

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) requiring therapy, 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 progression to symptomatic WM requiring therapy, amyloidosis or lymphoma was 6% at 1 year, 39% at 3 years, 59% at 5 years, and 68% at 10 years (Figure 1). The cumulative probability of progression was 12% per year for the first 5 years and then 2% per year for the next 5 years for the entire group. On multivariate analysis, the percentage of lymphoplasmacytic cells in the bone marrow, size of the serum M spike and hemoglobin value were significant independent risk factors for progression. The overall survival for the 48 SWM patients was 83% at 5 years and 50% at 9.6 years (Figure 2). The median survival after progressing to symptomatic WM was 5.1 years (Figure 3).

1. Kyle RA, Therneau TM, Rajkumar SV, et al. Long-term follow-up of IgM monoclonal gammopathy of undetermined significance. *Blood*. 2003;102(10):3759-3764.
2. Kyle RA, Benson JT, Larson DR, et al. Progression in smoldering Waldenstrom macroglobulinemia: long-term results. *Blood*. 2012;119(19):4462-4466. Prepublished on 2012/03/28 as DOI 10.1182/blood-2011-10-384768.

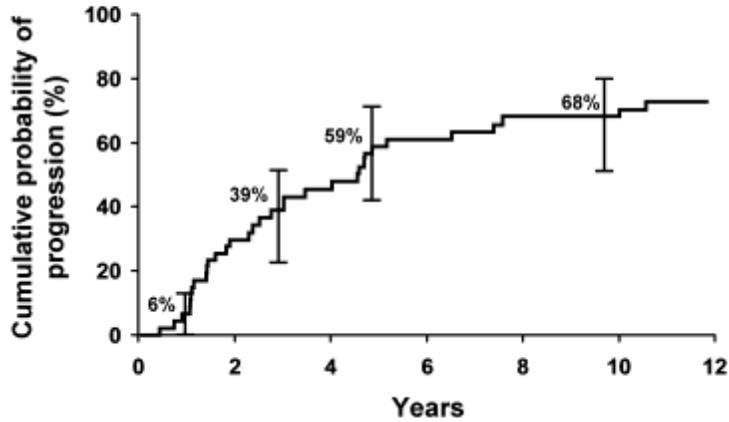


Figure 1: Cumulative probability of progression to symptomatic WM requiring therapy, amyloidosis, or lymphoma in the cohort of 48 patients with SWM.

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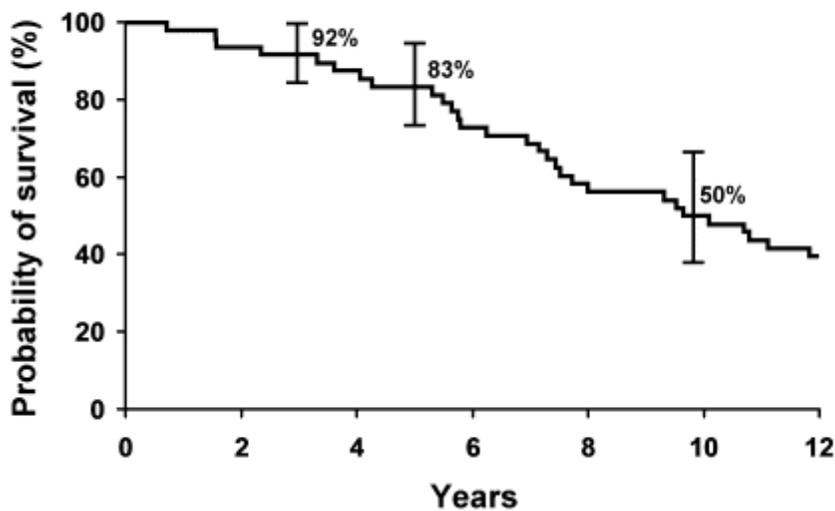


Figure 2: Probability of survival of SWM in 48 patients.

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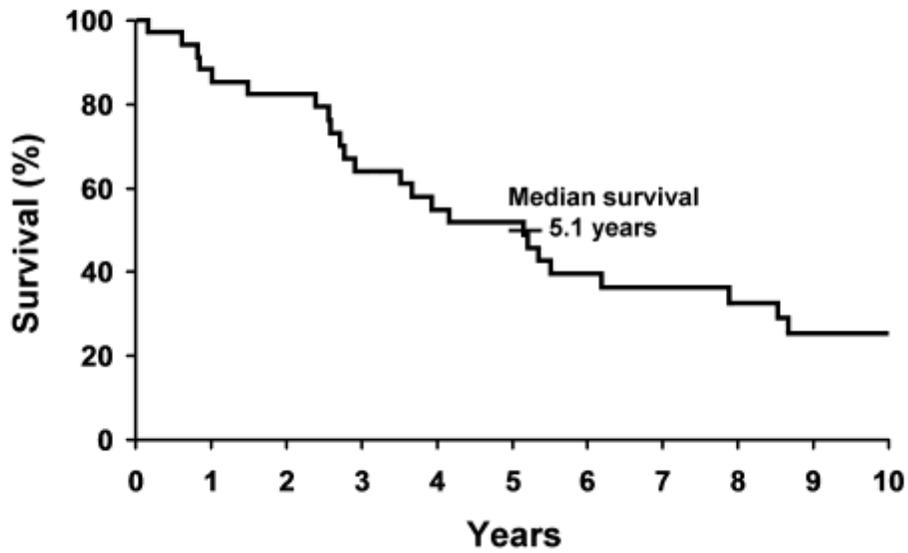


Figure 3: Probability of survival in 34 patients with SWM.

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