

Size of biomarker associated with improved survival following transplantation

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Among patients with severe aplastic anemia who received stem cell transplant from an unrelated donor, longer leukocyte (white blood cells) telomere length (a structure at the end of a chromosome) was associated with increased overall survival at 5 years, according to a study in the February 10 issue of *JAMA*.

Telomeres protect chromosome ends and are essential for maintaining chromosomal stability. Telomere length is a biological marker for cellular aging and the capacity to replicate. Aplastic anemia is a blood disorder where the bone marrow fails to make new blood cells, with one of the causes potentially being defects in telomere biology. Allogeneic (genetically different) hematopoietic (blood marrow) cell transplantation (HCT) is recommended as initial therapy for young patients with acquired severe aplastic anemia when a matched sibling donor is available, according to information in the article.

Shahinaz M. Gadalla, M.D., Ph.D., of the National Cancer Institute, National Institutes of Health, Rockville, M.D. and colleagues evaluated the association between recipient and donor pretransplant leukocyte telomere length with outcomes after unrelated donor allogeneic HCT for 330 patients with severe aplastic anemia. The patients and their unrelated donors had pre-HCT blood samples and other clinical results available at the Center for International Blood and Marrow Transplant Research. Patients underwent HCT between 1989 and 2007 in 84 centers and were followed-up to March 2013. Leukocyte telomere length for both recipient and donor analyses was categorized based on the leukocyte

telomere length tertiles (one of three groups) in the donors: long (third tertile) and short (first and second tertiles combined).

The researchers found that longer donor leukocyte telomere length was associated with a higher overall survival (5-year overall survival was 56 percent vs 40 percent in the short donor leukocyte telomere length group). After adjusting for donor age and clinical factors associated with survival following HCT in severe aplastic anemia, the risk of post-HCT all-cause mortality remained approximately 40 percent lower in patients receiving HCT from donors with long vs short leukocyte telomere length. Similar patterns were observed by subtypes of the disease.

There was no association between donor leukocyte telomere length and engraftment or graft-vs-host disease (a complication of bone marrow transplantation). Recipient telomere length was not associated with patient overall survival.

"Among patients with severe aplastic anemia who received unrelated donor allogeneic HCT, longer donor leukocyte telomere length was associated with increased overall survival at 3 and 5 years," the authors write. "This observational study suggests that donor leukocyte telomere length may have a role in long-term post-transplant survival."

"If donor leukocyte telomere length is shown to be associated with survival in other hematopoietic [stem cell transplant](#) (HSCT) patient populations, can leukocyte telomere length become one of the factors used to choose the best available donor in matched unrelated donor HSCT (or other types of HSCT)," ask Ayman Saad, M.D., Shin Mineishi, M.D., and Racquel Innis-Shelton, M.D., of the Blood and Marrow Transplantation & Cell Therapy Program, Birmingham, Alabama, in an accompanying editorial.

"The test to determine leukocyte telomere length is widely available, but

it is left to each center to determine whether to use it and if so, which test to use. If the procedure is not well standardized, comparison between centers would be difficult or impossible. In addition, leukocyte telomere length may change with aging; thus, leukocyte telomere length results would need to be repeated each time confirmatory typing is performed on the same donor."

"Many questions and issues need to be resolved before leukocyte telomere length can be used as one of the factors to determine the best available donor. Nevertheless, the report by Gadalla et al opens up a new area of scientific investigation. Further studies are warranted to define and optimize the potential role of leukocyte [telomere length](#) in selecting donors and improving outcomes for [patients](#) with severe aplastic anemia who receive HSCT."

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