

Guidelines for the Management of Bladder Cancer

Date Approved by Network Governance	July 2012
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Changes Between Version 3 and 4

Sections 5.2 and 8 updated

1. Scope of the guideline

1.1 This Guidance has been produced to support the following:

- the management of patients presenting with symptoms suspicious of bladder cancer.
- the management of patients found to have bladder cancer.

2. Guideline background

- 2.1 These guidelines are based on the 2 week wait Guidelines for Referral¹ (www.dh.gov.uk), Improving Outcomes for Urological Cancer – Manual² (www.nice.org.uk) and the European Association of Urology (EAU) Clinical Guidelines^{3,4} (www.uroweb.org). They have been written by the Pan Birmingham Cancer Network, Network Site Specific Group (NSSG) which consists of local urology teams based at University Hospital Birmingham NHS Foundation Trust (UHBFT), Sandwell and West Birmingham Hospitals NHS Trust (SWBH), Heart of England NHS Foundation Trust (HEFT) and Walsall Healthcare NHS Trust (WHT).
- 2.2 In line with the Improving Outcomes Guidance for Urology² the Pan Birmingham Cancer Network has two designated centres for the location of major pelvic surgery. All patients in the Network requiring a cystectomy will be referred to either HEFT or UHBFT. Within these cancer centres, surgery will be carried out by those surgeons doing 5 or more radical procedures per year. A minimum of 50 radical procedures will be carried out at each of the centres per year.

Guideline statements

3. Referral from GPs

- 3.1 Patients with suspected urological cancer (for details see paragraph 5.2) should be referred from GPs to local urology units according to the 2 week wait criteria².
- 3.2 Referrals deemed inappropriate by consultant urologists will be notified to the referring GP and to the relevant Commissioner according to agreed protocols to improve the quality of future referrals.
- 3.3 GPs will be notified of the diagnosis of cancer within 24 hours of the diagnosis being made, and will be kept informed of all aspects of the patients care.

4. Multi disciplinary teams (MDTs)

Each team will hold regular MDT meetings. All patients with proven urological malignancy will be discussed by an MDT. Normally this will be the local MDT in the first instance, and the overall responsibility for the patient's management rests with the local MDT until referral has been agreed.

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5. Referral

5.1 The most common presentation is haematuria, which should be referred as a 2 week wait. Local units should offer a haematuria clinic appointment to these patients, which should include an immediate flexible cystoscopy.

5.2 2 week wait referrals should be made:

- a) in all adult patients of any age who present with painless visible or dipstick haematuria.
- b) in all adult patients age 40 years and older who present with recurrent or persistent urinary tract infection associated with haematuria.
- c) in patients aged 50 years and older who are found to have unexplained microscopic haematuria (if under 50, assuming there is no proteinuria or raised creatinine, a non-urgent referral should be made).
- d) in all patients with symptoms suggestive of urinary infection who present with visible haematuria, investigations should be undertaken to diagnose and treat the infection before consideration of referral. If infection is not confirmed the patient should be referred urgently.

5.3 Other patients with microscopic haematuria:

If the patient is under 50 years old urine should be tested for protein and serum creatinine. If these are raised the patient should be referred to a renal physician, if normal the patient should be referred to an urologist.

6. Diagnosis and staging

6.1 Physical examination, including digital rectal examination and/or bimanual pelvic palpitation, is recommended when haematuria is found.

6.2 Clinical diagnosis at flexible cystoscopy should be followed by urgent tumour resection, which provides confirmation of the diagnosis and staging and grading information.

6.3 All patients should have imaging of the upper urinary tract to look for urothelial tumours. No randomized trial evidence exists as to the most appropriate form of imaging and therefore local preference will dictate. IVU is the accepted modality but CT urography may be used when expertise exists. In the investigation of haematuria, retrograde studies are indicated if cytology is positive or haematuria is continuing and non invasive investigations are normal. Further imaging may not be necessary if cytology is negative, haematuria does not recur and non invasive investigations are normal.

6.4 Superficial (pTa and pT1) tumours that are G1 or G2 do not require further staging.

6.5 In cases of muscle invasive disease (pT2 or above) or G3 tumours a pelvic and abdominal CT should be performed. Ideally if muscle invasion is suspected the patient should undergo CT (or MRI) prior to biopsy. If CT (or MRI) is carried out

within 6 weeks of the biopsy the imaging cannot reliably depict the level of extra-vesical spread and the patient may be over-staged.

- 6.6 Although MRI will define muscle invasion more specifically than CT this information will not alter the treatment plan. MRI is therefore not obligatory.
- 6.7 A bone scan should be performed if bony symptoms are present or alkaline phosphatase level is elevated.

