

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

by Dries Deeren

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Title page

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

Dries Deeren¹

¹Hematology department, AZ Delta, Roeselare, Belgium

ORCID ID: 0000-0001-9599-2142

Corresponding author:

Dr. Dries Deeren, MD

Hematology department

AZ Delta

Deltalaan 1

B-8800 Roeselare

Belgium

Email: dries.deeren@azdelta.be

Phone: +32 51237322

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To the Editor,

We read with great interest the article by Dr. 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.

1. Causality versus correlation

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.

2. Disclosure of conflicts of interest

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?

3. Early referrals post-transplantation

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?

4. Objective and reproducible assessment of performance status and comorbidities

A major source of inter-center heterogeneity lies in the assessment of performance status and comorbidity. ECOG and Karnofsky scores remain subjective, and several items within the HCT-CI allow room for interpretation. How do the authors ensure that these clinical variables were evaluated consistently across centers?

5. Homogeneity within volume categories

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 explanations do the authors suggest?

6. Implications and implementation

If center-related factors 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.

Thank you.

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.