Cleveland Academy of Osteopathic Medicine

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The Ohio State University
Wexner Medical Center

Cutaneous Squamous Cell Carcinoma: A Focus on Diagnosis and Staging

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Disclosures

I have no relevant disclosures related to this presentation.

Basics of Cutaneous Squamous Cell Carcinoma

Second most common cutaneous malignancy

UV radiation

High cure rate if treated early

New emerging medical & surgical treatments

Fig. 1. Keratinocyte & Melanocyte Stem Cell (Bolognia)

Fig. 2. (Bolognia)

How big of a problem is this in the US?

Lets dive into the data…

Image goes here

Cutaneous squamous cell carcinoma: Estimated incidence of disease, nodal metastasis, and deaths from disease in the United States, 2012

Pritesh S. Karia, MPH, Jiali Han, PhD, and Chrysalyne D. Schmults, MD, MSCE
Boston, Massachusetts

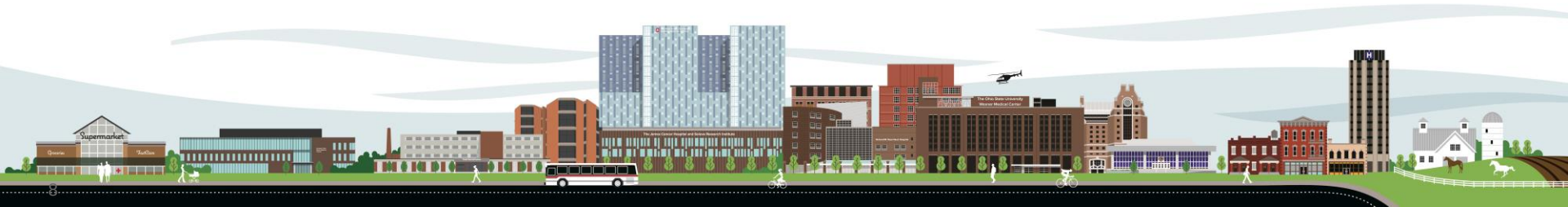
What are the facts?

Over 700,000 new cases of cutaneous SCC diagnosed yearly

Approximately 4% of patients will develop nodal metastasis

1.5% will die from the disease

“High-risk” subset has been identified



Risk Factors

Environmental Exposure

Phenotype

Genetic Syndromes

Predisposing Clinical Settings

Immunosuppression

Immunosuppression

Solid Organ Transplant Patient 65-250 x the risk of cSCC!!!

Heart & Lung Transplant

Less risk for hematopoietic stem cell transplant

Chronic Lymphocytic Leukemia

Multi-disciplinary approach needed for this population

What about the actinic keratosis?

0.075% - 0.096% per lesion per year

Typical patient has 7.7 AKs

Rate of development is 10.2% in 10 years

Some studies have shown rates higher (13-20%)

Fig. 3.(Bolognia)

Identification of SCC

Squamous cell carcinoma in-situ

Most commonly an erythematous and slightly scaly plaque

Sun-exposed areas

Elderly individuals

Younger individuals with significant photodamage

Anogenital regions can also be affected

Fig. 4.(Bolognia)

Fig. 5.(Bolognia)

Fig. 6.(Bolognia)

Fig. 7.(Bolognia)

Invasive squamous cell carcinoma

Vast array of clinical presentations

Sun-exposed areas

Exophytic or plaque-like

Associated scale to dense hyperkeratosis

Fig. 8.(Bolognia)

Fig. 9.(Bolognia)

Fig. 10.(Bolognia)

Fig. 11.(Bolognia)

Fig. 12.(Bolognia)

Factors associated with recurrence & metastasis

Tumor diameter >2cm

- 2x risk of recurrence
- 3x risk of metastasis
- 19-fold increase in disease-specific death

Tumor depth >2mm

- 10-fold risk of recurrence
- 11-fold risk of metastasis

Perineural Invasion

- 47% recurrence and metastatic rate after wide excision

Staging of squamous cell carcinoma

Evolution of Staging - AJCC 6

- All nonmelanoma skin cancers were grouped together for the purpose of staging

- Incorporated at least 82 different types of tumors

- This included cutaneous SCC

- Staging remained unchanged for 20 years until 2010

Cutaneous SCC receives its own staging system with AJCC 7

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor ≤2 cm in greatest dimension with <2 high-risk features*
T2	Tumor >2 cm in greatest dimension with or without one additional high-risk feature,* *or* any size with ≥2 high-risk features*
T3	Tumor with invasion of maxilla, mandible, orbit, or temporal bone
T4	Tumor with invasion of skeleton (axial or appendicular) or perineural invasion of skull base

* High-risk features include depth (>2-mm thickness; Clark level ≥IV); perineural invasion; location (primary site ear; primary site nonglabrous lip); and differentiation (poorly differentiated or undifferentiated).

