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Progression risk-based classification of Asymptomatic Waldenström Macroglobulinemia: a large single-center study.

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Purpose. Waldenström macroglobulinemia (WM) is a non-Hodgkin's lymphoplasmacytic lymphoma characterized by over production of monoclonal IgM protein. It hasn't been clear how to distinguish the asymptomatic patients who will progress from those who will not. The existing classification was based on rather small studies. A new risk stratification is needed, yet the rarity of the disease and the ensuing sparsity of data represent a practical challenge.

Patients and Methods. We obtained clinical data of all WM patients who had been diagnosed and followed up at Dana-Farber Cancer Institute from 1982 to the end of 2014. Only patients with asymptomatic WM at the time of diagnosis were included in this study to determine the risk factors of disease progression. Patients with asymptomatic disease who were diagnosed with other malignancies before or after diagnosis with WM, had potential chemotherapy-related effects on disease course, or progressed to other types of lymphoproliferative disorders or Amyloidosis were excluded.

Results. A total of 439 patients were included in the study. During the 35-year study period, 317 patients had progressed to symptomatic WM. The median time to progression was 3.9 (95% CI 3.2–4.6) years. In the multivariate model, IgM ≥ 5,000 mg/dL (adjusted HR 3.97;

95% CI 1.94–8.12; $p < 0.001$), BM involvement percentage ≥ 70% (adjusted HR 2.66; 95% CI 1.76–4.03; $p < 0.001$), β2-microglobulin ≥ 4.0 mg/dL (adjusted HR 2.15; 95% CI 1.11–4.16; $p = 0.024$), and albumin < 3.5 g/dL (adjusted HR 2.94; 95% CI 1.60–5.41; $p = 0.001$) were independent predictors of disease progression. A scoring system was built by incorporating these discrete values and divided the patients into low-risk (scores 0–1) and high-risk (scores 2–3) groups **(Figure 1)**. The 2-year cumulative rate of progression was 71.4% (95% CI 51.8%–88.35%) for the high-risk group and 25.8% (95% CI 19.7%–33.2%) for the low-risk group (HR 5.22; 95% CI 3.10–8.80; $p < 0.001$). We also built a proportional hazards model of the same four variables that divided the cohort into 3 risk groups with a median time to progression (TTP) of 1.8 years (95% CI 1.64–2.13), 4.6 years (95% CI 4.31–5.15), 8.12 years (95% CI 7.33–8.13), respectively.

Conclusion. We have assembled the largest cohort of asymptomatic WM patients to date, and we thus have developed a robust classification that could improve patient monitoring and care. This risk stratification system can help in defining patients with high risk features and thus improve the management of asymptomatic WM patients.

Figure 1. Cumulative probability of disease progression among patients with different risk scores