Online Calculators: Prognosis for Non-Hodgkin and Hodgkin Lymphoma

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Lymphomas are a heterogenous group of lymphoid malignancies with varied patterns of clinical behavior, response to treatment, and prognosis (National Comprehensive Cancer Network [NCCN], 2010). A main goal of therapy is to achieve the best possible response with minimum toxicity. Identifying patients as having low-, intermediate-, or high-risk disease enables clinicians to discuss prognosis and possible treatment options. For example, in certain situations, patients with low-risk disease may be able to defer therapy while patients with high-risk disease may require aggressive or investigational therapy.

There are prognostic indices for Hodgkin lymphoma and several subtypes of non-Hodgkin lymphoma—including diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), and mantle cell lymphoma (MCL)—that assign relative risk based on probability of long-term survival. These prognostic indices are available as online calculators at http://www.qxmd.com/calculate-online/hematology. The site is free and the calculators can be downloaded as free applications for the Android, Blackberry, iPad, or iPhone.

Follicular Lymphoma

Follicular lymphoma is the second most common subtype of non-Hodgkin lymphoma seen in adults. Most follicular lymphomas are indolent, so although the disease is generally considered to be incurable, it is associated with a median survival of over 10 years. Patients with low-risk disease who are asymptomatic may maintain a good quality of life without any treatment. Patients with higher-risk disease may benefit from initial therapy with chemotherapy and rituximab (Rituxan).

The Follicular Lymphoma International Prognostic Index (FLIPI) was developed to assess risk and assist with the choice of therapy to avoid toxicity and preserve quality of life (Solal-Céligny et al., 2004). The data were derived from univariate and multivariate analyses of characteristics of 4,167 patients with FL diagnosed between 1985 and 1992. This index was then tested on 919 patients. Five adverse prognostic factors were selected: age (> 60 vs. ≤ 60 years), Ann Arbor stage (III/IV vs. I/II), hemoglobin level (< 12.0 vs. ≥ 12.0 g/dL), number of nodal areas (> 4 vs. ≤ 4), and serum lactate dehydrogenase (LDH) level (above normal vs. normal or below). The mnemonic NoLASH may be useful to remember the factors: number of Nodal areas, LDH, Age, Stage, and Hemoglobin level.

Three risk groups were defined: low risk (0 or 1 adverse factor, 36% of patients), intermediate risk (2 factors, 37% of patients), and poor risk (≥ 3 adverse factors, 27% of patients). Overall survival at 10 years is estimated to be 71% for low-risk patients, 51% for intermediate-risk patients, and 35% for high-risk patients.

Diffuse Large B-Cell Lymphoma

Diffuse large B-cell lymphoma is the most common subtype of non-Hodgkin lymphoma in adults. Diffuse large B-cell lymphoma is an aggressive lymphoma that is potentially curable with intensive combination chemotherapy and rituximab. The original International Prognostic Index (IPI; The International Non-Hodgkin's Lymphoma Prognostic Factors Project, 1993) derived data from 2,031 patients with DLBCL who were treated with a combination chemotherapy regimen containing doxorubicin between 1982 and 1987.

Five adverse prognostic factors were selected: age (> 60 vs. ≤ 60 years), Eastern Cooperative Oncology Group performance status[1] (0–2 vs. 3–4), serum LDH level (above normal vs. normal or below), extranodal sites (0 or 1 vs. ≥ 2), and Ann

[1]Eastern Cooperative Oncology Group scale: 0 = patient has no symptoms, 1 = patient has symptoms but is ambulatory, 2 = patient is bedridden less than half the day, 3 = patient is bedridden half the day or longer, 4 = patient is chronically bedridden and requires assistance with the activities of daily living.

Arbor stage (III/IV vs. I/II). The mnemonic APLES may be useful to remember the factors: Age, Performance status, LDH, Extranodal sites, and Stage.

Four risk groups were identified: low risk (0 or 1 factor, 35% of patients), low-intermediate risk (2 factors, 27% of patients), high-intermediate risk (3 factors, 22% of patients), and high risk (4 or 5 factors, 16% of patients). The 5-year overall survival rate was estimated to be 71% for low-risk patients, 51% for low-intermediate–risk patients, 43% for high-intermediate–risk patients, and 26% for high-risk patients.

