available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Review – Education
Editorial by XXX on pp. x–y of this issue

Updates in the Eighth Edition of the Tumor-Node-Metastasis Staging Classification for Urologic Cancers

Gladell P. Paner[a,b,*], *Walter M. Stadler*[c], *Donna E. Hansel*[d], *Rodolfo Montironi*[e], *Daniel W. Lin*[f], *Mahul B. Amin*[g,h]

[a] *Department of Pathology, University of Chicago, Chicago, IL, USA;* [b] *Department of Surgery (Urology), University of Chicago, Chicago, IL, USA;* [c] *Department of Medicine (Hematology/Oncology), University of Chicago, Chicago, IL, USA;* [d] *Departments of Pathology and Urology, University of California, San Diego, CA, USA;* [e] *Department of Pathological Anatomy and Histopathology, School of Medicine, Polytechnic University of the Marche Region, Ancona, Italy;* [f] *Department of Urology, University of Washington and Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA, USA;* [g] *Department of Pathology and Laboratory Medicine, University of Tennessee Health Science Center, Memphis, TN, USA;* [h] *Department of Urology, University of Tennessee Health Science Center, Memphis, TN, USA*

Article info

Article history:
Accepted December 14, 2017

Associate Editor:
James Catto

Keywords:
Bladder
Genitourinary
Kidney
Penis
Prostate
Staging
Testis
TNM
Ureter
Urethra
Urinary
Urologic

Abstract

The Tumor-Node-Metastasis (TNM) classification on cancer staging, jointly developed by the American Joint Commission on Cancer (AJCC) and the Union for International Cancer Control (UICC), has been updated to its 8th edition with two contemporaneous versions published by the AJCC and UICC. While the goal of the AJCC and UICC is to have identical TNM staging systems, differences exist between these two publications including in the staging of urologic cancers. Among several new facets in the AJCC staging manual, a select few of greater import include an expanded section on imaging, presentation of levels of evidence for significant changes, and endorsement of risk assessment models that pass the AJCC quality criteria such as in prostate cancer. The updates for urologic cancers in the AJCC stage categories can be grouped into: (1) newly defined TNM categories and prognostic stage groupings, (2) clarifications and refinements of previously defined categories, and (3) more systematic and expanded presentation of prognostic factors. Changes are harmonized with the current reporting and treatment guidelines. Contributions from genitourinary pathology are evident in the AJCC classification from many of the International Society of Urological Pathology (ISUP) consensus conferences on prostate, kidney, testicular, and penile neoplasms that addressed staging issues and the timely publication of the 4th edition of the World Health Organization (WHO) classification of urinary and male genital organ tumors. New grading approaches for penile (WHO/ISUP grade), prostate (Grade group), and kidney (WHO/ISUP nucleolar grade) cancers were adopted in the AJCC system. Many of these updates in the AJCC staging manual are also included in the 8th UICC TNM edition. In an effort to achieve the optimal staging recommendations for urologic cancers, updates in the 8th TNM edition were generated through the acquisition of best evidences, tapping interdisciplinary resources including consensus recommendations, and enhanced data analysis.

Patient summary: In this report, we explain the seminal changes in the 8th edition of the Tumor-Node-Metastasis staging system for urologic cancers. Major stage category definitional changes are in Tumor-Node-Metastasis classifications of testicular, penile, and prostate cancer which improve patient stratification for prognosis and management.

* Corresponding author. Department of Pathology, The University of Chicago, 5841 South Maryland Avenue, Room AMB S626 – MC 6101, Chicago, IL 60637, USA. Tel. +1 773 702 2824; Fax: +1 773 834 7644.
E-mail address: Gladell.Paner@uchospitals.edu (G.P. Paner).

https://doi.org/10.1016/j.eururo.2017.12.018
0302-2838/

1. Introduction

The Tumor-Node-Metastasis (TNM) staging system has been recognized globally for decades as the benchmark in staging cancers for: (1) cancer classification, (2) prognostication, (3) management, (4) data registry, and (5) clinical trials and research. In late 2016, the American Joint Committee on Cancer (AJCC) published its 8th edition of the *AJCC Cancer Staging Manual* (8E AJCC), with an implementation date of January 1, 2018 for clinical practice and cancer registry reporting [1]. Changes in stage classifications were guided by the principle of building on its "population-based" approach and refining towards a more "personalized" paradigm to cancer staging, exemplified by the expansion of nonanatomic factors in its *prognostic stage groups* for select cancers. The 8E AJCC demonstrates transparency behind major changes by providing *levels of evidence*, established by its Evidence-Based Medicine and Statistics Core (Table 1) [2]. Through the AJCC Precision Medicine Core, select *risk assessment models* for individualized prognosis were endorsed and will be continually updated on the AJCC website (cancerstaging.org) [3].

