

Shorter biological marker length in aplastic anemia patients linked to higher relapse, death rates

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Among patients receiving immunosuppressive therapy for severe aplastic anemia (a condition in which the bone marrow is unable to produce blood cells), the length of telomeres (chromosome markers of biological aging) was not related to the response to treatment but was associated with a higher rate of relapse (return to low blood cell counts) and lower overall survival, according to a study in the September 22/29 issue of *JAMA*.

Severe aplastic anemia is characterized by life-threatening cytopenias (blood cell count below normal), but this condition can be treated by [bone marrow transplantation](#) or immunosuppressive drugs. In older patients, and when an appropriate matched sibling donor is not available, immunosuppression can be effective, although relapse and clonal evolution (the appearance of chromosome abnormalities in [bone marrow cells](#) that accompany hematologic malignancy) can occur in many patients, according to background information in the article. Recently, target cell abnormalities have been identified as risk factors in bone marrow failure. "Mutations in telomerase complex genes resulting in extremely short telomeres have been described in some patients with apparently acquired severe aplastic anemia," the authors write. Telomeres, a structure at the end of a chromosome that shortens with each cell division, function as protective caps to prevent erosion of genomic DNA during cell division. [Genetic factors](#) and environmental stressors can shorten the length of the telomere.

Phillip Scheinberg, M.D., of the National Institutes of Health, Bethesda, Md., and colleagues conducted a study to determine the effect of telomere attrition in acquired severe aplastic anemia by measuring telomere length prior to immunosuppressive therapy. The study included 183 patients with severe aplastic anemia who were treated from 2000 to 2008. The pretreatment leukocyte ([white blood cells](#) involved in defending the body against infectious disease) age-adjusted telomere length of patients with severe aplastic anemia enrolled in [immunosuppression](#) protocols was analyzed for correlation with clinical outcomes.

One hundred and four patients (57 percent) responded to immunosuppressive therapy. The researchers found that there was no correlation between telomere length (measured pretreatment) and the probability of response to the therapy. The response rate for patients in the first quartile (shortest telomere lengths) was 56.5 percent; in the second quartile, 54.3 percent; in the third quartile, 60 percent; and in the fourth quartile, 56.5 percent. Additional analysis demonstrated that telomere length was associated with relapse, clonal evolution, and mortality. Telomere length was inversely correlated with the probability of disease relapse. The probability of clonal evolution was higher in patients in the first quartile (24.5 percent) than in quartiles 2 through 4 (8.4 percent).

"Survival between these 2 groups differed, with 66 percent surviving 6 years in the first quartile compared with 83.8 percent in quartiles 2 through 4," the researchers write.

"In conclusion, our data show that in a cohort of patients with severe aplastic anemia receiving immunosuppressive therapy, [telomere](#) length was not associated with response but was associated with risk of relapse, clonal evolution, and overall survival."

More information: JAMA. 2010;304[12]:1358-1364.

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