

## Comment on “Prognostic value of sentinel lymph node biopsy according to Breslow thickness for cutaneous melanoma”



*To the Editor:* Stiegel et al recently reported a single-institution, retrospective cohort study of cutaneous melanoma patients who underwent sentinel lymph node (SLN) biopsy.<sup>1</sup> Their stated objective was “to measure how much, if any, further prognostic information is gained by determining SLN status than that which is known from Breslow thickness (BT).” To address this question, they ran Cox regression analyses for overall survival, including BT and SLN status as dependent variables. Reporting a *P* value of .067 for SLN status, they concluded “SLN status could not improve the prognostic ability of the model compared with that provided by BT alone.” In our view, this conclusion is not supported for several reasons.

First, the analyses performed did not measure the additional prognostic information provided by SLN status over and above that provided by BT. The authors inappropriately used a multivariate analysis that investigated the independent association between SLN status and overall survival while adjusting for BT. More appropriate statistical methods that quantify the improvement offered by additional covariates, including C-statistic or net reclassification improvement, should have been applied.<sup>2</sup>

Second, arguing that a negative SLN did not confer a statistically significant survival advantage for any BT subgroup solely on the basis of a *P* value > .05 is misleading. It cannot be concluded from a *P* value of .067 in a retrospective study that was probably underpowered that there was no association or no evidence of an effect.<sup>3</sup>

Third, the authors claimed the study was powered appropriately to directly compare overall survival for SLN status by BT. However, no information was provided about the power calculation or the level of power. Post-hoc determination of power has been widely criticized in the statistical literature on the basis that power provides no valid information beyond that provided by *P* values and confidence limits.<sup>4</sup> In fact, the very wide confidence intervals that were reported in the study indicate a lack of power in the subgroup analyses.

Fourth, overall survival was used to assess the therapeutic benefit of SLN status. Disease-specific survival would have been a more appropriate

outcome in a situation where patients can have relatively long survival and many die from other causes. Furthermore, given that this was an observational study, a more rigorous analysis accounting for other known confounding variables (eg, ulceration, age) was required.

Fifth, the quality of the data is concerning. The fact that 34.3% of the biopsy specimens were transected at the base means that BT measurements in these specimens were inevitably unreliable, with probable underestimation of the true thickness of the tumors and inclusion in the 0.01-1 mm thickness group of many thicker tumors that were misclassified.

For all of these reasons, the claim that for a melanoma of given BT, knowledge of SLN status does not improve prognostic accuracy is not justified, nor is the claim consistent with data from a large, prospective, multicentre randomized controlled trial, the first Multicenter Selective Lymphadenectomy Trial, which demonstrated the important prognostic information provided by knowledge of SLN status for melanomas in all BT categories.<sup>5</sup>

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