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Performance of the American Joint Committee on Cancer Staging Manual, 8th Edition vs the Brigham and Women's Hospital Tumor Classification System for Cutaneous Squamous Cell Carcinoma

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IMPORTANCE Brigham and Women's tumor classification (BWH) better predicts poor outcomes than American Joint Committee on Cancer (AJCC) 7th edition (AJCC 7). AJCC 8th edition (AJCC 8) has not been evaluated.

OBJECTIVES To compare BWH and AJCC 8 tumor classifications for head and neck cutaneous squamous cell carcinoma (HNCSCC).

DESIGN, SETTING, AND PARTICIPANTS A total of 459 patients with 680 HNCSCCs in this cohort study were staged via BWH and AJCC 8 classifications and poor outcomes (ie, local recurrence [LR], nodal metastasis [NM], disease specific death [DSD], and overall survival [OS]) were compared. The study was carried out at a single academic tertiary care center in Boston, Massachusetts.

MAIN OUTCOMES AND MEASURES Distinctiveness (outcome differences between tumor class), homogeneity (outcome similarity within tumor class), monotonicity (outcome worsening with increasing tumor class), and C statistic.

RESULTS A total of 680 HNCSCCs in 459 patients were included in this study, of which 313 (68%) were men with the mean (SD) age of 70.2 (12.7) years. The AJCC 8 (T3/T4) and BWH (T2b/T3) high tumor classes accounted for 121 (18%) vs 63 (9%), 17 (71%) vs 16 (70%), and 11 (85%) vs 12 (92%) of total cases, metastases, and deaths, respectively. The AJCC 8 T2 and T3 comprised 23% of cases and had statistically indistinguishable outcomes. The BWH had higher specificity (93%) and positive predictive value (30%) for identifying cases at risk for metastasis or death. C statistics showed BWH to be superior in predicting NM and DSD (P = .01 and P = .005, respectively), but there was no difference for LR and OS.

CONCLUSIONS AND RELEVANCE Lack of distinction between AJCC T2 and T3 resulted in a 23% subset of HNCSCCs with significant risk of metastasis and death—too large of a group for routine nodal staging or consideration of adjuvant therapy. The BWH identifies the same number of poor outcomes in a 9% subset of HNCSCCs, thus minimizing inappropriate upstaging of low-risk disease.

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Supplemental content

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Although most cutaneous squamous cell carcinomas (CSCC) have an excellent prognosis and are cured with surgical excision alone, a small subset of tumors have a high risk of poor outcomes with 3.7% to 5.2% developing metastases and 2.8% dying of disease.[1-4] Most deaths (70%) are owing to unresectable locoregional disease (including local and nodal disease) rather than distant organ metastases.[2] Identification of such tumors with significant risk of recurrence, progression to unresectability, or death is challenging owing to lack of accurate CSCC risk stratification. The American Joint Committee on Cancer (AJCC) Tumor Classification, 7th edition (AJCC 7) for CSCC introduced several prognostic factors besides tumor diameter.[5,6] However, AJCC staging has suffered from an inability to validate and refine the system via population-based data because CSCC is excluded from the Surveillance, Epidemiology, and End Results Program.

The Brigham and Women's Hospital (BWH) system is an alternative tumor classification system. Prior analysis of a single institution cohort demonstrated that the BWH staging system offers improved distinctiveness, homogeneity, and monotonicity over AJCC 7.[6] A systematic review[7] of sentinel node biopsy in CSCC demonstrated that BWH T2b/T3 tumors have a high risk of sentinel node positivity (29.4%). Such data prompted the recommendation of some form of nodal staging for BWH T2b/T3 CSCCs.[8]

