Do high-volume centers really save more lives? A call for scientific rigor and transparency. Comment on: "Does size matter? Center-specific characteristics and survival after allogeneic hematopoietic cell transplantation for acute myeloid leukemia: an analysis of the German Registry for Stem Cell Transplantation and Cell Therapy"

We read with great interest the article by Bethge and colleagues on the observed association between transplant center volume and outcomes after allogeneic stem cell transplantation for acute myeloid leukemia.[1] We would like to raise several comments and questions that we believe are essential to correctly interpret the presented data.

The authors repeatedly refer to an "effect" or a "prognostic impact" of transplant volume on outcome. However, the study is observational in nature, which implies at most a statistical correlation. Demonstrating a causal relationship would require a randomized study in which patients are assigned to different types of centers. What arguments or additional analyses do the authors propose to support the assumption of causality?

In addition, despite rigorous statistical modeling, subtle biases may persist due to differences between patients treated at university hospitals and those treated elsewhere. For example, is it possible that patients referred to non-university centers are, on average, less mobile or have less access to psychosocial support or informal caregiving networks? Such differences, though difficult to measure, could influence outcomes independently of center experience.

The manuscript explicitly states that there are no conflicts of interest. In the context of a pharmaceutical study, financial or other conflicts would rightly be expected to be disclosed. The authors note that similar data in Germany have already informed policy decisions. Transparency seems essential in this context: which authors are affiliated with high-volume or university centers? Are any authors involved with governmental agencies or health insurance institutions?

In clinical practice, patients are sometimes referred back to their original center relatively soon after stem cell infusion for further follow-up. How was this situation accounted for in the analysis? In other words, how do the authors differentiate between the potential effect of the transplanting center and that of the center responsible for post-transplant care?

A major source of inter-center heterogeneity lies in the assessment of performance status and comorbidity. Eastern Cooperative Oncology Group and Karnofsky scores remain subjective, and several items within the Hematopoietic Cell Transplantation-specific Comorbidity Index allow room for interpretation. How do the authors ensure that these clinical variables were evaluated consistently across centers?

Centers were grouped based on annual transplant numbers. Could the authors indicate the degree of overlap in outcomes between centers across different categories? For example, were there low-volume centers with excellent outcomes, or high-volume centers with significantly poorer outcomes? If so, what suggestions would the authors make to explain this?

If center-related factors do indeed explain differences in outcomes, it is in the interest of patients, referring physicians, and transplant centers to identify and broadly implement these factors. Rather than advocating for centralization, an alternative approach could be to improve performance across all centers. What recommendations do the authors make in this regard?

We hope these questions will contribute to an open and constructive scientific dialogue, with the shared goal of achieving the best possible care for patients undergoing allogeneic stem cell transplantation.

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Disclosures

DD is affiliated with a non-university, JACIE-accredited stem cell transplantation center performing fewer than 40 allogeneic transplants per year.

References

1. Bethge W, Flossdorf S, Hanke F, et al. Does size matter? Center-specific characteristics and survival after allogeneic hematopoietic cell transplantation for acute myeloid leukemia: an analysis of the German Registry for Stem Cell Transplantation and Cell Therapy. Haematologica. 2025;110(6):1292-1303.