The International Prognostic Index in aggressive B-cell lymphoma

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TITLE	A predictive model for aggressive non-Hodgkin's lymphoma.
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Prognostication and risk assessment are standard components of a clinical workup for a patient with a newly diagnosed hematologic malignancy. The information given by a prognostic tool provides guidance for treatment selection, helps to define clinical trial eligibility, and is useful for patient counseling. The development of an accurate measure of prognosis that can be broadly applied in a disease setting is a deceptively difficult endeavor. It requires assembly of a dataset that has a sufficiently large number of entries for statistical modeling, is representative of patients with the disease, and has adequate follow-up to assess clinically relevant outcomes. Furthermore, information in models may become clinically obsolete as new therapies are developed and/or the natural history of the disease evolves.

The International Prognostic Index (IPI)[1] was published in 1993 and has been a clinically relevant prognostic tool in aggressive B-cell lymphoma for 30 years. The fact that we are still using the model to define patient populations in this disease in 2023 is frankly remarkable. The patients used to develop the model received combination chemotherapy containing anthracycline on clinical trials between 1982 and 1987. In the mid 1980s, pathology subtypes were based on International Working Formulation, Kiel or Rappaport classifications, CD20 was a relatively recently discovered protein, and rituximab was still a decade away from being available for these patients. The computational tools available for modeling at the time the IPI was developed were also greatly limited compared to the smartphone/point-of-care apps, modern data visualization, and advanced modeling and data science techniques available to clinicians and researchers today. However, the product-of-its-time simplicity of the IPI model has made it appealing and approachable for clinicians. A score of five dichotomous variables (age, stage, lactate dehydrogenase, Eastern Cooperative Oncology Group Performance Status, and number of involved extranodal sites) (Table 1), while inefficient from a statistical approach, can easily be computed in real-time without the need for electronic tools or reference charts. The variables in the model are part of standard workups and can be applied in most clinical settings. Efforts to modify the IPI have made marginal improvements in the prognostication of aggressive B-cell lymphoma and the IPI retains a strong prognostic capability in the rituximab era (Figure 1).[2] As the classification and management of aggressive B-cell lymphoma continues to evolve and increase in complexity, a simple five-variable model built from patients treated in the 1980s remains the standard for patient prognostication and determination of clinical trial eligibility in 2023.

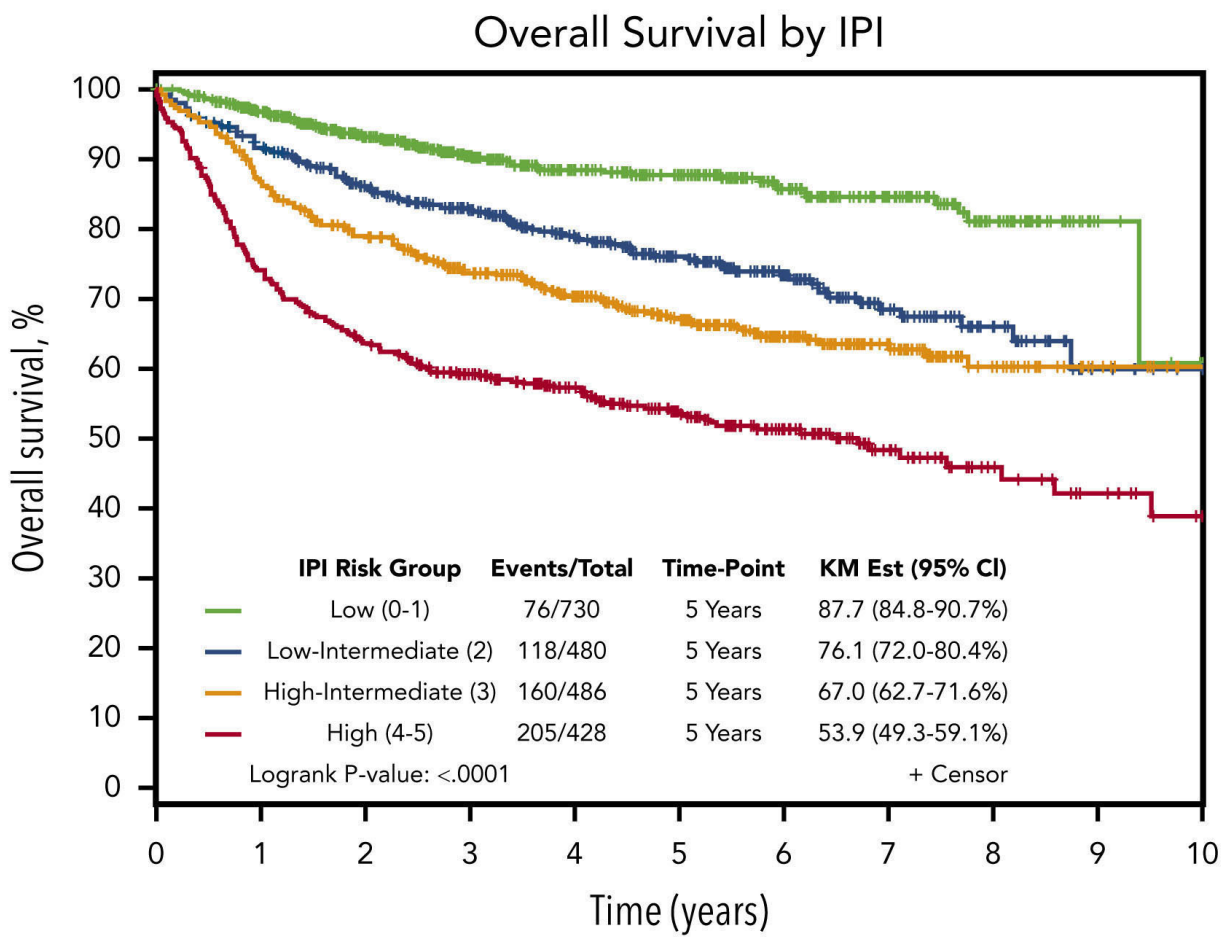
Table 1. Variables used to calculate the International Prognostic Index score.

Category	Number of points
Age >60 years	+1
Stage III/IV	+1
ECOG Performance Status ≥2	+1
LDH >upper limit of normal	+1
≥2 Extranodal sites	+1
IPI score	Sum of Points

ECOG: Eastern Cooperative Oncology Group; LDH: lactate dehydrogenase; IPI: International Prognostic Index.

Disclosure

No conflicts of interest to disclose.



Patients-at-Risk

Low (0-1)	730	650	493	344	267	227	159	102	46	6	1
Low-Intermediate (2)	480	431	370	315	260	194	133	69	36	9	4
High-Intermediate (3)	486	418	368	315	260	201	135	83	38	19	9
High (4-5)	428	315	268	227	184	136	92	50	27	18	9

Figure 1. Prognostic discrimination of the International Prognostic Index score with regard to overall survival. Figure modified with permission, from Ruppert *et al.*[2] IPI: International Prognostic Index; KM est: estimated Kaplan-Meier; 95% CI: 95% confidence interval.

References

1. International Non-Hodgkin's Lymphoma Prognostic Factors Project. A predictive model for aggressive non-Hodgkin's lymphoma. N Engl J Med. 1993;329(14):987-994.
2. Ruppert AS, Dixon JG, Salles G, et al. International prognostic indices in diffuse large B-cell lymphoma: a comparison of IPI, R-IPI, and NCCN-IPI. Blood. 2020;135(23):2041-2048.