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REVIEW

Decoding the UICC 9th Edition TNM Staging in Head and Neck Cancer: Key Updates for Clinical Practice

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Abstract

Accurate cancer staging is fundamental to treatment planning, outcome prediction, clinical research, and policy development. The Union for International Cancer Control (UICC) 9th edition TNM classification introduces several key updates in head and neck squamous cell carcinoma (HNSCC). These include the incorporation of extranodal extension (ENE) into nodal staging for nasopharyngeal carcinoma (NPC) and HPV-associated oropharyngeal carcinoma, restructuring of stage grouping in NPC with stage IV now restricted to distant metastasis, modifications to both T and N categories in salivary gland carcinoma, and the addition of parathyroid carcinoma as a newly staged entity. These refinements aim to improve risk stratification and provide a framework for more precise and personalized treatment strategies. This review summarizes the major and minor changes and discusses their clinical implications, while emphasizing the need for further evidence to validate the prognostic utility of these recommendations.

Keywords: AJCC, UICC, Extranodal extension, TNM classification, Cancer staging

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Introduction

Cancer staging is essential for patient care, prognostication, treatment and research. A stable cancer staging system not only aids clinicians in treatment planning and prognostication but also helps to evaluate the treatment outcome and facilitate information exchange among various centers, which ultimately contributes to cancer research and support cancer control activities [1]. Between 1943 and 1952, Pierre Denoix introduced a systematic approach to stage cancer in solid tumours based on three anatomic characteristics: tumour (T), lymph node spread (N) and distant spread (M) [2]. In 1968, Union for International Cancer Control (UICC) published the first edition of the TNM classification [3]. The American Joint Committee of Cancer (AJCC) reported a similar but separate TNM classification in 1977 [4]. The two staging systems merged in 1987 and evolved over the last three decades. The AJCC/UICC TNM staging system is a major tool used by oncologists worldwide to record the extent of malignancy at presentation before treatment clinical TNM (cTNM), after surgery pathological TNM (pTNM) and at recurrence (rTNM) [5]. The 9th edition of the UICC/AJCC TNM classification was released in 2025 with some major modifications [6]. In this review article, we discuss the changes made in head and neck squamous cell carcinoma (HNSCC) and their rationale.

Summary of the changes made in the 9th edition of UICC TNM staging system

In case of pathological nodal staging minimum 6 lymph nodes are to be examined in selective nodal dissection (SND) specimen and 15 lymph nodes for radical or modified radical neck dissection (RND or MRND) specimen. The definition of Extranodal extension (ENE) is thoroughly elaborated whether detected clinically, pathologically or by imaging. ENE is introduced in the nodal staging of Nasopharyngeal carcinoma and HPV

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associated Oropharyngeal carcinoma. Stage grouping of nasopharyngeal carcinoma has undergone significant alteration. Stage grouping has been introduced for mucosal melanoma of the head and neck region. Modifications have been made to both T and N staging of salivary gland carcinoma, along with corresponding changes in stage grouping. Introduction of new TNM staging for parathyroid carcinoma in the 9th edition.

Major Modifications

Nasopharyngeal carcinoma

In nasopharyngeal carcinoma (NPC), 83% of new cases are reported from Asia with distinct characteristics and therapeutic implications [7]. In the 8th edition TNM staging system multiple important changes were made in both T and N stage like introduction of T0 stage for EBV positive cervical lymphadenopathy with unknown primary, replacement of 'infratemporal fossa/ masticator space' by specific description of soft tissue involvement, clubbing of N3a and N3b into N3 and stage IVA and IVB into IVA [8]. In the updated AJCC 9th edition, the criteria for cT4-stage tumors have been slightly adjusted specifically, cancers that invade past the outer surface of the lateral pterygoid muscle are now explicitly included. Advanced clinical or radiological ENE is now included as cN3 disease. M1 stage is divided into M1a: ≤3 metastatic lesions and M1b: >3 metastatic lesions. Stage grouping in nasopharyngeal carcinoma has undergone several major changes in the 9th edition, including: i. merging stage I and II into stage I; ii. Down-classifying stage III and IVA to II and III respectively; iii. Restriction of stage IV to distant metastasis only, and; iv. Subdivision of stage I and IV. The study conducted by the collaborative efforts from the endemic centers, the China Anticancer Association and the AJCC/UICC committee, has come to the conclusion that TNM-9 is superior to TNM-8 in major statistical aspects and improves the prognostication for NPC [9]. Table 1A and 1B give the detail description of the new TNM staging.[1, 9].

