1142P. Personalized follow-up in cutaneous squamous cell carcinoma: integrating a clinicopathological model for absolute metastatic risk into staging systems

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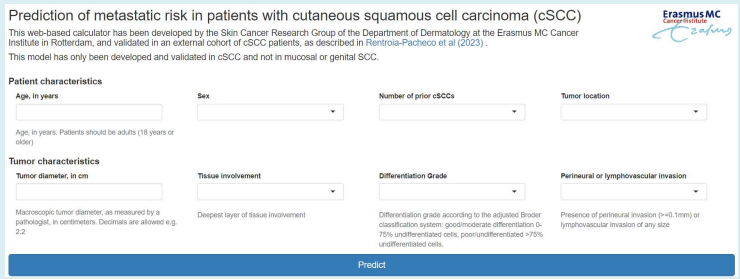
Introduction

Cutaneous squamous cell carcinoma (**cSCC**) is the 2nd most common skin cancer, with a death toll comparable to melanoma, despite its low propensity to metastasize (2%-5%).

Accurate identification of high risk patients remains an unmet need in the field. Therefore, we sought to improve the risk stratification of American Joint Committee on Cancer (**AJCC**) and the Brigham and Women's Hospital (**BWH**) staging systems by integrating a recently developed clinicopathological (**CP**) model predicting absolute metastatic risk.

Clinicopathological model

For a given cSCC patient, the model takes as input eight clinicopathological variables to compute his/her absolute risk of developing loco-regional or distant metastases within a certain time point (1, 3 and 5 years).



The model is available as a web-based calculator[1]:

How would you use this model? Please answer our 2 minutes survey:

SCAN ME

Methods

Nationwide cohort[1] (N=12325)

Nested case control cohort[1] (N=390)

Within staging systems low-risk (AJCC: T1-T2 and BWH: T1-T2a) and staging systems high-risk (AJCC: T3-T4 and BWH: T2b-T3) groups, we tried to discriminate patients with increased metastatic risk. Using the nested case control cohort, we defined a **CP model risk threshold** for each risk group:

- Using the CP model, we computed the risk of developing metastases (CP model risk) within 5-years.
- Based on the CP model risk, we binarized patients into **CP High-Risk** and **CP Low-Risk**.
- We computed statistics and performance metrics in the intended-use population (nationwide cohort) using weighted metrics, as required by a nested case-control cohort design.

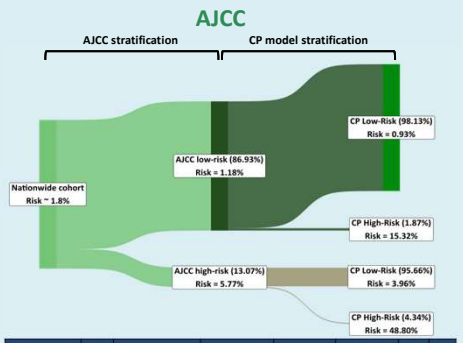
Results

In the **low-risk group as per AJCC and BWH,** the metastatic risk is respectively 1.18% and 1.26%. Within this group, **CP High-Risk patients** are defined as those with CP model risk above 1% and:

- They represent respectively 1.87% and 2.34% of the AJCC and BWH groups.
- They have metastatic risk comparable or higher than risk in staging systems high-risk (15.32% in AJCC, 12.97% in BWH).
- They would be offered a more intense follow-up regimen (e.g., comparable to staging systems high-risk group).

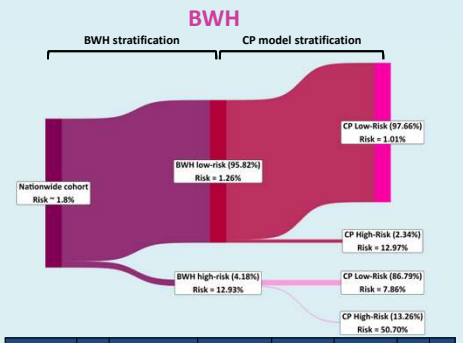
In the **high-risk group as per AJCC and BWH,** the metastatic risk is respectively 5.77% and 12.93%. Within this group, **CP High-Risk patients** are defined as those with CP model risk above 3.5% and:

- They represent respectively 4.34% and 13.26% of the AJCC and BWH groups (~0.6% of the nationwide cohort).
- They have increased metastatic risk of 48.80% in AJCC and 50.70% in BWH.
- They could be offered more intensive follow-up and treatment (e.g., adjuvant treatment).



AJCC risk group	NPV (%)	Risk in CP Low-Risk (=100-NPV) (%)	Risk in CP High-Risk (= PPV) (%)	Specificity (%)	Sensitivity (%)	LR+	LR-
AJCC high-risk	96.04	3.96	48.80	97.40	32.77	18.21	0.69
AJCC low-risk	99.07	0.93	15.32	98.37	21.90	15.56	0.79

Figure 1 *Sankey plot and performance metrics of stratification by CP model in combination with AJCC staging system (NPV: Negative Predictive Value, PPV: Positive Predictive Value, LR: Likelihood Ratio).*



BWH risk group	NPV (%)	Risk in CP Low-Risk (=100-NPV) (%)	Risk in CP High-Risk (= PPV) (%)	Specificity (%)	Sensitivity (%)	LR+	LR-
BWH high-risk	92.14	7.86	50.70	91.83	46.94	8.05	0.58
BWH low-risk	97.66	1.01	12.97	97.91	21.79	11.73	0.80

Figure 2 *Sankey plot and performance metrics of stratification by CP model in combination with BWH staging system (NPV: Negative Predictive Value, PPV: Positive Predictive Value, LR: Likelihood Ratio (LR)).*

Conclusion

Our risk model allows for more refined risk stratification within AJCC and BWH risk groups, leading to:

- Identification of high risk patients which require intense follow-up, and could be considered for treatments.
- Help clinicians, dermatologists, radiotherapists, and clinical oncologists in making more personalized decisions about follow-up schedules and treatments.

References

1. Rentroia-Pacheco, B., Tokez, S., Bramer, E. M., Venables, Z. C., van de Werken, H. J., Bellomo, D., ... & Wakkee, M. (2023). Personalised decision making to predict absolute metastatic risk in cutaneous squamous cell carcinoma: development and validation of a clinico-pathological model. EClinicalMedicine, 63.

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Sponsors: PPP Allowance made available by Health-Holland, Top Sector Life Sciences & Health, to stimulate public private partnerships.