

ANALYSIS OF 452 PATIENTS WITH ASYMPTOMATIC IgM MONOCLONAL GAMMOPATHY: A PROGNOSTIC INDEX TO PREDICT EVOLUTION TO SYMPTOMATIC WALDENSTRÖM MACROGLOBULINEMIA. E. Morra¹, C. Cesana¹, C. Klersy², M. Varettoni³, L. Cavanna⁴, B. Canesi⁵, E. Tresoldi¹, L. Barbarano¹, M. Lazzarino³; ¹Hematology and ⁵Rheumatology, Niguarda Hospital, Milan; ²Scientific Direction and ³Hematology, IRCCS Policlinico S. Matteo University of Pavia; ⁴Hematology and Oncology, Ospedale Civile, Piacenza, on behalf of the Hematology/Oncology Studies and Trials (HOST) Group, Italy.

Criteria to identify asymptomatic IgM monoclonal gammopathies (MG) with the highest likelihood of progression to symptomatic Waldenström Macroglobulinemia (WM) are largely undetermined. To assess whether simple parameters detected at diagnosis may predict the risk of evolution, we analyzed 452 patients (253 males, 199 females) with asymptomatic IgM MG diagnosed from 1975 to 2001 (median follow-up 49 months, range 12-233). Cumulative probability of survival was calculated by means of the Kaplan-Meier estimator. Univariate and multivariate Cox models were used to identify possible predictors of transformation. Median age was 66 years (23-91). Median IgM monoclonal component (MC) level was 800 mg/dL (100-4,480). Median bone marrow (BM) lymphoplasmacytoid (LP) infiltration was 6% (0-90%). Forty-one cases (9.1%) evolved to symptomatic WM (n=36) or other malignant lymphoproliferative disorders (n=5), the median interval from diagnosis being 53 months (12-154). At univariate analysis, variables associated with the probability of evolution were: IgM MC level, Hb level, peripheral blood lymphocytosis ($>4 \times 10^9/L$), degree of BM LP involvement ($>10\%$), ESR (≥ 40 mm/h) and detectable Bence Jones proteinuria. At multivariate analysis, IgM MC, Hb and lymphocytosis proved to be independent factors predicting evolution ($p < 0.0001$). Assuming a label (x) for each variable ($x_1 = \text{MC level in mg/dL}$, $x_2 = \text{Hb in g/dL}$, $x_3 = 1$ if lymphocytes $> 4 \times 10^9/L$, and $x_3 = 0$ if lymphocytes $\leq 4 \times 10^9/L$), a prognostic index ($\text{PI} = 0.0009x_1 - 0.2278x_2 + 2.299x_3$) was calculated for each patient. Three risk groups were identified on the basis of PI distribution tertiles. The highest evolution risk was identified by the third tertile ($\text{PI} > -1.92$). All the patients with $\text{MC} > 3,000$ mg/dL and with lymphocytes $> 4 \times 10^9/L$, and the majority of patients with $\text{Hb} < 12$ g/dL entered this prognostic subgroup, characterized by event-free survival rates at 5 and 10 yrs of 76% (95%CI, 68-87%) and 59% (95%CI, 40-75%), respectively. Patients with asymptomatic IgM MG showing these hematological features at diagnosis need careful clinical monitoring in view of an early treatment of the disease.