

IgM Monoclonal Gammopathy of Undetermined Significance (MGUS) and Smoldering Waldenstrom's Macroglobulinemia (SWM)

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Monoclonal gammopathy of undetermined significance (MGUS) was diagnosed in 213 Mayo Clinic patients who were residents of 11 counties in Southeastern Minnesota from 1960 to 1994. During long-term followup 29 (14%) developed non-Hodgkin's lymphoma (n = 17), Waldenstrom's macroglobulinemia (n = 6), chronic lymphocytic leukemia (n = 3), and AL amyloidosis (n = 3) with relative risks of 15-, 262-, 6- and 16-fold respectively. The cumulative probability of progression to one of these disorders was 10% at 5 years, 18% at 10 years, and 24% at 15 years – approximately 1.5% per year. Risk for progression at 10 years after the diagnosis of MGUS was 14% with an initial monoclonal protein concentration of 0.5 g/dL or less, 26% with 1.5 g/dL, 34% for 2.0 g/dL and 41% for more than 2.5 g/dL. The concentration of serum monoclonal protein at diagnosis and the initial serum albumin value were the only independent predictors of progression with multivariate analysis.

Smoldering Waldenstrom's macroglobulinemia was defined as a serum monoclonal protein ≥ 3 g/dL and/or $\geq 10\%$ bone marrow lymphoplasmacytic infiltration but no evidence of end-organ damage such as symptomatic anemia, constitutional symptoms, hyperviscosity, symptomatic lymphadenopathy or hepatosplenomegaly that can be attributed to a lympho-plasma cell proliferative disorder. Forty-eight patients with SWM were identified at Mayo Clinic from 1974 to 1995. During 285 cumulative person-years of follow-up (median 15.4 years) 34 (71%) progressed to Waldenstrom's macroglobulinemia (WM), 1 to AL amyloidosis and 1 to lymphoma (total 36, 75%). On the basis of the SEER data, one would expect 0.004 cases of WM; thus the relative risk of progression was increased 8,034 fold. The median time of progression to WM was 4.6 years. The cumulative probability of progressing to SWM, amyloidosis or lymphoma was 6% at 1 year, 39% at 3 years and 59% at 5 years (12% per year). On multivariate analysis, the size of the serum M protein spike, hemoglobin value and number of lymphoplasmacytic cells in the bone marrow at diagnosis were significant independent risk factors for progression. The median survival after progression to symptomatic WM was 5.1 years.