
Authors
Andrew D. Zelenetz, Elaine S. Jaffe, Ranjana H. Advani, Nancy Lee Harris, Richard T. Hoppe, Michael P. Link, Steven T. Rosen, John P. Leonard

Emerging Prognostic Factors for Clinical Care
Reed-Sternberg cells represent the minority of cells in a node involved by HL. The tumor microenvironment is composed of a mixed inflammatory infiltrate. There have been several reports that the extent of infiltration of macrophages as measured by CD68 is associated with an adverse outcome. However, the cutoffs defining CD68 positivity vary among studies. This assay must be standardized before it can be routinely used in clinical practice.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Definition</th>
<th>Clinical significance</th>
<th>Level of evidence</th>
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<tr>
<td>CD68 infiltration</td>
<td>IHC for CD68 as a surrogate for macrophage infiltration, cutoff for CD68 expression differ by study</td>
<td>Most studies suggest poor prognosis if extensive macrophage infiltration, cutoffs not established</td>
<td>III</td>
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Risk Assessment Models
Risk assessment models and prognostic tools play an important role in cancer medicine because they provide a mechanism to integrate disparate data elements into a process that leads to decreased prognostic heterogeneity. Such processes are useful for (1) identifying and characterizing important prognostic factors, (2) improving prognostic predictions for individual patients, and (3) designing, conducting, and analyzing clinical trials. The most common type of prognostic tool is a prognostic calculator that provides time-specific outcome (e.g., 5-year OS) probability predictions for individual patients based on their demographic, clinical, and tumor characteristics. The prognostic nomogram developed by Yang et al is an example of a risk calculator. Another type of prognostic tool is a prognostic classifier that places patients into ordered prognostic risk classes (either directly or based on cutoffs for individual probability estimates). The remaining tools referenced in this chapter (e.g., IPI, MIPI, FLIPI, and CLL-IPI) are prognostic classifiers. The AJCC Precision Medicine Core (PMC) developed and published criteria for critical evaluation of prognostic calculators, which are presented and discussed in Chapter 4. The prognostic nomogram developed by Yang et al meets all but one of the AJCC PMC criteria because it lacks discussion of how missing data were treated.

Recommendations for Clinical Trial Stratification
The authors have not provided any recommendations for clinical trial stratification at this time.

Bibliography