so that, ultimately, a tool of this kind can be implemented widely to empower patients, carers and professionals alike.

Liverpool care pathway

The Liverpool Care Pathway (LCP)³⁹ for the dying patient was developed to transfer the hospice model of care into other settings,

e.g. hospital, community, nursing home. It was established by the Specialist Palliative Care Team in Liverpool at the Royal Liverpool University Hospitals and the team at the Marie Curie Centre Liverpool.

Diagnosing and subsequently managing the dying phase can cause great anxiety to those working in the general clinical sector.⁴⁰ A 'bad' death can have a lasting impact on health professionals, impacting on how future death related issues are managed.

The pathway is a multiprofessional document which provides an evidence-based framework for end-of-life care, and is a key recommendation in the Supportive and Palliative Care Guidelines issued by the National Institute of Clinical Excellence. The pathway replaces all other documentation and empowers health professionals to 'deliver high quality care to dying patients, their carers and relatives'.³⁹ It provides guidance on providing optimal comfort measures and symptom control, and on providing a holistic approach to the care of the patients in the last 48 h of life. It places particular importance on maximizing communication between all members of the multidisciplinary team. It focuses those caring for patients in the dying phase not only on the control of physical symptoms but also on the more spiritual aspects of their suffering.

The LCP states that following diagnosis of the dying phase, an initial assessment should be made which includes assessing current medications and discontinuing non-essentials. This involves reviewing the appropriateness of oral medications and having a provision of medications that can be given via the subcutaneous route. Subcutaneous medications should be available to be given regularly via a continuous subcutaneous infusion and on an 'as required' basis.

The pathway recommends that subcutaneous medications should, at least, be available to control the four common symptoms known to occur in the dying phase. These include pain, agitation, respiratory tract secretions and nausea and vomiting. Therefore, analgesia, sedatives, antiemetics and anticholinergic medications should be available to be given via the subcutaneous during the dying phase.

A patient is considered appropriate to be placed on the pathway once the multiprofessional team has agreed that the patient is dying. The patient may also be bed bound, only able to take sips of fluids, semi-comatose and no longer able to take tablets.

Conclusion

Despite great advancement in palliative medicine in recent years, there is still a long way to go. In most urological journals and textbooks,

palliative care is given a disproportionately small amount of space,¹³ especially considering the great need, particularly in prostate cancer. We hope this paper has outlined some general principles that can be applied to advanced prostate cancer and other terminal illnesses and provide a basis for further learning, to improve the quality of life for all people with life-limiting illness.

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