A major limitation to AJCC 7 is that the bulk of poor outcomes (local recurrence [LR], nodal metastasis [NM], or death from CSCC [DSD]) occurred in AJCC 7 T2 because higher tumor classes (AJCC 7 T3 and T4) were reserved for bone invasion.[6] The AJCC Cancer Staging Manual, 8th Edition (AJCC 8) was brought into clinical use in January 2018 and includes an updated CSCC tumor classification for cases located on the head and neck only.[9]

A recent analysis of head and neck CSCC (HNCSCC) tumors showed that AJCC 8 had superior homogeneity and monotonicity to AJCC 7 because a greater number of tumors (AJCC 7: 0.7% vs AJCC 8: 17.8%) and 70% of poor outcomes occurred in AJCC 8 T3 and T4 classes.[10] This is an improvement over AJCC 7, wherein only 14% of poor outcomes occurred in AJCC 7 T3/T4 classes. Another recent study found that AJCC 7, AJCC 8, and BWH tumor classifications did not identify CSCC tumors at risk for metastasis.[11] However, information on the primary tumor was unavailable in many metastatic cases, prohibiting accurate T staging.

The purpose of the present study was to compare the performance of AJCC8 and BWH tumor classifications (summarized in **Table 1**) in patients diagnosed with CSCC of the head and neck without evidence of distant metastesis (N0M0) with regard to distinctiveness, homogeneity, and monotonicity as defined below. The sensitivity and specificity of high tumor classes (AJCC 8 T3/T4 and BWH T2b/T3) to predict poor outcomes were also evaluated.

Key Points

Question How does the performance of American Joint Committee on Cancer Staging Manual, 8th Edition (AJCC 8) compare with Brigham and Women's Hospital Tumor Classification System (BWH) in patients diagnosed with cutaneous squamous cell carcinoma of the head and neck (HNCSCC)?

Findings In this cohort study of 459 patients with 680 HNCSCC, twice as many tumors were classified as AJCC 8 (T3/T4) high tumor class compared with BWH (T2b/T3) high tumor classes (AJCC 8 18% vs BWH 9%). The AJCC 8 T2 and T3 comprised 23% of cases and had statistically indistinguishable outcomes, whereas the BWH had higher specificity (93%) and positive predictive value (30%) for identifying cases at risk for metastasis or death; C statistics showed BWH to be superior in predicting nodal metastasis and disease-specific death.

Meaning There was a lack of distinction between AJCC T2 and T3 results in a subset of 23% of HNCSCC with significant risk of metastasis and death whereas BWH identified the same number of poor outcomes in a 9% subset of HNCSCC, thus minimizing inappropriate upstaging of low-risk disease.

Methods

Data Collection

The study was approved by the Partners Human Research Committee, which waived written informed consent because all data were deidentified. Data used in the present study included the subset of CSCCs located on the head and neck (HNCSCC) from a previously published Brigham and Women's CSCC cohort study.[12] Data collection procedures have been previously published.[6,12] In brief, patients with CSCC diagnosed at BWH from January 1, 2000, through December 31, 2009, were identified via a department of pathology electronic database. Pathology reports were reviewed and noncutaneous SCC, in situ CSCC, and recurrent CSCC were excluded. Only tumors located on the head and neck were included in the present analysis because AJCC 8 staging system is specific for HNCSCC. Tumors were classified according to BWH and AJCC 8 tumor classifications. The medical records of all eligible patients were reviewed for features of the primary tumor needed for tumor classification (clinical diameter, millimeter and/or anatomic depth of invasion, and presence and location and/or caliber of perineural invasion with nerve caliber measured and recorded if absent in pathology report) and analyzed by outcomes of interest (LR, NM, DSD, and overall survival [OS]). When risk factors were not reported on the pathology report or Mohs operative note, they were assumed to be absent. Pathologists and Mohs surgeons at BWH routinely report histologic differentiation, the presence of perineural invasion (PNI), and tumor invasion beyond the dermis. Thus, if there was no mention of depth of invasion, PNI, or differentiation, the tumor was assumed to be well differentiated, less than 6 mm, and confined to fat with no PNI. Histologic review was performed for cases with reported PNI to ensure there was tumor present in the nerve sheath and to record millimeter caliber of involved nerves.