Management

7. Superficial disease

Initial resection of a bladder tumour should be followed as soon as possible (ideally within 6 hours, otherwise within 24 hours) by a single instillation of intravesical chemotherapy if the tumour is thought to be superficial. Tumours should then be assessed depending on stage, grade, size, multiplicity and the presence of recurrence at cystoscopy after 3 months.

- 7.1 Low risk: pTa G1, single tumour less than 3 cm. These tumours require a follow up cystoscopy at three months, then annually if clear.
- 7.2 Intermediate risk: G1 tumours other than those above and all G2 tumours. In cases where multiple tumours are present, or where there is recurrence at 3 months, a 6 week course of intravesical chemotherapy or BCG should be considered.
- 7.3 Follow up for low and intermediate risk: Discharging patients from follow-up should be done on a case by case basis as there is always a risk of recurrence. This risk is low in 'low risk patients' who have not had a recurrence within 5 years. Annual cytology may be considered in patients with high grade disease following discussion of the options with the patient. Annual cytology is not usually recommended for those patients with low grade tumours. Patients should be advised to re-present without delay if they have any further haematuria.
- 7.4 High risk: pT1 G3 tumours and carcinoma in situ. These patients should receive an immediate 6 week course of intravesical BCG, although primary cystectomy may be employed. Follow up should be life-long.
- 7.5 Tumour recurrences: should be treated by immediate resection or cystodiathermy. If persistent recurrences occur a 6 week course of intravesical chemotherapy or BCG should be employed.

8. Invasive disease

- 8.1 In the absence of metastatic disease and other significant co-morbidity, treatment options for patients with invasive disease (i.e. T2 tumours and above) include cystectomy with ileal conduit formation, cystectomy with formation of a neo-bladder, and radiotherapy all with or without 3-4 cycles of neo-adjuvant chemotherapy. Unless there are specific contra-indications, all three options should be discussed with the patient prior to formulating a management plan.
- 8.2 Where neoadjuvant chemotherapy is given, rigorous attention must be paid to scheduling of subsequent treatments, preferably by the pre-booking of slots for surgery or radiotherapy as appropriate, to prevent undue delays between treatment modalities. Most patients should be fit for their subsequent therapy by 4 weeks after the last chemotherapy injection (or possibly sooner). Interim check cystoscopy after 2-3 cycles of chemotherapy (can be a flexible scope) is recommended to ensure that disease is not worsening on chemotherapy.
- 8.3 All patients suitable for radical treatment should be reviewed by an oncologist as well as a surgeon.
- a) patients in whom radical surgery is considered should be referred to one of the specialist urology teams (UHBFT or HEFT).
 - b) radiotherapy (with or without synchronous chemotherapy) will be performed at UHBFT but arranged by the local team.
- 8.4 Chemotherapy should be considered in appropriate cases and should be given as a neo-adjuvant to radiotherapy or surgery.
- 8.5 Based on the results of the BC2001 trial patients receiving radical radiotherapy should be offered synchronous chemotherapy with continuous infusion 5FU plus a single bolus of mitomycin C on day 1. The trial showed a 50% reduction in invasive recurrence with no increase in late toxicity or impact on bladder capacity at 1 year. The synchronous regimen toxicity was not adversely impacted by prior neoadjuvant chemotherapy.

9. Non transitional cell carcinoma (TCC) bladder cancer

Careful case by case management of these patients is required including discussion at the specialist MDT. Specialist histopathological review may be required, with consideration to the fact that the primary tumour may not be arising from the bladder.

10. Follow-up

10.1 Superficial disease

Follow up of superficial disease is by cystoscopy, the frequency and duration of follow-up depends on the risk at presentation and the presence of recurrences (see above).

10.2 Invasive disease

- a) Follow up after radiotherapy is by regular (usually 6 monthly) cystoscopy.
- b) Follow up after cystectomy is by clinical assessment and CT scanning (see comment below).
- c) The best method of examining the upper tracts following cystectomy is loopogram.
- d) A CT chest/abdo/pelvis should be performed (at around 6 months from start of treatment (either RT or surgery) for most patients) to assess for lymph or local recurrence. Subsequent CT scanning may be required in some cases but need not be carried out routinely.

11. Management of recurrence

11.1 Superficial recurrences are dealt with endoscopically. Intravesical chemotherapy or BCG should be considered if recurrences are multiple or frequent.

11.2 Superficial recurrences after radiotherapy are dealt with endoscopically. Intravesical chemotherapy, or in advanced cases, salvage cystectomy, should be considered.

11.3 Invasive recurrences after radiotherapy are best dealt with by salvage cystectomy if the patients condition allows (in other cases chemotherapy may be appropriate.)

