Management of Low-risk and Intermediate-risk Non–Muscle-invasive Bladder Carcinoma

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KEYWORDS

• Non–muscle-invasive bladder cancer • Risk groups • Intermediate risk • Low risk
• Treatment

KEY POINTS

- Bladder cancer is a frequent and expensive malignancy with high rates of recurrence.
- Good initial transurethral resection of the bladder tumor is crucial for adequate staging and prognosis.
- In low-risk and intermediate-risk non–muscle-invasive bladder cancer, 1 immediate instillation of chemotherapy is recommended.
- Adherence to international guidelines remains insufficient, resulting in high recurrence rates. New safe and effective therapies are needed.

INTRODUCTION

Bladder cancer (BC) is a frequent and costly disease: it is reported to be the most expensive cancer per patient, and it is the 11th most commonly diagnosed cancer and the 14th leading cause of cancer deaths worldwide.[1,2] In the United States in 2012, there were an estimated 73,510 cases of BC, with 55,600 and 17,910 cases in men and women, respectively.[3] Risk factors for BC include tobacco use (50%), exposure to aromatic amines and polycyclic aromatic hydrocarbons other than in tobacco (10%), and genetic predisposition and aging.[1,4,5] The most common histologic subtype of BC is urothelial carcinoma, accounting for more than 90% of all bladder tumors.[6] Approximately 75% of patients with BC present with non–muscle-invasive BC (NMIBC), ie, Ta (70%), T1 (20%), and carcinoma in situ (CIS; 10%). The

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remainder of patients present with tumors invading the detrusor muscle (stage T2), the perivesical tissue (T3), the organs surrounding the bladder (T4), or metastatic disease.[5,7]

NON–MUSCLE-INVASIVE BLADDER CANCER

Stage Ta tumors have a papillary configuration, are confined to the urothelium, and do not penetrate into the lamina propria or detrusor muscle. Stage T1 tumors originate from the urothelium but penetrate the basement membrane separating the urothelium from the deeper layers. They invade into the lamina propria, but do not reach the detrusor muscle.

At present, 2 classifications are used for grading of papillary NMIBC (World Health Organization [WHO] 1973 and 2004; **Box 1**).[8] 1973 WHO grade 1 carcinomas have been reassigned to papillary urothelial neoplasms of low malignant potential and low-grade carcinomas in the 2004 WHO classification. It is a subject of controversy that grade 2 carcinomas have been eliminated in the 2004 WHO classification and reassigned to either low-grade or high-grade carcinomas. The 2004 WHO classification contains a detailed histologic description of the various grades in order to minimize diagnostic variability among pathologists. However, so far, published comparisons do not clearly confirm better reproducibility for the WHO 2004 classification compared with the 1973 WHO classification.[9,10]

Several studies have compared the two classifications concerning prognostic implications with conflicting results.[10–14] Until the prognostic role of this classification has been validated by more prospective trials with sufficient follow-up, both classifications should be used, because it is indicated by the 2014 European Association of Urology (EAU) guideline on NMIBC as a grade A recommendation.[15] Moreover, most clinical trials published so far have been performed using the 1973 WHO classification, meaning that recommendations from current guidelines are still based on this version.

CIS is a high-grade carcinoma confined to the urothelium, but with a flat nonpapillary configuration. Unlike a papillary tumor, CIS appears as reddened and velvety mucosa and is slightly elevated, although sometimes it is not visible. The diagnosis of CIS is based on the histology of biopsies from the bladder wall.

Box1
WHO grading 1973 and 2004

1973 WHO grading

Urothelial papilloma

Grade 1: well differentiated

Grade 2: moderately differentiated

Grade 3: poorly differentiated

2004 WHO grading

Urothelial papilloma

Papillary urothelial neoplasm of low malignant potential

Low-grade papillary urothelial carcinoma

High-grade papillary urothelial carcinoma

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