Statistical Analyses

Cox proportional hazards regression with competing risks was performed for LR, NM, and DSD. Death from non-CSCC causes was considered a competing event. Cox proportional hazards regression models were used for overall survival (OS) owing to the

absence of competing risks for this outcome. Overall survival was calculated by patient rather than for each individual tumor. Survival time for each end point of interest was calculated from the date of CSCC tumor diagnosis to date of outcome occurrence. For tumors without any poor outcome, survival time was censored on the date of death or medical record review if patient was alive at the time of data collection. The proportional hazards assumption was checked using Schoenfeld residuals. Cumulative incidence function curves for LR, NM, and DSD, and Kaplan-Meier survival curves for OS were generated by BWH tumor classification for HNCSCC. The curves for AJCC 8 for this cohort have previously been published, but are displayed in the **Figure** to facilitate comparison with BWH.[10]

For analyses comparing high vs low tumor classes, high tumor class for BWH was considered BWH T2b or T3 and AJCC 8 was considered AJCC 8 T3, T4a, and T4b. Performance of tumor classification system was assessed in terms of homogeneity (outcomes are similar within tumor class), monotonicity (outcomes worsen with increasing tumor class), and distinctiveness (outcomes differ between tumor class). To evaluate tumor classification homogeneity and monotonicity, the proportion of poor outcomes occurring in low and high tumor classes was compared using the McNemar test. To evaluate tumor classification distinctiveness, the 10-year cumulative incidences with corresponding 95% confidence intervals (CI) and C statistic were compared by tumor classification system by outcome. Discrimination was measured by the C statistic (or concordance statistic), which is a measure of the area under the receiver operating characteristic (ROC) curve and is used to determine distinctiveness. The C statistic in the present study is the probability a tumor with a poor outcome had a higher chance of being high tumor class in the modeled data than a randomly chosen patient without the outcome in the same model. A value of 1.0 indicates the model (in this case, high vs low tumor class) has perfect distinctiveness whereas a value of 0.5 indicates the model has no distinctiveness. The Gray test was used for statistical comparisons of cumulative incidence estimates and log-rank test was used to compare cumulative survival estimates. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the high tumor class' ability to predict NM and DSD (considered as 1 outcome for this analysis) were calculated. Sensitivity and specificity were compared using the McNemar test.

All reported *P* values were 2-sided with type I error (α <.05) considered to be statistically significant. Statistical analyses were performed using SAS statistical software (version 9.4, SAS Institute) and Stata statistical software (version 14.0, StataCorp).

Results

The pathology database search yielded a total of 1980 primary CSCC cases. After medical record review, 1152 tumors not located on head and neck region and 148 tumors with insufficient primary tumor information were excluded, leaving a total of 680 HNCSCC in 459 patients. One additional tumor was excluded from BWH staging analysis owing to missing tumor diameter, but was able to be staged as an AJCC 8 T3 based on presence of PNI in the subcutaneous fat (eTable in the Supplement).

Table 1. Summary of the BWH and AJCC 8 Tumor Classification Systems

Tumor Staging System	Definition
AJCC 8th Edition	
T1	<2 cm in greatest diameter
T2	≥2 cm, but <4 cm in greatest diameter
T3	Tumor ≥4 cm in greatest diameter or minor bone invasion or perineural invasion or deep invasion[a]
T4a	Tumor with gross cortical bone and/or marrow invasion
T4b	Tumor with skull bone invasion and/or skull base foramen involvement
BWH	
T1	0 High-risk factors[b]
T2a	1 High-risk factor
T2b	2-3 High-risk factors
T3	4 High-risk factors or bone invasion

Abbreviations: AJCC, American Joint Committee on Cancer; BWH, Brigham and Women's Hospital; T, tumor stage from TNM staging system.

