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

Barbara Rentroia-Pacheco, MSc[1], Lara Pozza MSc[2], Domenico Bellomo,PhD[2], Sheril Alex, PhD[2], Jvalini Dwarkasing PhD[2], Antien L. Mooyaart, PhD[3], Loes M. Hollestein,PhD[1,4], Marlies Wakkee, PhD[1]

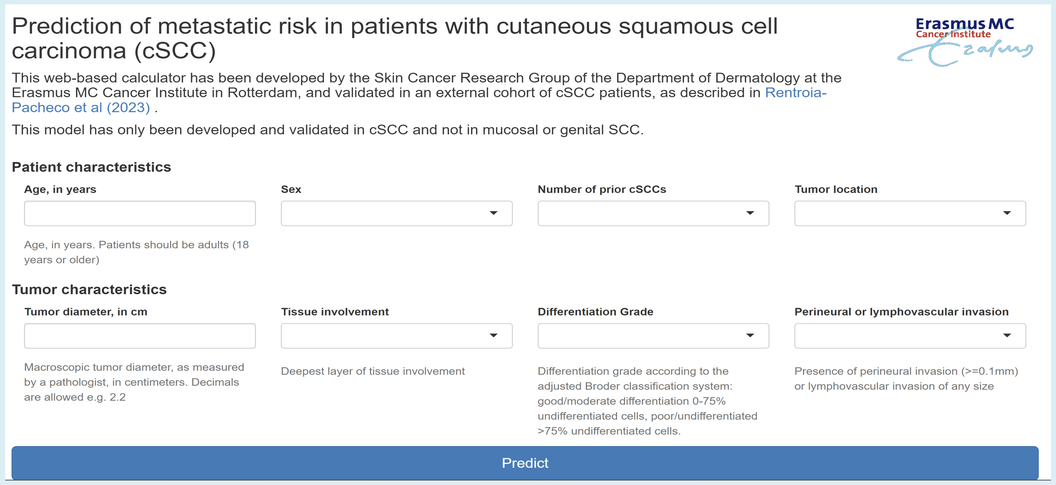
[1]Department of Dermatology, Erasmus Medical Center, Rotterdam, The Netherlands [2]SkylineDx B.V., Rotterdam, The Netherlands [3]Department of Pathology, Erasmus University Medical Center, Rotterdam, The Netherlands [4]Department of Research, Netherlands Comprehensive Cancer Organization (IKNL), Utrecht, The Netherlands

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.

Absolute risk model



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

Methods

Nationwide cohort

→ Nested case control cohort (N=390)

Within staging systems low-risk group (AJCC: T1-T2 and BWH: T1-T2a), we tried to discriminate a large fraction of patients with very low metastatic risk from a smaller group with increased risk:

- We computed 5-year metastatic risk with the CP model.
- We binarized the metastatic risk into **CP High-Risk** and **CP Low-Risk**, so as to have a CP Low-Risk, with halved metastatic risk.
- We computed statistics and performance metrics in the intended-use population 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 about 1%. Within this group:

- **CP Low-Risk patients**:
  - Are 2/3 of the group.
  - Have a very low metastatic risk of about 0.5%.
  - Require a much less intense follow-up regimen.
- **CP High-Risk patients**,
  - Are 1/3 of the group.
  - Have metastatic risk of about 3%.
  - Require regular or more intense follow-up schedules.

Figure 1 *Risk stratification of cSCC patients with the CP model in combination with AJCC and BWH staging systems.*

Staging system	NPV	Risk in CP Low-Risk (=100-NPV)	Risk in CP High-Risk (= PPV)	Specificity	Sensitivity	LR+	LR-
AJCC	99.52	0.48	2.70	69.12	71.81	2.33	0.41
BWH	99.51	0.49	2.60	63.61	76.06	2.10	0.38

Negative predictive value (NPV), Positive predictive value (PPV), Likelihood ratio (LR)

Table 1 *Performance metrics based on the confusion matrix.*

Conclusion

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

- Potentially forgo intensive follow-up regimens in two-thirds of the low-risk patients.
- More personalized decisions about follow-up schedules.
- Improvement in managing healthcare resources, which is very relevant for a cancer with such a high incidence.

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.