

Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer: AUA/SUO Guideline

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Purpose: Although associated with an overall favorable survival rate, the heterogeneity of non-muscle invasive bladder cancer (NMIBC) affects patients' rates of recurrence and progression. Risk stratification should influence evaluation, treatment and surveillance. This guideline attempts to provide a clinical framework for the management of NMIBC.

Materials and Methods: A systematic review utilized research from the Agency for Healthcare Research and Quality (AHRQ) and additional supplementation by the authors and consultant methodologists. Evidence-based statements were based on body of evidence strength Grade A, B, or C and were designated as Strong, Moderate, and Conditional Recommendations with additional statements presented in the form of Clinical Principles or Expert Opinions.¹

Results: A risk-stratified approach categorizes patients into broad groups of low-, intermediate-, and high-risk. Importantly, the evaluation and treatment algorithm takes into account tumor characteristics and uniquely considers a patient's response to therapy. The 38 statements vary in level of evidence, but none include Grade A evidence, and many were Grade C.

Conclusion: The intensity and scope of care for NMIBC should focus on patient, disease, and treatment response characteristics. This guideline attempts to improve a clinician's ability to evaluate and treat each patient, but higher quality evidence in future trials will be essential to improve level of care for these patients.

Key Words: urinary bladder neoplasms, cystectomy, drug therapy, immunotherapy

BACKGROUND

Epidemiology

NMIBC represents approximately 80% of the 74,000 estimated new bladder cancer cases diagnosed in the United States in 2015 and primarily affects Caucasian Americans and those older than 65 years.²⁻⁵ National registry data from the U.S.

Surveillance Epidemiology and End Results program demonstrates that the incidence of all stages of NMIBC has been relatively stable from 1988-2006.⁵ Multiple factors are associated with bladder carcinogenesis; however, tobacco smoking is the most significant and common risk factor.⁶

Abbreviations and Acronyms

AUA = American Urological Association
BCG = bacillus Calmette-Guérin
CIS = carcinoma *in situ*
EORTC = European Organization for Research and Treatment of Cancer
FDA = Food and Drug Administration
LVI = lymphovascular invasion
NMIBC = non-muscle invasive bladder cancer
SUO = Society of Urologic Oncology
TURBT = transurethral resection of bladder tumor
WLC = white light cystoscopy

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The complete guideline is available at <http://www.auanet.org/common/pdf/education/clinical-guidance/Non-Muscle-Invasive-Bladder-Cancer.pdf>.

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For another article on a related topic see page 1270.

Staging and Grading

Staging for bladder cancer is separated into clinical and pathologic stage, as outlined by the American Joint Committee on Cancer.⁷ Pathological staging is based on the extent of disease following surgical resection of the bladder and adjacent pelvic lymph nodes.

Tumor grade is an important prognostic factor for determining risk of recurrence and progression. The World Health Organization/International Society of Urological Pathology 2004 classification, which designates tumors as “low-” or “high-grade,” is currently the most widely utilized system in the U.S.^{8,9}

Prognosis

The cancer-specific survival in high-grade NMIBC is approximately 70-85% at 10 years.^{10,11} Long-term follow-up of low-grade Ta lesions demonstrates a progression rate of approximately 6%, whereas high-grade T1 lesions have an increased chance of progression of approximately 17%.^{10,12} Therefore, the ability to predict recurrence and progression risk based on patient-specific disease characteristics holds prognostic significance.

METHODOLOGY

The AUA categorizes body of evidence strength as Grade A, B, or C based on both individual study

quality and consideration of study design, consistency of findings across studies, adequacy of sample sizes, and generalizability of samples, settings, and treatments for the purposes of the Guideline.

Evidence-based statements are provided as *Strong*, *Moderate*, and *Conditional Recommendations* with additional statements provided in the form of *Clinical Principles* or *Expert Opinion* (table 1).

GUIDELINE STATEMENTS

Diagnosis. 1. **At the time of resection of suspected bladder cancer, a clinician should perform a thorough cystoscopic examination of a patient’s entire urethra and bladder that evaluates and documents tumor size, location, configuration, number, and mucosal abnormalities. (Clinical Principle)**

2. **At initial diagnosis of a patient with bladder cancer, a clinician should perform complete visual resection of the bladder tumor(s), when technically feasible. (Clinical Principle)**

3. **A clinician should perform upper urinary tract imaging as a component of the initial evaluation of a patient with bladder cancer. (Clinical Principle)**

Table 1. AUA nomenclature linking statement type to level of certainty, magnitude of benefit or risk/burden, and body of evidence strength

	Evidence Strength A (High Certainty)	Evidence Strength B (Moderate Certainty)	Evidence Strength C (Low Certainty)
Strong Recommendation (Net benefit or harm substantial)	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) is substantial Applies to most patients in most circumstances and future research is unlikely to change confidence	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) is substantial Applies to most patients in most circumstances but better evidence could change confidence	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) appears substantial Applies to most patients in most circumstances but better evidence is likely to change confidence (rarely used to support a Strong Recommendation)
Moderate Recommendation (Net benefit or harm moderate)	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) is moderate Applies to most patients in most circumstances and future research is unlikely to change confidence	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) is moderate Applies to most patients in most circumstances but better evidence could change confidence	Benefits > Risks/Burdens (or vice versa) Net benefit (or net harm) appears moderate Applies to most patients in most circumstances but better evidence is likely to change confidence
Conditional Recommendation (No apparent net benefit or harm)	Benefits = Risks/Burdens Best action depends on individual patient circumstances Future research unlikely to change confidence	Benefits = Risks/Burdens Best action appears to depend on individual patient circumstances Better evidence could change confidence	Balance between Benefits & Risks/Burdens unclear Alternative strategies may be equally reasonable Better evidence likely to change confidence
Clinical Principle	A statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature		
Expert Opinion	A statement, achieved by consensus of the Panel, that is based on members’ clinical training, experience, knowledge, and judgment for which there is no evidence		

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