11.4 Recurrence after cystectomy may be treated with radiotherapy or chemotherapy.

12. Intravesical chemotherapy and BCG

12.1 Intravesical chemotherapy is indicated in cases of multiple and recurrent superficial tumour. It involves the administration of 6 – 8 doses of either mitomycin c or epirubicin into the bladder at weekly intervals on an outpatient basis.

12.2 Intravesical BCG is given for the same indications and for carcinoma in situ. It is generally considered to be superior in efficacy but may result in a higher incidence of side effects. 6 doses are given at weekly intervals, usually followed by 3 maintenance doses. Further maintenance therapy may be appropriate if tolerated.

13. Metastatic disease

- 13.1 Radiotherapy can provide effective palliation for symptoms of locally advanced or metastatic disease.
- 13.2 Chemotherapy may be appropriate in cases of metastatic disease where the patient has a good performance status and renal function: Treatment is purely palliative and should be selected according to the patient's needs but may include systemic chemotherapy with CMV or MVAC. Combinations with cisplatin are more effective than those without^{5,6}. Gemcitabine plus platinum has equivalent survival to MVAC but is much less toxic.

14. Staging

- 14.1 Staging data for 70% of all cancers (90% of stageable cancers) should be collected electronically and transferred to the West Midlands Cancer Intelligence Unit (WMCIU).
- 14.2 All Trusts
 - a) All Trusts should send electronic extracts from their histopathology system regularly to the WMCIU
 - b) All Trusts should send imaging extracts for cancer patients electronically to the WMCIU regularly, or establish remote access for the WMCIU to their radiology information system
- 14.3 For cancers diagnosed clinically or those that have not had surgery
 - a) Clinical TNM stage should be recorded on the MDT database
- 14.4 For those with invasive cancer who have had surgery
 - a) MDTs should record the full cancer registry dataset onto their MDT database at the time of discussion at the MDT meeting and send extracts to the WMCIU on a regular basis

15. Performance status

All patients should have their performance status recorded at the onto the MDT database at the MDT. This should be done using the WHO classification which will ensure it is in line with the cancer outcomes and services dataset guidance

16. Patient information and counselling

- 16.1 All patients diagnosed with a metastasis to **any bone**, or who have **myeloma**, should receive information about the possibility of developing metastasis to the spine. This is essential to enable patients to report signs of spinal metastases

early, thereby offering treatment options that may prevent damage to the spinal cord and unnecessary disability.

- 16.2 This information should be offered by a senior cancer clinician (for example a CNS or consultant). The patients should be advised about what to look for and what to do in the event that they have symptoms and/or signs of spinal metastases.
- 16.3 Patients should be provided with information about the symptoms and/or signs of spinal cord compression and what to do if they develop them. This discussion should be supported by written information in the form of the PBCN Patient Information on Cancer that has Spread to the Bone (Bone Metastases) and the Patient Alert Card (<http://www.birminghamcancer.nhs.uk/staff/clinical-guidelines/bone-cancer>)
- 16.4 All patients, and with their consent, their partners should be given access to appropriate written information during their investigation and treatment, and on diagnosis should be given the opportunity to discuss their management with a clinical nurse specialist who is a member of the relevant MDT. The patient should have a method of access to the Urology team at all times.
- 16.5 Access to psychological counselling will be available if required.

17. Palliative care

- 17.1 Palliative care services will be made available to all patients as deemed appropriate by the MDT.

18. Clinical trials

- 18.1 Wherever possible, patients who are eligible should be offered the opportunity to participate in National Institute for Health Research portfolio clinical trials and other well designed studies.
- 18.2 Where a study is only open at one Trust in the Network, patients should be referred for trial entry. A list of studies available at each Trust is available from Pan Birmingham Cancer Research Network. Email: PBCRN@westmidlands.nhs.uk .
- 18.3 Patients who have been recruited into a clinical trial will be followed up as defined in the protocol.

Monitoring of the Guideline

Adherence to the Network guidelines may from time to time be formally monitored.

References

- 1 Department of Health, 2000. Referral guidelines for suspected cancers
- 2 NICE, 2002. Improving Outcomes in Urological Cancers - The Manual.
- 3 European Association of Urology, 2006. Guidelines on TaT1 (Non-muscle invasive) Bladder Cancer
- 4 European Association of Urology, 2006. Guidelines on Bladder Cancer, Muscle Invasive and Metastatic
- 5 Mead GM, Russell M, Clark P, et al. *British Journal of Cancer* 1998;**78**:1067-1075
- 6 Saxman SB, Propert KJ, Einhorn LH, et al. *Journal of Clinical Oncology* 1997;**15**:2564-2569.)

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