HPV associated Oropharyngeal carcinoma

UICC/AJCC in their 8th version introduced a separate TNM classification for HPV associated oropharyngeal carcinoma due to increased incidence of HPV positive oropharyngeal carcinoma in Western countries presented with distinct clinical features and more favorable prognosis [10]. The inclusion of all ipsilateral lymph nodes ≤6 cm within cN1 disease and the classification of T1–2N1 disease as stage I introduce inherent heterogeneity in that stage which might augment inconsistent result in the deintensification trials [11]. iENE is a dependable factor for assessing the risk of distant metastasis in HPV associated oropharyngeal carcinoma [11]. Thus extracting the iENE positive cohort from the cN1 group has improved the treatment outcome and survival [11]. Thus ipsilateral node

Table 1A. UICC 9th Edition Clinical T, N and M Stage of Nasopharyngeal carcinoma

T stage	Primary tumour
cTx	Primary tumour cannot be assessed
cT0	No evidence of primary tumour, but EBV positive cervical node (s) metastasis
cTis	Carcinoma-in-situ
cT1	Tumour confined to nasopharynx or extends to nasal cavity and/or oropharynx without parapharyngeal extension
cT2	Tumour with parapharyngeal extension or invasion to medial pterygoid, lateral pterygoid and/or prevertebral muscles
cT3	Tumour invades bony structures of skull base, cervical vertebrae, pterygoid structures and/or paranasal sinuses
cT4	Tumour with any of the following: Intracranial extension, Unequivocal clinical and/or radiological involvement of cranial nerves, Involvement of hypopharynx, Invading the orbit, Involvement of parotid gland, Infiltration beyond the anterolateral surface of the lateral pterygoid muscles
N stage	Nodal status
cNx	Regional lymph nodes cannot be assessed
cN0	No regional lymph node metastasis
cN1	Unilateral metastases in cervical lymph node (s) and/or unilateral or bilateral metastasis in retropharyngeal lymph nodes and 6 cm or less in greatest dimension and above the caudal border of cricoid cartilage *and without advanced clinical/ radiological extranodal extension#*
cN2	Bilateral metastasis in cervical lymph node (s) and 6cm or less in greatest dimension and above the caudal border of cricoid cartilage *and without advanced clinical/ radiological extranodal extension*
cN3	Metastasis in cervical lymph node (s) greater than 6 cm in greatest dimension or extension below the caudal border of cricoid cartilage or advanced clinical/ radiological extranodal extension
M stage	Distant metastasis
cM0	No distant metastasis
M1	Distant metastasis
M1a	*Three or fewer lesions in one or more organs*
M1b	*More than three lesions in one or more organs*

Footnote: changes are made in Italics, abbreviation: EBV, Epstein-Barr virus. # Advanced radiological and/or clinical extranodal extension is unequivocal evidence of tumour invasion into adjacent structures (i.e., skin, muscle, salivary gland and/or neurovascular bundles) identified by appropriate morphological imaging or clinical examination.

Table 1B. UICC 9th Edition Stage Grouping of Nasopharyngeal carcinoma

Stage 0	Tis	N0	M0
Stage IA	T1, T2	N0	M0
Stage IB	T0, T1, T2	N1	M0
Stage II	T0, T1, T2	N2	M0
	T3	N0, N1, N2	M0
Stage III	T4	Any N	M0
	Any T	N3	M0
Stage IVA	Any T	Any N	M1a
Stage IVB	Any T	Any N	M1b

Table 2A. UICC 9th Edition T, N and M stage of HPV Associated Oropharyngeal carcinoma