[a] Deep invasion defined as invasion beyond the subcutaneous fat or >6 mm (as measured from the granular layer of adjacent normal epidermis to the base of the tumor), perineural invasion defined as tumor cells in the nerve sheath of a nerve lying deeper than the dermis or measuring 0.1 mm or larger in caliber or presenting with clinical or radiographic involvement of named nerves without skull base invasion or transgression.

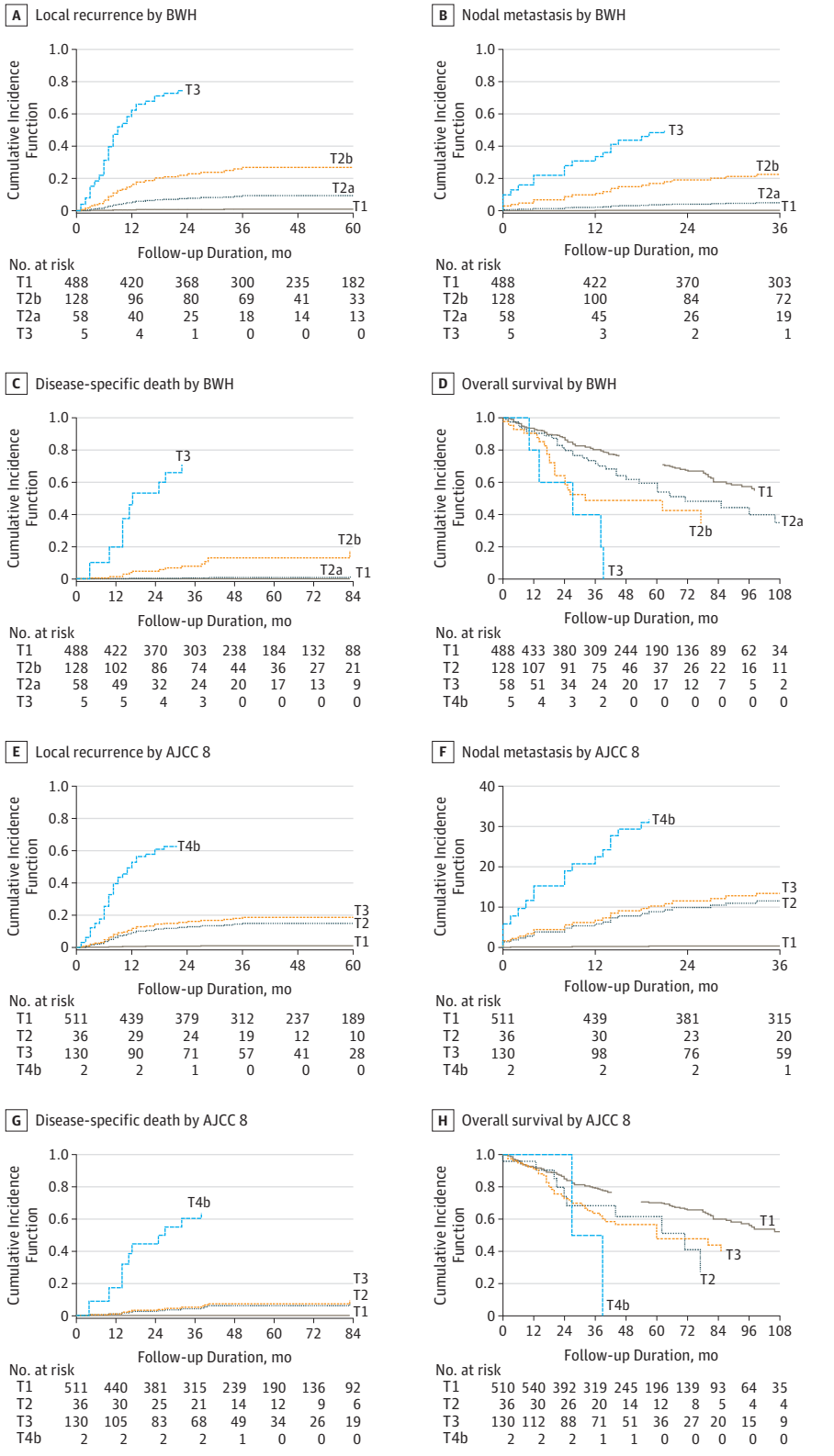
[b] BWH high-risk factors include tumor diameter ≥2 cm, poorly differentiated histology, perineural invasion of nerve(s) ≥0.1 mm in caliber, or tumor invasion beyond subcutaneous fat (excluding bone invasion, which upgrades tumor to BWH stage T3).