What data come out of AJCC 7?

JAMA Dermatol. 2013 Apr;149(4):402-10. doi: 10.1001/jamadermatol.2013.2456.

Evaluation of AJCC tumor staging for cutaneous squamous cell carcinoma and a proposed alternative tumor staging system.

Jambusaria-Pahlajani A[1], Kanetsky PA, Karia PS, Hwang WT, Gelfand JM, Whalen FM, Elenitsas R, Xu X, Schmults CD.

- 256 high-risk cutaneous SCC

T2 to T4 were clinically indistinguishable!

- Only 2% of cohort were stage T3/T4

- Most of the poor outcomes were clustered in stage T2
    - 69% of local recurrences
    - 83% of nodal metastasis
    - 92% of deaths

- Heterogenous T2 group

Alternative staging system was proposed

- Alternative staging system was based off of 4 risk factors

1. Poorly differentiated histologic characteristics
2. Diameter greater then 2 cm
3. Perineural Invasion
4. Invasion beyond subcutaneous fat

Table 3. Alternative T Staging System

Alternative T Staging System	Definition	Patients in Study Cohort, No. (%)
T0	In situ SCC	Not included
T1	0 Risk factors[a]	134 (52)
T2a	1 Risk factor[a]	67 (26)
T2b	2-3 Risk factors[a]	49 (19)
T3	4 Risk factors[a] or bone invasion	6 (2)

[a] Risk factors include tumor diameter 2 cm or greater, poorly differentiated histologic characteristics, perineural invasion, and tumor invasion beyond the subcutaneous fat (excluding bone invasion, which automatically upgrades tumor to alternative stage T3).

What was the goal of the alternative staging system?

- Break up the large AJCC T2 group

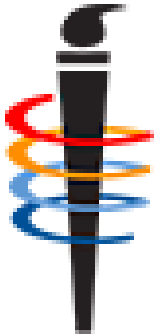
- T2a had rare poor outcomes

- T2b had significantly higher rates of poor outcomes

- T3 tumors were extremely rare

-Eliminated the need for a T4 category

October, 2016, 8th edition is released



AJCC

American Joint Committee on Cancer

Validating science. Improving patient care.

Head & Neck cSCC, AJCC 8 Tumor Staging

pT category	
Tx	Primary tumor cannot be identified
Tis	Carcinoma in situ
T1	Tumor <2 cm
T2	Tumor ≥2 cm but <4 cm
T3	Tumor >4 cm or minor bone erosion or PNI or deep invasion
T4a	Tumor with gross cortical bone/marrow invasion
T4b	Tumor with skill base invasion and/or skull base foramen involvement

Summary of the changes in AJCC 8

- T2 is limited to tumors >2cm, but <4cm

- T3 has been expanded to include tumors >4cm, or have 1 or more risk factors

- Risk factors for T3 upstaging
    - Invasion beyond subcutaneous tissue or >6mm
    - Perineural invasion
    - Minor bone invasion

- T4a = gross cortisol bone/marrow invasion; T4b = skull base or foramen involvement

Comparison of Tumor Classifications for Cutaneous Squamous Cell Carcinoma of the Head and Neck in the 7th vs 8th Edition of the *AJCC Cancer Staging Manual*

Pritesh S. Karia, MPH; Frederick C. Morgan, BSPH; Joseph A. Califano, MD; Chrysalyne D. Schmults, MD, MSCE