The original IPI was derived from data gathered during the prerituximab era. It is now standard of care to treat DLBCL with rituximab in addition to anthracycline-based chemotherapy as clinical trials have confirmed that rituximab improves the survival of individuals with diffuse large B-cell lymphoma. The revised IPI (R-IPI) was developed to predict the outcome of individuals receiving rituximab with chemotherapy (Sehn et al., 2007). The data were derived from 345 patients treated with R-CHOP (cyclophosphamide, doxorubicin HCl, vincristine [Oncovin], and prednisone plus rituximab) chemotherapy in British Columbia. The prognostic factors were applied to these patients according to the original IPI factors to determine overall survival in patients treated with R-CHOP. The risk categories were modified into three groups: very good risk (0 factors, 10% of patients), good risk (1 or 2 factors, 45% of patients), and poor risk (3 to 5 factors, 45% of patients). The 4-year overall survival rate was 94% for very-good-risk disease, 79% for good-risk disease, and 55% for poor-risk disease.

The QxMD calculator uses the R-IPI.

Mantle Cell Lymphoma

Mantle cell lymphoma is a rare non-Hodgkin lymphoma that accounts for 6% of all non-Hodgkin lymphomas in adults. The disease may have an indolent or aggressive course and is generally considered incurable despite intensive treatment with rituximab and chemotherapy.

The Mantle Cell Lymphoma International Prognostic Index (MIPI) was derived from a data set of 455 advanced-stage MCL patients treated within three clinical trials in Europe (Hoster et al., 2008). Initial cytoreductive chemotherapy comprised CHOP in 56% of the patients, R-CHOP in 31% of the patients, MCP (mitoxantrone, chlorambucil, and prednisone) in 11%, and other chemotherapy regimens in 2%. Of the 438 patients evaluable for treatment response, 351 (80%) achieved a complete or partial remission, and 80 (18%) achieved a complete remission. Treatment in remission was autologous stem cell transplant for 80 patients, interferon-alfa maintenance for 199 patients, and no therapy for 72 patients in remission.

Five prognostic factors were identified: age, performance status, LDH, leukocyte count, and cell proliferation (Ki-67). The first four prognostic factors were included in the MIPI. When the Ki-67 is available, a biologic MIPI (MIPIb) can be calculated.

The MIPI stratifies patients into three risk groups: low risk (44% of patients, median survival not reached after median 32 months follow-up and 5-year overall survival rate of 60%), intermediate risk (35% of patients, median survival 51 months), and high risk (21% of patients, median survival 29 months).

Hodgkin Lymphoma (Hodgkin Disease)

The Hasenclever International Prognostic Score (Hasenclever et al., 1998) was designed to predict 5-year freedom from progression of disease. With each additional adverse prognostic factor, the predicted rate of freedom of progression is reduced by approximately 8%. The score was developed and validated based on a set of patients treated in the 1980s with regimens including ABVD (doxorubicin [Adriamycin], bleomycin, vinblastine, and dacarbazine), MOPP (mustargen, vincristine, procarbazine, and prednisone), and similar hybrid regimens.

Seven adverse prognostic factors were identified: serum albumin level < 4 g/dL, hemoglobin level < 10.5 g/dL, male sex, age ≥ 45 years, Ann Arbor stage IV disease, leukocyte count ≥ 15,000/μL, and lymphocyte count < 600/ μL or < 8% of the white cell count, or both. The rate of freedom from progression of disease was stratified into five groups: 0 factors (7% of the patients), 84% FFP rate; 1 factor (22% of the patients), 77% FFP rate; 2 factors (29% of the patients), 67% FFP rate; 3 factors (23% of the patients), 60% FFP rate; 4 factors (12% of the patients), 51%; and 5 or more factors (7% of the patients), 42% FFP rate.

Conclusions

The evidence-based prognostic calculators available for follicular, diffuse large B-cell, mantle cell, and Hodgkin lymphomas can guide clinicians in predicting the probability of their patients' overall survival. Prognostic calculators can also be helpful when counseling patients about treatment options, for example, to minimize the intensity of treatment for patients with low-risk disease and ensure adequate treatment for patients with high-risk disease. Online prognostic calculators are convenient tools that allow advanced practice clinicians to easily access these clinical prediction models.

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