The Figure shows cumulative incidence function curves for LR, NM, and DSD, and Kaplan-Meier survival curves for OS by BWH and AJCC 8 tumor classification for HNCSCC.

Table 2 shows results of homogeneity and monotonicity evaluations for AJCC 8 vs BWH tumor classifications. The AJCC 8 (T3/T4) and BWH (T2b/T3) high tumor classes accounted for 121 (18%) and 63 (9%) of total cases and 50 (70%) DROs (22 [65%] LRs, 17 [71%] NMs, 11 [85%] DSDs) and 47 (67%) DROs (19 [56%] LRs, 16 [70%] NMs, 12 [92%] DSDs), respectively. The 2 systems had comparable monotonicity and homogeneity (McNemar *P* not significant for all end points of interest) capturing similar fractions of poor outcomes in high tumor classes.

The 10-year cumulative incidences of outcomes of interest by AJCC 8 and BWH tumor classifications are shown in **Table 3**. For both AJCC 8 and BWH tumor classification systems, most tumors were classified as T1 (AJCC 8: 523 [76.9%]; BWH: 488 [72%]). A smaller proportion of tumors were classified as AJCC 8 T2 (5.3%) compared with BWH T2a (19%) and the opposite trend was seen for AJCC 8 T3 (17.5%) compared with BWH T2b (8%). No tumors were classified as AJCC 8 T4a and only 2 tumors AJCC 8 T4b (0.3%). Similarly, only 5 tumors (1%) were staged as BWH T3. For AJCC 8, there was substantial overlap in the CIs for AJCC 8 T2 and T3, whereas for BWH T2b and T3 there was no overlap for LR and NM and only slight overlap for DSD (there is substantial overlap in CIs for OS for both systems). Calculation of C statistics by ROC analyses revealed similar discriminative ability between BWH and AJCC 8 tumor classification for LR (C statistic, 0.86; 95% CI, 0.79-0.92 vs C statistic, 0.81; 95% CI, 0.73-0.88; *P* = .09) and OS (C statistic, 0.54; 95% CI, 0.50-0.57 vs C statistic, 0.53;

Figure. Cumulative Incidence Function Curves



A, Local recurrence; B, nodal metastasis; and C, disease-specific death. D, Kaplan-Meier survival curves for overall survival by Brigham and Women's Hospital (BWH) tumor classification for cutaneous squamous cell carcinomas of the head and neck (HNCSCC). E, Cumulative incidence function curves for local recurrence; F, nodal metastasis; and G, disease-specific death. H, Kaplan-Meier survival curves for overall survival by American Joint Committee on Cancer 8th Edition (AJCC 8) tumor classification for HNCSCC. Figures E-H are adapted from figures previously published in *JAMA Dermatology*.[10]

Table 2. Evaluation of BWH and AJCC 8 Tumor Classification System Homogeneity and Monotonicity[a]