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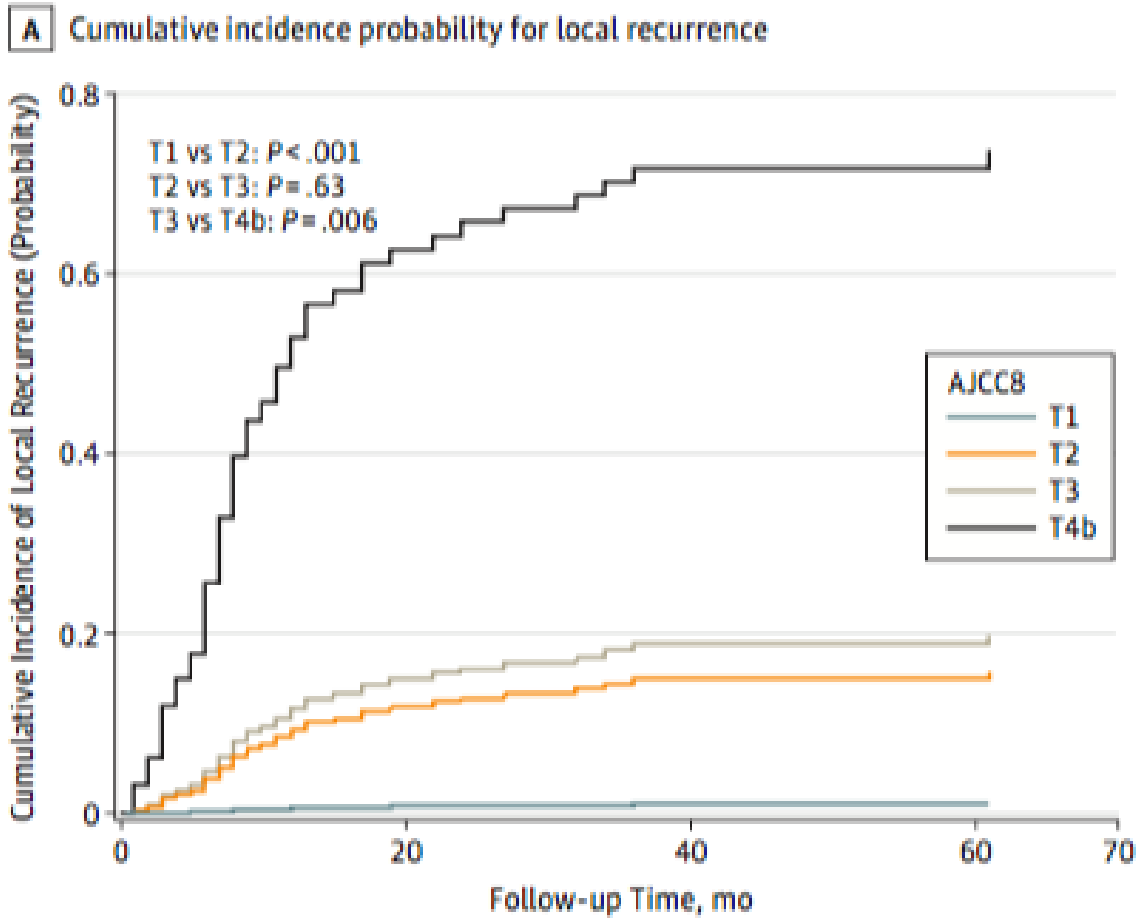
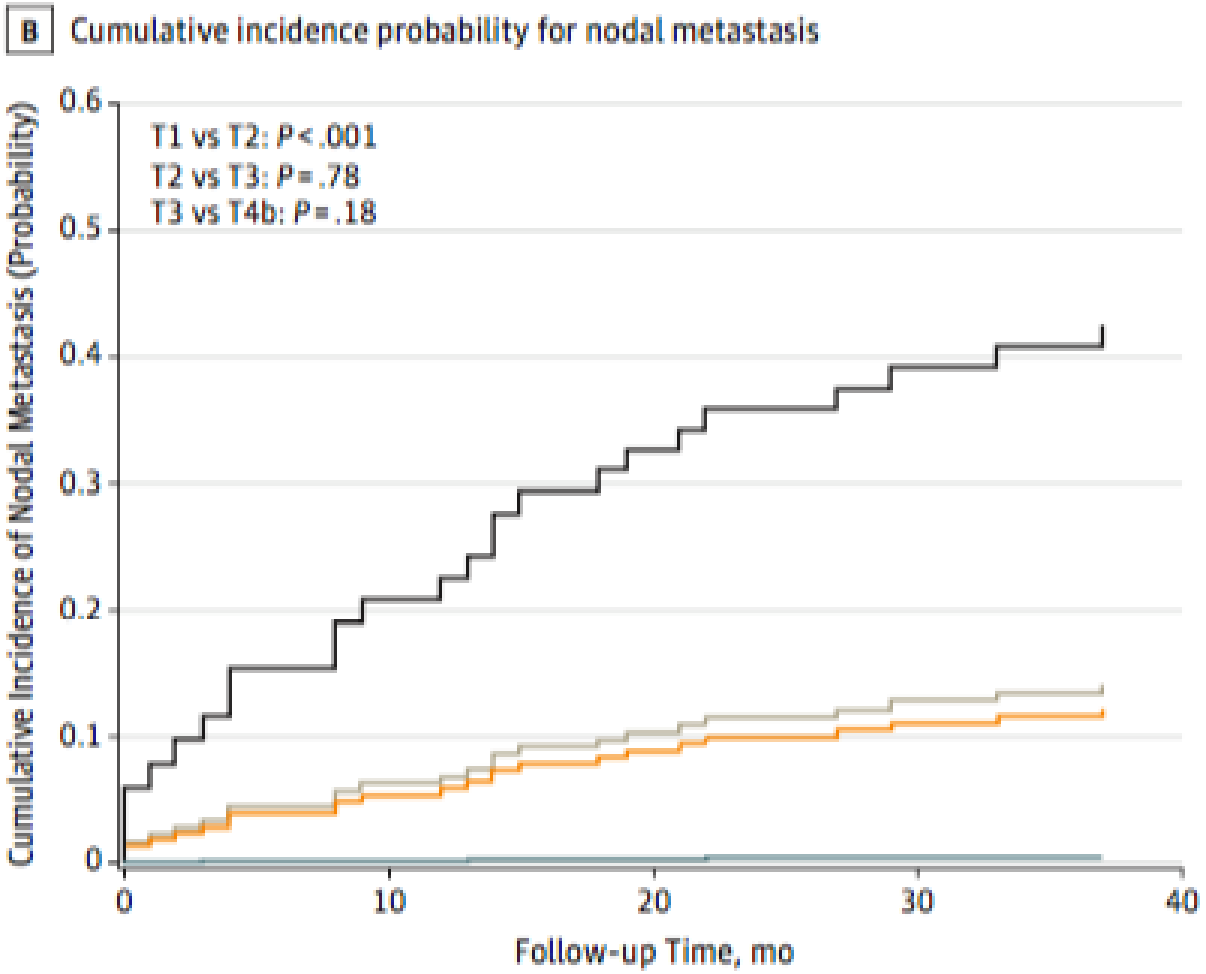
