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Diagnosis of Smoldering Multiple Myeloma

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To the Editor

In 2007, we reported in the *Journal* the diagnosis, natural history, and progression of smoldering multiple myeloma (SMM).¹ Consistent with the accepted definition of this disease,² patients with bone marrow containing 10% or more plasma cells and no evidence of end-organ damage attributable to the plasma-cell disorder were considered to have SMM; however, no upper limit of bone marrow involvement was defined. Since then, major advances in the field have led to evolving definitions of SMM, along with changes in therapy.³ Accordingly, the natural history described in our paper may not apply to patients with marked bone marrow infiltration. In order to define an upper limit of bone marrow involvement for SMM, we reassessed the cohort described in our original publication and found that only 6 of 276 patients (2%) had bone marrow containing 60% or more plasma cells. Furthermore, 4 of these 6 patients progressed to symptomatic myeloma 3 to 9 months after the diagnosis of SMM, and 1 of these patients died 13.5 months after the diagnosis, with no information available about whether or not the disease had progressed. In the 1 remaining patient, SMM progressed to myeloma 50 months after the diagnosis, which resulted in death within 2 years of that date. The median progression-free survival of these 6 patients was 7.7 months (95% confidence interval [CI], 0.4 to 14.9); 83% had progression or died by 14 months after the diagnosis.

We then studied all patients diagnosed with SMM at the Mayo Clinic from January 1996 through June 2010. This group comprised 655 patients who underwent a baseline bone marrow evaluation at the time of diagnosis; in 21 of these patients (3.2%), the percentage of bone marrow plasma cells was at least 60%. The median time to progression to symptomatic myeloma was significantly shorter among the patients with 60% or more bone marrow involvement, as compared with those having less than 60% involvement ($P < 0.001$) (Fig. 1). Progression to myeloma occurred within 2 years of the diagnosis in 95% of the patients with 60% or more bone marrow plasma cells, with a median time to progression of 7 months (95% CI, 1.0 to 12.9). We conclude that the natural history of SMM is based almost exclusively on data from patients in whom the number of bone marrow plasma cells is less than 60%. In patients without end-organ damage at diagnosis but with 60% or greater bone marrow involvement, the clinical course is characterized by progression to symptomatic myeloma within 2 years. Such patients should be considered to have myeloma that requires therapy at the time of diagnosis.

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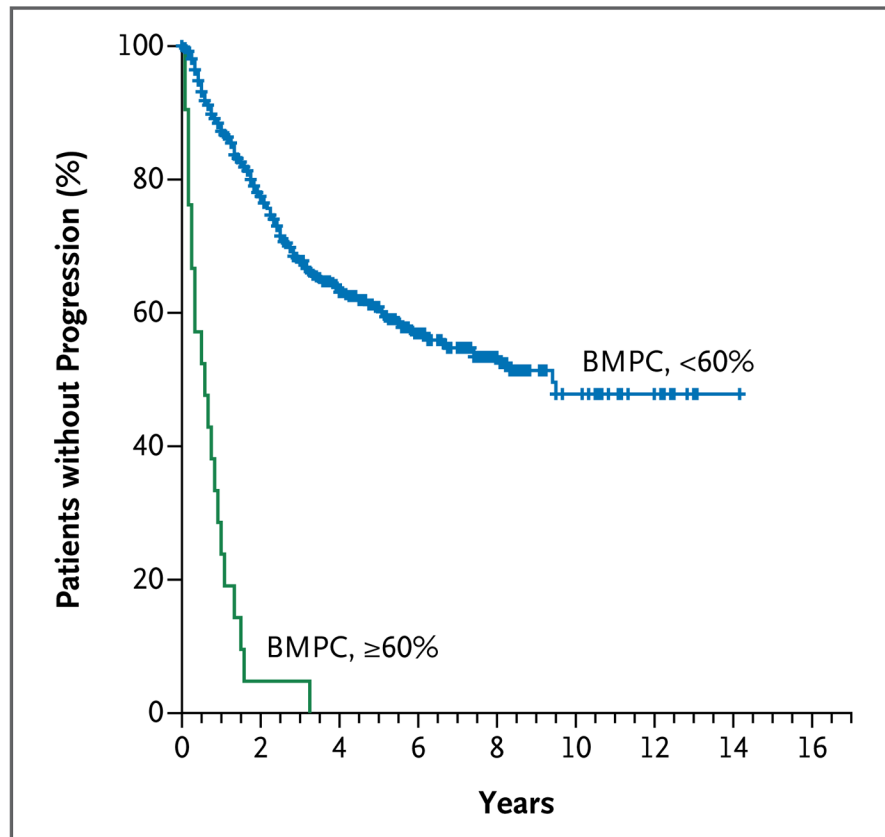


Figure 1. Time to Progression of Disease in Patients Diagnosed with Smoldering Multiple Myeloma, as Stratified According to the Percentage of Plasma Cells in the Bone Marrow (BMPC) at Baseline.