Tumor Classification	No./No. (%)			
	LR	NM	DSD	Overall Events
Homogeneity: Proportion of Poor Outcomes Occurring in Low Tumor Classes				
BWH T1/T2a	15/34 (44)	7/23 (30)	1/13 (8)	23/70 (33)
AJCC 8 T1/T2	12/34 (35)	7/24 (29)	2/13 (15)	21/71 (30)
P value	.46	.92	.53	.67
Monotonicity: Proportion of Poor Outcomes Occurring in High Tumor Classes				
BWH T2b/T3	19/34 (56)	16/23 (70)	12/13 (92)	47/70 (67)
AJCC 8 T3/T4a/T4b	22/34 (65)	17/24 (71)	11/13 (85)	50/71 (70)
P value	.46	.92	.54	.67

Abbreviations: AJCC, American Joint Committee on Cancer; BWH, Brigham and Women's Hospital; DSD, disease-specific death; LR, local recurrence; NM, nodal metastasis; T, tumor stage from TNM staging system.

[a] *P* values based on the McNemar test.

Table 3. Evaluation of BWH and AJCC 8 Tumor Classification System Distinctiveness

Tumor Classification	Tumors, No. (%)	Local Recurrence		Nodal Metastasis		Disease-Specific Death		Overall Survival[a]	
		Events, No.	10-y CIN (95% CI)	Events, No.	10-y CIN (95% CI)	Events, No.	10-y CIN (95% CI)	Events, No.	10-y Survival (95% CI)
BWH									
T1	488 (72)	4	0.9 (0.4-2.1)	1	0.2 (0.04-1.1)	0	NA	103	55.0 (47.0-62.2)
T2a	128 (19)	11	9.8 (5.4-17.7)	6	5.2 (2.3-11.9)	1	1.2 (0.1-12.2)	32	35.0 (19.2-51.2)
T2b	58 (8)	15	28.4 (18.9-42.8)	13	23.8 (14.8-38.4)	7	17.4 (9.0-33.8)	21	33.4 (14.6-53.6)
T3	5 (1)	4	84.2 (74.1-95.7)	3	62.1 (31.4-123.0)	5	94.8 (83.5-107.7)	5	0 (0.0-0.0)
AJCC 8									
T1	523 (76.9)	7	1.1 (0.4-2.6)	3	0.4 (0-1.9)	0	NA	113	52.4 (44.3-59.8)
T2	36 (5.3)	5	15.8 (7.5-33.0)	4	12.2 (5.4-27.6)	2	7.6 (4.4-13.1)	10	29.9 (7.5-57.0)
T3	119 (17.5)	20	19.7 (13.0-29.7)	16	14.1 (9.7-20.7)	9	9.3 (6.8-14.0)	35	39.5 (24.4-54.3)
T4a	0	0	NA	0	NA	0	NA	0	NA
T4b	2 (0.3)	2	73.6 (66.8-81.0)	1	42.6 (12.6-100)	2	82.2 (68.3-91.5)	2	0.0 (0.0-0.0)

Abbreviations: AJCC, American Joint Committee on Cancer; BWH, Brigham and Women's Hospital; CIN, cumulative incidence; T, tumor stage from TNM staging system.

[a] Overall survival was calculated for each patient. All other outcomes were calculated for each tumor.

95% CI, 0.50-0.56; *P* = .69). However, the BWH tumor classification demonstrated superior discriminative ability for NM (C statistic, 0.91; 95% CI, 0.85-0.96 vs C statistic, 0.84; 95% CI, 0.76-0.91; *P* = .01) and DSD (C statistic, 0.97; 95% CI, 0.94-0.99 vs C statistic, 0.91; 95% CI, 0.88-0.94; *P* = .005) compared with AJCC 8 tumor classification.