T stage	Primary tumour
cT0	No evidence of primary tumour, but p16 positive (HPV-associated) cervical node(s) metastasis present
cT1	Tumour 2 cm or less in greatest dimension
cT2	Tumour more than 2 cm but not more than 4 cm in greatest dimension
cT3	Tumour more than 4 cm in greatest dimension or extension to lingual surface of epiglottis
cT4	Tumour invades any of the following: larynx, deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus and styloglossus), medial or lateral pterygoid muscle, hard palate, mandible, pterygoid plates (medial and/ or lateral), nasopharynx, skull base, encases carotid artery
N stage	Nodal status
cNx	Regional lymph nodes cannot be assessed
cN0	No regional lymph node metastasis
cN1	Metastasis in ipsilateral lymph node (s), all 6 cm or less in greatest dimension, *without unequivocal imaging-detected and/or clinical extranodal extension*
cN2	Metastasis in ipsilateral lymph node (s), all 6 cm or less in greatest dimension, *with unequivocal imaging-detected and/or clinical extranodal extension** or Contralateral or bilateral metastasis in lymph node(s), all 6 cm or less in greatest dimension *without unequivocal imaging-detected and/or clinical extranodal extension*
cN3	Metastasis in lymph node (s) greater than 6 cm in greatest dimension or Contralateral or bilateral metastasis in lymph node (s) *with unequivocal imaging-detected and/or clinical extranodal extension*
M stage	Distant metastasis
M0	No distant metastasis
M1	Distant metastasis

Changes are made in italics, Abbreviation: HPV, Human Papilloma Virus; *Clinical extranodal extension is defined as the presence of skin involvement or soft tissue invasion with deep fixation to underlying muscle or adjacent anatomical structures or clinical signs of nerve involvement. Imaging is becoming a standard method of detecting unequivocal extranodal extension.

≤6 cm with unequivocal imaging detected and/or clinical ENE is now classified as cN2 stage and contralateral or bilateral node (s) with unequivocal imaging detected and/or clinical ENE is staged as cN3 disease (Table 2A) [1, 11]. Pathological nodal staging (Table 2B) [1, 11] has incorporated the following modifications: i. pN1 is divided into, pN1a: mets in 1 lymph node without definitive pENE and pN1b: mets in 2-4 lymph nodes without definitive pENE, ii. pN2: mets in 1-4 lymph nodes with definitive pENE or >4 lymph nodes without definitive pENE, iii. pN3: mets in >4 lymph nodes with definitive pENE. Stage grouping is summarized in table-2C [1, 11].

Salivary gland carcinoma

In the UICC 9th edition TNM classification major changes have been introduced in both T and N staging of salivary gland tumour. For cT3 tumors, the updated staging specifies gross extraparenchymal extension, including adjacent mucosal or soft-tissue involvement, without requiring deep structural invasion (e.g., bone or cartilage). cT4a is now described as invasion to immediately adjacent structures including skin, bone, cartilage, solid organ parenchyma, trachea, esophagus, named nerve. cT4b is now described as invasion beyond the adjacent structures eg., base of skull (except nasopharynx), carotid encasement, spinal column, intracranial, mediastinal structures, masticator space. Nodal staging (Table 3A) [1] is now being simplified. cN1 now includes 1-3 ipsilateral nodes without cENE or iENE. cN2 is involvement of >3 lymph nodes or any node with cENE or iENE. Subclassification of cN2: N2a, N2b and N2c is removed. cN3 is also removed. Pathological nodal staging also corroborates with the new clinical nodal stage (Table 3B) [1]. In stage grouping (Table 3C) [1] stage IV is limited to only distant spread with exclusion of further subdivision of stage IV into IVA, IVB and IVC. Stage III is now divided into IIIA and IIIB.

Table 2B. UICC 9th Edition Pathological Nodal Staging of HPV Associated Oropharyngeal carcinoma

pNx	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis in 1–4 lymph nodes *without definitive pathological extranodal extension**
pN1a	*Metastasis in 1 lymph node without definitive pathological extranodal Extension*
pN1b	*Metastasis in 2–4 lymph nodes without definitive pathological extranodal extension*
pN2	*1–4 lymph nodes with definitive pathological extranodal extension or Metastasis in >4 lymph nodes without definitive pathological extranodal extension*
pN3	*Metastasis in >4 lymph nodes with definitive pathological extranodal extension*

Changes are made in italics. * Pathological extranodal extension (pENE) should only be diagnosed when tumour that is present within the confines of a lymph node definitively transgresses through the entire thickness of the lymph node capsule into the surrounding connective tissue, with or without stromal reaction. A soft tissue deposit should be considered as at least one lymph node with extranodal extension if it occurs at a site where a regional lymph node would be expected.

