

Prognostic Markers in Waldenström Macroglobulinemia (WM)

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The Cox proportional hazard (PH) model is widely used for summarizing with a limited number of covariates the prognostic information required for the description of the outcome of patients. A large number of studies pointed out the very different survival of WM patients with symptomatic and asymptomatic disease. Median survival of the former subgroup of patients has been estimated approximately 5 to 10 years whereas it was not different from that of the general population in the latter subgroup. For this reason, we used the PH model in a large series of patients with symptomatic WM diagnosed between September 1979 and December 2001 and treated mainly by single alkylating agent (369 patients) or fludarabine (195 patients). Using the combination of age >65 years, hemoglobin ≤ 11.5 g/dL, platelet count $\leq 100 \times 10^9/L$, κ -2 microglobulin >3 mg/L, and M-protein >7.0 g/dL, low risk was defined by the presence of ≤ 1 adverse characteristic except age, high risk by the presence of >2 adverse characteristics and the remaining patients with 2 adverse characteristics or age >65yr had intermediate risk, with 5-year survival rates of 87%, 36% and 68% respectively. The prognostic system was effective in patients treated with alkylating agent or fludarabine. Few months later the system has been validated in patients who received rituximab alone or in combination with dexamethasone and cyclophosphamide, as first line therapy. This system was also effective for identifying a high-risk subgroup of patients in advanced phase, after a combination therapy including fludarabine.

Although this system appears useful for describing the outcome of WM patients treated with single agent chemotherapy, additional studies are required to assess the impact of new therapeutic agents on this system, to identify an optimal prognostic system for patients in advanced phase or with progressive disease and to evaluate the potential usefulness of additional covariates, such as CRP or LDH or new biological characteristics for improving the accuracy of the model for the prediction of the outcome of patients.