Soluble immune checkpoint proteins as predictive biomarkers for lymph node metastasis in penile cancer

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Abstract

Background: Penile cancer is a rare disease and its prognosis primarily depends on the presence of lymph node metastases (LNM). Unfortunately, no radiological methods is sensitive enough to detect occult LNM, currently no convincing predictive biomarkers are available. Immune checkpoint proteins are regulators of the immune system and play a significant role in tumor elimination. Previous studies have explored the predictive value of LNM for individual immune checkpoint proteins. However, limitations in the biomarkers analyzed restrict the ability to make accurate predictions. Therefore, identifying a sensitive, easily accessible panel of biomarkers to predict LNM in penile cancer is needed.

Objective: To evaluate the value of combining 14 soluble immune checkpoint proteins in predicting LNM in penile cancer patients.

Methods: Using multiplex Luminex assay, the circulating levels of 14 immune checkpoint proteins - BTLA, GITR, HVEM, IDO, LAG-3, PD-1, PD-L1, PD-L2, TIM-3, CD28, CD27, CD137, CD80 and CD152- were measured in plasma obtained from penile cancer patients. This study enrolled two independent cohorts: the exploratory cohort, including 205 patients, and the validation cohort, including 90 patients. To evaluate the value of a panel of checkpoint proteins in predicting LNM, a prediction model was created using logistic regression.

Results: PD-L1 was undetectable in 43% of the samples and was therefore excluded from the analyses. For the exploratory cohort, the prediction model showed an accuracy of 77.8 (95% CI: 71.2 - 83.5, p=0.23) and identified patients with LNM with a 12.8 % sensitivity and 99.3 % specificity. The positive predictive value (PPV) and negative predictive value (NPV) were 85.7 % and 77.5 %, respectively.

For the validation cohort, the model showed an accuracy of 63.4 (95% CI: 52.1 - 73.8, p=0.72) and identified patients with LNM with a 14.3 % sensitivity and 88.9 % specificity. The PPV and NPV were 40.0 % and 66.7 %, respectively.

The panel showed an area-under-the-curve of 0.68 (95% CI: 0.59 - 0.77) for the exploratory cohort and 0.51 (95% CI: 0.37 - 0.64) for the validation cohort.

Conclusion: Our study provides no evidence that soluble immune checkpoint proteins serve as predictive biomarkers for LNM in penile cancer.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.