Table 4 shows the sensitivity, specificity, PPV, and NPV of the high stages of the BWH (T2b and T3) and AJCC 8 (T3, T4a, and T4b) tumor classification systems to detect NM and DSD. The sensitivity, probability that an NM/DSD will be a high tumor class, of both staging systems is similar (AJCC 8, 0.78 vs BWH, 0.73; McNemar *P* = .20). The specificity, probability that someone without NM/DSD will be a low tumor class, was higher with BWH (AJCC 8, 0.85 vs BWH, 0.93; McNemar *P* < .001). The PPV, probability of developing a NM/DSD with a high-class tumor, was higher for BWH (AJCC8, 0.17 vs BWH, 0.30) because 50% more cases were high tumor class under AJCC 8 compared with BWH, but both high tumor classes detected the same number of poor outcomes. The NPV, probability of not developing a NM/DSD if the tumor was a low tumor class, was high for both classification systems, as expected for a disease with few poor outcomes overall (AJCC 8/BWH, 0.99).

Discussion

Although both tumor classification systems have similar monotonicity and homogeneity, the BWH staging system was found to be more distinct than AJCC 8, with a higher specificity (93%) and PPV (30%) for identifying cases at risk for metastasis and death. The AJCC 8 is limited owing to equivalent risks for all end points of interest between AJCC 8 T2 and T3 tumors. This results in a large (155 [23%] of the cohort) heterogeneous AJCC 8 T2/T3 group with an approximate 13% risk of NM and 8% risk of DSD. Conversely, most poor outcomes (16 [70%] NM and 12 [92%] DSD) were confined to just 63 (9%) of the cohort in BWH T2b/T3. The BWH T2b group had a 24% risk of NM, consistent with prior data, and a 17% risk of DSD.[6,7] Rare (n = 5) T3 cases had a high risk of poor outcomes, with 3 of 5 developing nodal metastases and all 5 dying from disease.

One reason for the equivalent outcomes in AJCC 8 T2 and T3 is that poor differentiation is not a risk factor. Approximately 50% of nodal metastasis and overall death in AJCC 8 T2 occurred in patients with poorly differentiated tumors, increasing the risk of poor outcomes in this group. The risk of poor outcomes was lower in AJCC 8 T3 compared with BWH T2b because AJCC 8 T3

Table 4. Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value of BWH and AJCC 8 Tumor Classification High Stages (AJCC 8, T3/T4 and BWH, T2b/T3) to Detect NM/DSD

Variable	AJCC 8	BWH	*P* Value[a]
Sensitivity	0.78	0.73	.20
Specificity	0.85	0.93	<.001
Positive predictive value	0.17	0.30	NA[b]
Negative predictive value	0.99	0.99	NA[b]

Abbreviations: AJCC, American Joint Committee on Cancer; BWH, Brigham and Women's Hospital; DSD, disease specific death; NM, nodal metastasis; T, tumor stage from TNM staging system.

[a] *P* values based on the McNemar test.

[b] *P* values cannot be estimated for positive and negative predictive values because they are based on prevalence of disease.

tumors are only required to have 1 of 4 risk factors whereas 2 risk factors are required for BWH T2b tumor class. Of the 130 AJCC 8 T3, 101 (78%) only had 1 risk factor, with 74 being upstaged to T3 owing to PNI, 24 owing to depth beyond fat, 2 owing to diameter larger than 4 cm, and 1 owing to minor bone erosion. The AJCC 8 excluded differentiation because the designation of well, moderate, and poor differentiation may differ between centers, limiting clinical application. The decision to use a single risk factor for upstaging was based on insufficient data to quantify the prognostic impact of accumulating risk factors with only 2 cohort studies having investigated this methodology.[5,6] Upstaging on a sole risk factor and not including poor differentiation appear to result in convergence of AJCC 8 T2 and T3 such that their risks of poor outcomes are identical.

