Diagnosis and Staging of Bladder Cancer

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KEYWORDS

• Bladder cancer • Urothelial carcinoma of the bladder • Staging • Diagnosis
• Cystoscopy • Imaging • Screening • Biomarkers

KEY POINTS

- The current recommendations do not support routine bladder cancer (BCa) screening because of insufficient evidence and lack of understanding of the effects of screening in the case of overdiagnosis and overtreatment. However, the results of existing studies suggest that BCa screening may be important in high-risk populations.
- Currently, the combination of urine cytology and cystoscopy remains the gold standard for diagnosing patients with BCa. Less invasive urine biomarkers have been investigated over time, but their performance remains subpar with respect to specificity compared with cytology alone. It is unlikely that a new marker will be used to replace the conventional urine cytology and cystoscopy.
- The cornerstone of diagnosis and subsequent management of BCa is the cystoscopic examination of the lower urinary tract. Specifically, white light cystoscopy (WLC) remains the gold standard, despite its limitations. Recently, new optical diagnostic methods have been designed to improve the accuracy of WLC, such as fluorescence cystoscopy, narrow-band imaging, and optical coherence tomography; their role is currently under investigation.
- Transurethral resection of bladder tumor under regional or general anesthesia is the gold standard to excise (and potentially cure) all visible tumors and to provide specimens for staging and grading of BCa.

SCREENING, DIAGNOSIS, AND EVALUATION IN BLADDER CANCER SCREENING

Bladder cancer (BCa) is a heterogeneous disease with a variable natural history. Most patients (70%) present with superficial tumors (stages Ta, T1, or carcinoma in situ).[1]

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However, 3 out of 10 patients present with muscle-invasive disease (T2–4) with a high risk of death from distant metastases. Moreover, roughly between 50% and 70% of superficial tumors do recur, and approximately 10% to 20% of them progress to muscle-invasive disease.[2] However, BCa has a relatively low ratio of mortality versus incidence of new cases.[3] In consequence, there is the danger of overdiagnosis and overtreatment.

Hence, the goal and challenge of screening would be to detect the disease at an earlier stage, consequently improving morbidity and survival, but, more importantly, to be able to identify the tumors that are more likely to become muscle-invasive cancers. Such early detection of tumors could allow for earlier curative intervention and could potentially preclude the need for unnecessary surgical treatment or chemotherapy and lower the costs associated with treatment.

To date, an estimated 75,000 new cases of urinary BCa will be diagnosed in the United States (56,390 men and 18,300 women) in 2014.[4] In the same year, approximately 16,000 new deaths (11,170 men and 4410 women) are expected. BCa is the fourth most common cancer and is 3 times more common in men than in women in the United States.[5] It has also been previously reported that the age-adjusted incidence of BCa seems to be increasing over time: from 21.0 to 25.5 per 100,000 person-years between 1973 and 2009 (+0.2% per year, $P = .001$).

Two landmark studies have evaluated the effect of screening for BCa. Messing and colleagues[6] performed an important assessment based on 1575 cases ($\geq$50-year-old men screened at home using hematuria dipsticks) and 509 controls (nonscreened). Those who showed positive results underwent cystoscopy (n = 283), and 21 (7.4%) of them were diagnosed with BCa. The primary results of that study indicated that earlier detection of BCa could result in a lower proportion of invasive cancers among high-grade and/or muscle-invasive diseases in screened versus nonscreened men (10% vs 60%, $P = .002$) and a significant reduction in mortality caused by the disease (0% vs 20%, $P = .02$). Britton and colleagues[7] examined 2356 men aged 60 years and older for dipstick hematuria. The test was positive in 20% of men, and BCa was ultimately diagnosed in 17 individuals (5.3%). Of those, 9 patients had high-risk non–muscle-invasive BCa. At a 7-year follow-up, 5 out of 9 patients progressed to muscle-invasive disease and 3 out of 9 died of the disease.

Partly owning to an overall low incidence of the disease (25.5 per 100,000 person-years in 2009), screening for BCa is currently not recommended as a standard of care during routine clinical practice.[5] The challenge being that a clearly defined high-risk population needs to be identified, so as to avoid the usual harms in screening, such as unnecessary diagnostic-related treatments (ie, cystoscopy and biopsy, transurethral resection of bladder tumor [TURBT], intravesical chemotherapy), and overdiagnosis.[3,8] Wu and colleagues[9] generated a model based on large case-control data (n = 678 cases and n = 678 controls) for the prediction of BCa risk using established risk factors, such as smoking and well-known occupational exposure (eg, diesel, aromatic amines, dry cleaning fluids, radioactive materials, arsenic). At internal validation, the model demonstrated an area under the curve of 80%. However, the model is impeded by the lack of external validation.

Similarly, Vickers and colleagues[10] using data from the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial attempted to create a risk score in order to identify those at higher risk of developing BCa. The study comprised 49,873 persons for the training set and 99,746 individuals for the external validation set. The investigators showed that the trade-off between the number of patients screened and invasive/high-grade tumors avoided was more optimal when restricting screening to a high-risk population instead of the whole population (57 vs 38 per 100,000), hence supporting the strategy to screen a high-risk population only.