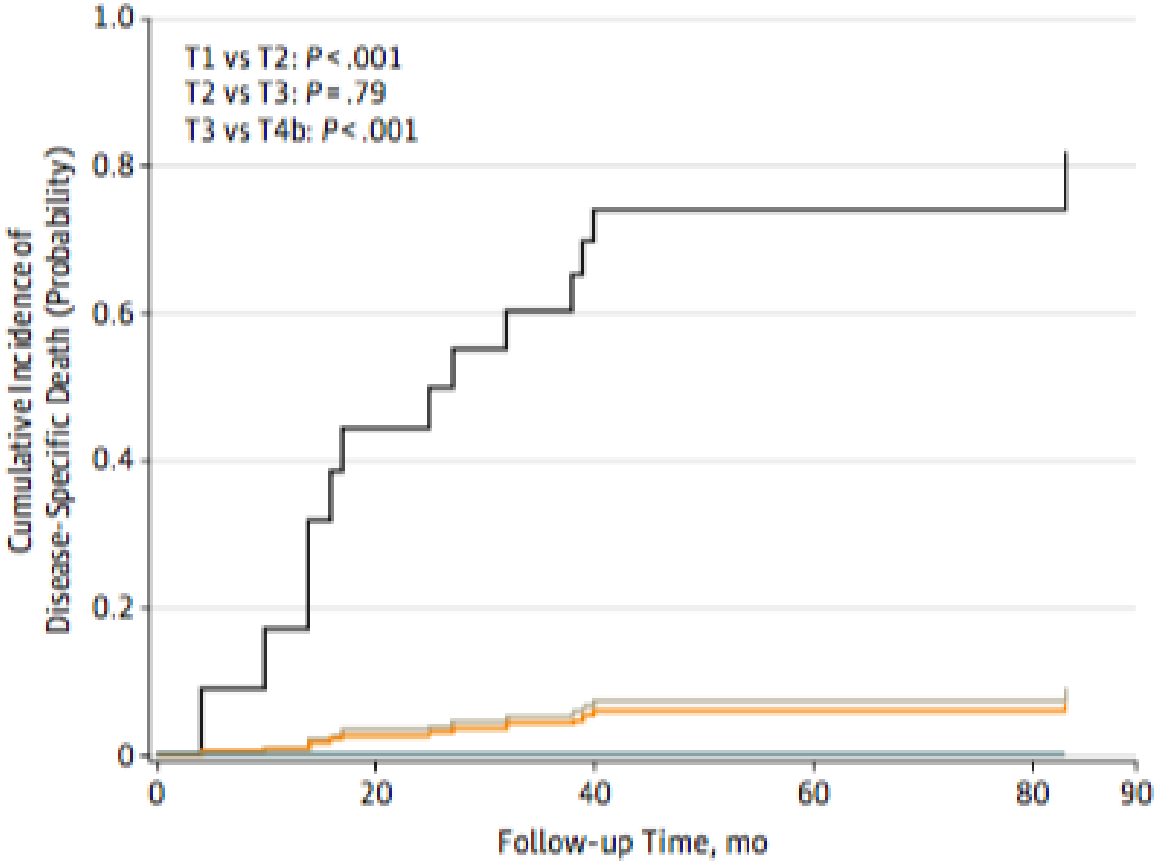