Risk stratification for CSCC is central to clinical treatment because it allows identification of tumors that are at high risk for poor outcomes and may benefit from lymph node evaluation or adjuvant therapy. A recent retrospective cohort study and retrospective review of published literature supported the use of radiologic imaging for high-stage CSCCs (BWH T2b/T3 tumors)[8,13] and, although data are limited, sentinel lymph node biopsy (SLNB) of high-risk tumors is more sensitive than radiologic imaging and allows early identification and treatment of nodal metatstasis.[7] However, it is important to select only the subset of cases likely to benefit from additional workup and treatment owing to the morbidity and costs associated with such procedures. Because AJCC 8 T2 and T3 grades have similar risks of nodal metastases (10-year cumulative incidence rates of 12% and 14%, respectively) and account for approximately a quarter of all HNCSCC in this cohort, it is difficult to use AJCC 8 to select tumors appropriate for nodal staging or adjuvant care. On the other hand, the BWH T2b grade contained only 58 (8%) of the cohort and had a much higher risk of nodal metastasis compared with BWH T2a (10-year cumulative incidence rates of 24% vs 5%, respectively). Based on the positive predictive value of BWH, a high tumor class tumor has a 30% risk of developing a metastasis or dying from disease. This risk is substantial enough to warrant nodal screening and close surveillance. Conversely, the specificity of the BWH indicates that patients who are BWH low tumor class have a 93% chance of never developing metastasis or dying from disease. Thus, these cases as a group, are unlikely to benefit from additional staging or treatment.

To our knowledge, only 2 prior studies compare the AJCC 8 and BWH tumor classification systems. Roshcer et al[11] performed a study of 103 CSCC tumors with metastasis and 81 without metastasis. The authors concluded that neither AJCC 8 nor BWH adequately risk stratify CSCC tumors. However, primary tumor characteristics needed for BWH classification were not available for many metastatic cases such that BWH tumor class could not be accurately assigned (8% missing tumor diameter, 19% depth of invasion, 15% differentiation, and 100% millimeter diameter of involved nerves) underscoring the need for prospective data collection or careful retrospective T-classification in validation studies. A recent analysis by Marrazzo et al[14] found the overall risk of NM to be 4.8%. Of the 647 HNCSCC treated with Mohs micrographic surgery in a private practice, most poor outcomes occured in AJCC 8 T2 whereas BWH T2B/T3 identified 79% of LR, 77% of NM, and 100% of DM, which is similar to the analysis presented herein.

Limitations

The primary limitation of our analysis is that it is based on a single-institution cohort. This is particularly important with regard to factors that may not be uniformly measured across centers such as measurement of perineural invasion (which has specific parameters in both BWH and AJCC 8 staging) and grading of differentiation. These will require standardization before tumor classification systems can be validated in multicenter studies. Another limitation is that an independent review of histologic analyses was not undertaken, except for cases with PNI, and so it was assumed that risk factors were absent if not reported. Some pathologic features were not routinely recorded, such as tissue level of PNI and millimeter tumor depth, and could have altered AJCC 8 staging in a few cases. However, AJCC 8 intentionally allows 2 ways of classifying PNI (tissue level or nerve caliber) and tumor depth (millimeter or tissue level) to allow flexibility in accordance with various current reporting standards. One of these methods was employed in all cases in the present study. The current analysis thus reflects how the staging systems may perform under current histologic reporting practices. Finally, the analysis presented herein used a subset of the cohort from which the BWH staging system was derived and so verification of the BWH staging system was not feasible. However, this would not influence the performance of AJCC 8, including the lack of distinction noted between AJCC 8 T2 and T3.

Conclusions

Although both AJCC 8 and BWH high tumor classes capture most poor outcomes, twice the number of tumors are staged as a high tumor class by AJCC 8. Use of BWH tumor classification may minimize the number of patients recommended for radiologic evaluation, close surveillance, and possible adjuvant therapy while still identifying most patients at risk for recurrence, metastasis, and death. Additional cohort or population-based studies with accurate tumor classification are needed to further validate and compare current CSCC staging systems and to provide data for future refinements to AJCC staging.

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Study concept and design: Ruiz, Karia, Schmults.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Ruiz.
Critical revision of the manuscript for important intellectual content: All authors.
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