Parathyroid carcinoma

The Staging system for parathyroid carcinoma has been newly introduced in the head and neck carcinoma chapter in the updated 9th version of UICC TNM classification. It is summarized in Table 4 [1].

Minor Modifications

Oral cavity carcinoma

A minor change is incorporated in the T stage which is superficial invasion of adjacent skin (dry vermilion or vermilion border) is insufficient for classification as cT4a

Laryngeal carcinoma

No significant modification is incorporated except the removal of tumour invasion into the paraglottic space and/or inner cortex of thyroid cartilage from cT3 stage in subglottic carcinoma.

Malignant melanoma of upper aerodigestive tract

In the previous AJCC 8th edition TNM staging there was no prognostic stage grouping. In UICC 9th edition TNM staging, stage III and IV are introduced as there is no T1, T2 disease as well as stage I and II due to the aggressive nature of mucosal melanomas.

Carcinoma of skin of the head and neck region

In the new TNM classification stage IV is subdivided into stage IVA and IVB. Stage IVA includes N2, N3, T4 disease and stage IVB encompass distant metastasis i.e., M1 disease.

No Modification

UICC 9th edition TNM classification corroborates with the 8th edition AJCC TNM classification for HPV independent oropharynx, hypopharynx, nasal cavity and paranasal sinus and cervical lymphadenopathy with unknown primary, thyroid carcinoma.

Clinical and prognostic implication of Extranodal extension in HNSCC

The lymph node capsule acts as a natural barrier to tumor spread, and extranodal extension (ENE) refers to the transgression of this capsule by malignant cells into surrounding tissues [12]. ENE can be identified in three distinct ways: clinical ENE (cENE), defined by clinical signs of invasion into adjacent structures such as skin, muscle, or nerves; pathological ENE (pENE), confirmed by histopathological demonstration of tumor cells extending beyond the lymph node capsule into perinodal tissue; and imaging-detected ENE (iENE), characterized by unequivocal radiological evidence of capsular breach, often manifesting as invasion into fat, muscle, or neurovascular structures.

ENE has long been recognized as an adverse prognostic marker in head and neck cancers [13]. In HPV-independent oropharyngeal and non-oropharyngeal squamous cell carcinomas, the presence of ENE correlates with higher rates of distant metastasis and inferior survival outcomes, and was therefore incorporated into the nodal staging in the 8th edition TNM classification [14]. However, its role in virus-associated malignancies, such as EBV-related nasopharyngeal carcinoma (NPC) and HPV-associated oropharyngeal carcinoma, remained controversial due to conflicting evidence [12].

Recent studies have clarified this uncertainty. In a meta-analysis both ungraded and unambiguous advanced radiological ENE, defined as unequivocal evidence of tumour invasion into surrounding structures like skin, muscles or neurovascular bundles detected clinically or by imaging, was found to be associated with inferior overall survival (OS) and distant metastasis free survival

Table 2C. UICC 9th Edition Stage Grouping of HPV Associated Oropharyngeal carcinoma

Stage I	T0, T1, T2	N0, N1	M0
Stage II	T0, T1, T2	N2	M0
	T3	N0, N1, N2	M0
Stage III	Any T	N3	M0
	T4	Any N	M0
Stage IV	Any T	Any N	M1

Table 3A. UICC 9th Edition T, N and M Staging of Salivary Gland Carcinoma

T stage	Primary tumour
cTx	Primary tumour cannot be assessed
cT0	No evidence of primary tumour
cTis	Carcinoma in situ
cT1	Tumour 2 cm or less in greatest dimension without extraparenchymal extension
cT2	Tumour more than 2 cm but not more than 4 cm in greatest dimension without extraparenchymal extension
cT3	Tumour more than 4 cm, or gross extraparenchymal or adjacent site mucosal/ soft tissue extension beyond site without structural involvement
cT4a	Tumour invades immediately adjacent structures, including skin, bone*, cartilage, solid organ parenchyma, oesophagus, trachea, and/or named nerve
cT4b	Tumour invades beyond adjacent structures, e.g. encasement of carotid artery, and/or base of skull invasion (except nasopharynx), and/or spinal column invasion, and/or intracranial invasion, and/or orbital apex, and/or prevertebral space, and/or mediastinal structures, and/or masticator space, etc.
N stage	Nodal status
cNx	Regional lymph nodes cannot be assessed
cN0	No regional lymph node metastasis
cN1	*Metastasis in 1–3 ipsilateral lymph node(s) without unequivocal imaging-detected** or clinical extranodal extension*
cN2	*Metastasis in more than 3 lymph nodes or any lymph node with unequivocal imaging-detected and/or clinical extranodal extension*
M stage	Distant metastasis
M0	No distant metastasis
M1	Distant metastasis