A Cumulative incidence probability for local recurrence
Cumulative Incidence of Local Recurrence (Probability)
0.8
0.6
0.4
0.2
0
T1 vs T2: P < .001
T2 vs T3: P = .63
T3 vs T4b: P = .006
AJCC8
T1
T2
T3
T4b
0
20
40
60
70
Follow-up Time, mo



C Cumulative incidence probability for disease-specific death



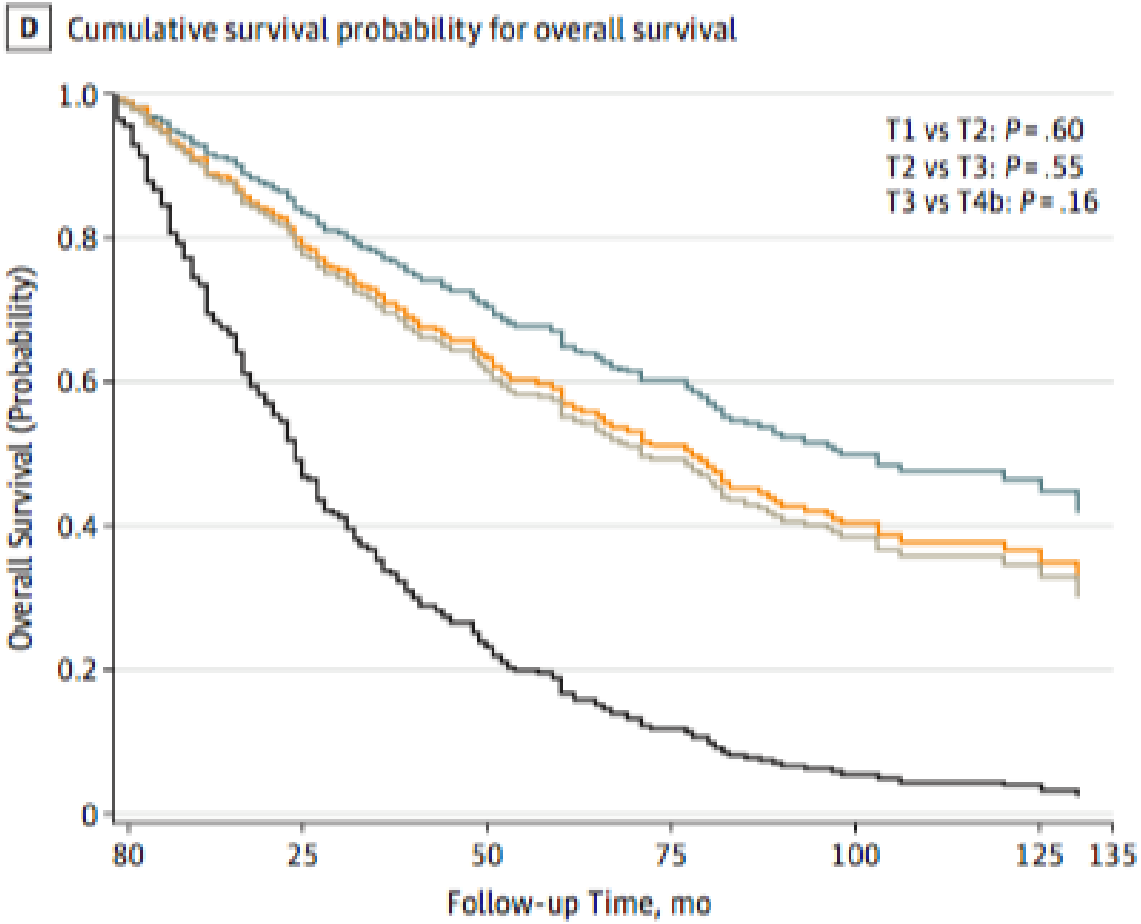


Table 3. Evaluation of the Seventh and Eighth Editions of the *AJCC Cancer Staging Manual* (*AJCC 7* and *AJCC 8*) Tumor Classification System Homogeneity and Monotonicity

Tumor Classification	LR	NM	DSD	Overall Events
	Homogeneity: Proportion of Poor Outcomes Occurring in Low Tumor Categories, No. (%)			
AJCC 7 T1/T2	30 of 34 (88.2)	21 of 24 (87.5)	8 of 13 (61.5)	59 of 71 (83.1)
AJCC 8 T1/T2	12 of 34 (35.3)	7 of 24 (29.2)	2 of 13 (15.3)	21 of 71 (29.6)
	Monotonicity: Proportion of Poor Outcomes Occurring in High Tumor Categories, No. (%)			
AJCC 7 T3/T4	4 of 34 (11.8)	3 of 24 (12.5)	5 of 13 (38.5)	12 of 71 (16.9)
AJCC 8 T3/T4a/T4b	22 of 34 (64.7)	17 of 24 (70.8)	11 of 13 (84.6)	50 of 71 (70.4)

Abbreviations: DSD, disease-specific death; LR, local recurrence; NM, nodal metastasis.

Table 4. Number of Tumors of 680 Upgraded and Downgraded Using the *AJCC Cancer Staging Manual, Eighth Edition* (*AJCC 8*) Tumor Classification System

Changes From *AJCC 7* to *AJCC 8*	Tumors, No.	Disease-Related Outcomes, No.		
		LR	NM	DSD
Upgrading				
T1→T2	8	1	1	0
T1→T3	20	0	0	0
T2→T3	96	18	14	6
Downgrading				
T2→T1	101	4	2	0

Abbreviations: DSD, disease-specific death; LR, local recurrence; NM, nodal metastasis.

What are the good things that came from AJCC 8?

- More tumors (17.8%) were classified into high tumor categories
    - Accounted for 70.4% of poor outcomes
        - 64.7% of Local Recurrence
        - 70.8% of Nodal Metastasis
        - 84.6% of Disease Specific Death

- >4cm in size or the addition of one high risk factor classifies a tumor at stage T3
    - Shifted many tumors from T2 to T3
    - Lead to superior homogeneity and monotonicity, with greater separation between low- and high-risk tumors

What areas still require some improvement?