The 8E AJCC has divided chapters presented in the Genitourinary section of the 7th edition into two separate sections—Male Genital Organs (3 chapters) and Kidney and Urinary Tract (4 chapters). The updates and emphasis in the 8E AJCC are most evident in the pathological aspects of staging and other prognostic factors. Besides the actual revisions in the TNM categories, attention was also devoted to: (1) clarify stage category definitions by using contemporary histoanatomic terminology used by practicing pathologists, (2) updating tumor histologic classifications, and (3) presenting prognostic factors in a more systematic and expanded manner. Since the publication of the 7th edition, the International Society of Urological Pathology (ISUP) had conducted consensus conferences on prostate cancer in 2009, kidney cancer in 2012, and testicular and penile cancers in 2015, the proceedings of which have informed several pathologic staging issues [4–10]. The 4th edition of the World Health Organization (WHO) classification for urologic cancers was published in early 2016 and was incorporated as the histologic classification system in the 8E AJCC [11]. Urologic specimen handling strategies including those provided by ISUP and the College of American Pathologists are also recommended [4–10,12].

Table 1 – American Joint Commission on Cancer levels of evidence[a]

Level	Evidence
I	The available evidence includes consistent results from multiple large, well-designed, and well-conducted national and international studies in appropriate patient populations, with appropriate endpoints, and appropriate treatments. Both prospective studies and retrospective population-based registry studies are acceptable; studies should be evaluated based on methodology rather than chronology.
II	The available evidence is obtained from at least one large, well-designed, and well-conducted study in appropriate patient populations and with appropriate endpoints and with external validation.
III	The available evidence is somewhat problematic due to one or more factors, such as: number, size, or quality of individual studies, inconsistency of results across individual studies, appropriateness of patient population used in one or more study, or appropriateness of outcomes used in one or more study.
IV	The available evidence is insufficient because appropriate studies have not yet been performed.

[a] Reproduced from Amin et al [1].

The 8E AJCC is a compendium of all currently available information on the staging of adult cancers for most clinically important anatomic sites developed by the AJCC in cooperation with the UICC. While the two organizations work closely together at every level to create a staging schema that is largely identical between the two organizations; some significant differences exist. The differences arise as UICC aims to maintain its focus on cancer incidence and surveillance across the world and hence requires international applicability across all countries, particularly those that are severely economically restrained. AJCC's vision is to build on the anatomic basis of the extent of disease foundation of the TNM classification developed robustly over the past seven editions and judiciously incorporate nonanatomic factors critical in cancer classification and prognostication. Thus, AJCC aims to meet both the cancer surveillance and registry needs while gaining increased clinical relevance at the individual patient care level. Contemporaneous to the 1024-page 8E AJCC manual, the UICC published its more condensed 253-page 8th edition of the *TNM Classification of Malignant Tumours* (8E UICC) [13]. The UICC has retained many of the categories unchanged from the 7th TNM edition. Some genitourinary pathology experts have criticized the UICC for publishing its 8th edition TNM version with fewer updates and exclusion of major ISUP recommendations in urologic cancers [14]. This review summarizes the changes in the 8th TNM staging edition for penile, prostate, testicular, kidney, bladder, and urinary tract cancers (Tables 2–7).

1.1. Penile cancer

Significant changes in skin-derived (nonurethral) penile cancer have been promulgated over past editions. Ta is now significantly expanded to noninvasive *localized squamous cell carcinoma (SCC)* from the previous noninvasive verrucous carcinoma (level of evidence II). The older definition was confusing to pathologists who may deem it is applicable to all verrucous carcinomas; most of which have broad pushing invasion and its extent can be difficult to assess. The new definition does not permit any overt destructive invasion in well sampled verrucous carcinoma and also encompasses other noninvasive SCC types such as basaloid, warty, papillary, and mixed types [11,15]. Ta is analogous to noninvasive papillary urothelial carcinoma of the urinary tract that contrasts the Tis for flat carcinoma in situ (CIS) or penile intraepithelial neoplasia.

The corpora are covered externally by varying tissue layers at the different regions of the penis (glans, foreskin, and shaft). The 8E AJCC has revised the definition of T1 or noncorporal invasive cancers according to penile region-

Please cite this article in press as: Stadler WM, et al. Updates in the Eighth Edition of the Tumor-Node-Metastasis Staging Classification for Urologic Cancers. Eur Urol (2018), https://doi.org/10.1016/j.eururo.2017.12.018