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The number of tumor cells spread to sentinel lymph nodes affects melanoma prognosis

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Cancer cell spread to the sentinel node—the lymph node to which cancer cells are most likely to spread from a primary tumor—is a risk factor for melanoma death. According to a study published in this week's *PLOS Medicine* by Anja Ulmer, Christoph Klein and colleagues from the Universities of Tübingen and Regensburg, Germany, the prognosis of a patient largely depends on the number of disseminated cancer cells per million lymphocytes in the sentinel node. Even very low numbers were found to be predictive for reduced survival.

The leading cause of death from skin disease is melanoma, which is the most dangerous type of skin cancer. When melanoma metastasizes and spreads to other parts of the body, treatment options become limited and the prognosis is poor. Melanoma staging (and prognosis) is currently focused on the primary tumor itself, with characteristics like tumor thickness, mitotic rate, and ulceration (break in the skin caused by the tumor) indicating the likelihood that the tumor has started to spread. Looking for tumor cells in the sentinel nodes is done for patients who are at increased risk for spread, but standard procedures for how to measure spread to the nodes and how to integrate this information with the tumor histology are needed. Since melanoma is one of the deadliest cancers, better predictors of prognosis for melanoma patients are needed for patient information and to determine treatment options.

The researchers prospectively collected a large number of samples for this relatively rare cancer: 1,834 sentinel lymph nodes from 1,027 patients with melanoma who had been followed for 5 years after the

samples were taken. They labelled disseminated cancer cells (DCCs) in the lymph nodes through the use of a marker for melanoma cells, counted them, and calculated DCC density. They then asked whether DCC density was related to a patient's survival. They found that patients with high DCC density in the lymph nodes were more likely to die from melanoma within 5 years. A 10-fold increase in DCC density nearly doubled the risk of death. The authors then created a model based on tumor thickness, tumor ulceration, and lymph-node DCC density that provided survival prediction superior to that of a model based on the current standard staging recommendations. The researchers show that their new model predicts patients' prognosis more accurately. It classified 13% of patients in this cohort correctly as high risk for progression, which the standard model did not. This group of patients could potentially have benefitted from more aggressive treatments. The new model also correctly identified a group of low risk patients who had excellent long-term outcomes, whereas the standard model overestimated their risk of death.

These results need to be validated in an independent study, however, in order to establish how this methodology could be used in a clinical setting.

The authors say: "Our study shows that the extent of metastatic dissemination largely determines the disease courses of patients. The better we are able to predict the risk of patients to die from melanoma the better can we balance cost and benefit of potentially toxic therapies. For early melanoma, this might become even more important as novel drugs to prevent lethal metastasis are currently under investigation.

More information: Ulmer A, Dietz K, Hodak I, Polzer B, Scheitler S, et al. (2014) Quantitative Measurement of Melanoma Spread in Sentinel Lymph Nodes and Survival. PLoS Med 11(2): e1001604. DOI: 10.1371/journal.pmed.1001604