- T4 remains rarely used
    - 0, T4a tumors & 2, T4b tumors

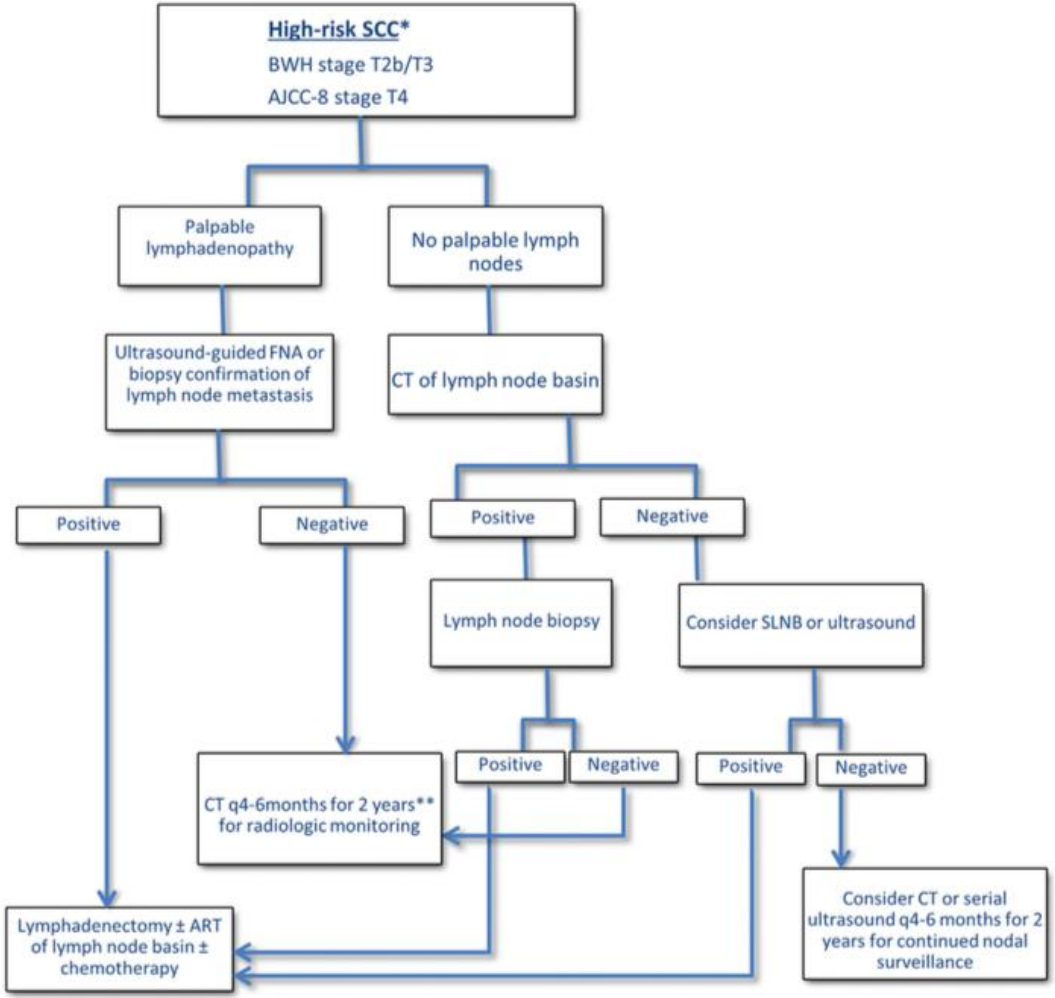
- 95% confidence intervals overlapped between T2 & T3 for all end points
    - Clinicians should recognize that some T2 tumors may develop poor outcomes

- Though acknowledged, poor differentiation was removed as a risk factor for inclusion in tumor classification
    - Accounts for most of the failures in stage T1 & T2
    - Of the cases that were elevated from T1 or T2 to stage T3, only those with poor differentiation had an elevated risk of poor outcomes.

Cutaneous squamous cell carcinoma

Management of advanced and high-stage tumors

Syril Keena T. Que, MD,[a] Fiona O. Zwald, MD,[b] and Chrysalyne D. Schmults, MD, MSCE[a]
Boston, Massachusetts, and Washington, District of Columbia


High-risk SCC*
BWH stage T2b/T3
AJCC-8 stage T4
Palpable lymphadenopathy
No palpable lymph nodes
Ultrasound-guided FNA or biopsy confirmation of lymph node metastasis
CT of lymph node basin
Positive
Negative
Positive
Negative
Lymph node biopsy
Consider SLNB or ultrasound
Positive
Negative
Positive
Negative
CT q4-6months for 2 years** for radiologic monitoring
Lymphadenectomy ± ART of lymph node basin ± chemotherapy
Consider CT or serial ultrasound q4-6 months for 2 years for continued nodal surveillance

Monitoring

- Low-risk
    - Every 6 months

- High-risk (Stage T2b)
    - Every 4 months
    - Skin & lymph nodes
    - Imaging?

Take-home Points

- BEWARE the squamous cell

- Cutaneous squamous cell carcinoma is a very common malignancy with potentially serious consequences

- Staging tumors allows clinicians to stratify the risk of poor disease related outcomes

- Monitor your patients closely or refer to a board-certified dermatologist for regular skin exams

Thank You!

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