Changes are made in italics. *Destruction of intrinsic sinus bones is not considered bone invasion for skull base tumours. Erosion of cortical bone is not considered bone invasion; a minor salivary gland tumour arising within the bone is not considered bone invasion. ** Extranodal extension can be detected clinically or radiologically. Imaging-detected Extranodal extension (iENE) on appropriate morphological imaging refers to unequivocal radiologic signs of tumour invasion through the capsule of a lymph node into either perinodal fat or adjacent tissues (e.g. skin, muscle or neurovascular structures) or a coalescent nodal mass (A coalescent nodal mass comprises ≥2 adjacent lymph nodes that have lost their intervening tissue planes and capsules to merge into a single indivisible structure).

Table 3B. UICC 9th Edition Pathological Nodal Staging of Salivary Gland Carcinoma

pNx	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis in 1–3 lymph node without definitive pathological extranodal extension
pN2	Metastasis in >3 lymph nodes or Metastasis in any lymph node with definitive pathological extranodal extension

Table 3C. UICC 9th Edition Stage Grouping of Salivary Gland Tumour

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3, T4	N0	M0
	T1, T2	N1	M0
Stage IIIB	T1, T2	N2	M0
	T3, T4	N1, N2	M0
Stage IV	Any T	Any N	M1

(DMFS) for NPC [15]. Similarly, multiple large-scale analyses have confirmed the prognostic significance of ENE in HPV-associated oropharyngeal carcinoma, where both iENE and cENE predict inferior disease control and survival [16-19]. These data provided the basis for the UICC 9th edition TNM classification, which now incorporates ENE into nodal staging for both NPC and HPV-associated oropharyngeal carcinoma. This change acknowledges ENE as a biologically meaningful event across both virus-associated and virus-independent head and neck cancers. By integrating ENE into staging, the updated system enhances risk stratification, informs treatment intensification or de-intensification strategies, and lays the groundwork for future clinical trials aimed at personalizing therapy.

In conclusion, the UICC 9th edition TNM classification reflects a deeper understanding of tumor biology and integrates emerging prognostic evidence into staging

Table 4. UICC 9th Edition T, N and M Staging for Parathyroid Carcinoma

T stage	Primary tumour
cTx	Primary tumour cannot be assessed
cT0	No evidence of primary tumour
cT1	Limited to the parathyroid gland or any tumour with minimal extra-parathyroid soft tissue extension without direct invasion of the thyroid gland
cT2	Tumour of any size with invasion into the thyroid gland
cT3	Tumour of any size with invasion into adjacent skeletal muscle, recurrent laryngeal nerve, trachea, oesophagus, thymus or direct invasion into adjacent lymph node(s)
cT4	Tumour of any size with direct invasion into major blood vessels or spine
N stage	Nodal status
cNx	Regional lymph nodes cannot be assessed
cN0	No regional lymph node metastasis
cN1a	Metastasis in Level VI (pretracheal, paratracheal and prelaryngeal/Delphian lymph nodes) or upper/superior mediastinal lymph nodes
cN1b	Metastasis in other unilateral, bilateral or contralateral cervical (Levels I, II, III, IV or V) or retropharyngeal node
M stage	Distant metastasis
M0	No distant metastasis
M1	Distant metastasis

practice. The most impactful advancement is the universal incorporation of ENE in virus-associated head and neck cancers, a change expected to enhance prognostic accuracy and guide therapeutic decision-making. Other important reforms include restructuring of nasopharyngeal carcinoma stage grouping, refinement of salivary gland staging, and the introduction of parathyroid carcinoma staging. Collectively, these updates establish a stronger foundation for risk-adapted treatment, personalized therapy, and the design of future clinical trials; however, their clinical utility will require validation through real-world multicentric studies.

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Statement of Transparency and Principles

• Author declares no conflict of interest

• Ethical approval and informed consent were not required as this is a narrative review of published literature.

• All authors have contributed to implementation of this research.

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