

Response to 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 thank Dr. Deeren¹ for his interest in our work² and his comments and questions. We would like to reply as follows. Concerning causality *versus* correlation, our study was a retrospective registry-based analysis and as such can only explore correlations and try to exclude confounders by statistical methods. A randomized study seems unrealistic in this setting, so for the next level of evidence we had to rely on a retrospective study. Nevertheless, we acknowledge the limitations of an observational registry-based analysis. The wording was chosen very cautiously to reflect the level of evidence based on the nature of our study. We never claimed causality and cautioned for possible bias and confounders. However, the presence of each individual risk factor identified in our models predicts an increased hazard of death compared to its absence independent of causality. Therefore, as long as the opposite is not proven (in the case of center volume that small sizes do not harm), there is no good reason not to consider those factors, particularly if a direct causal correlation is very plausible, as is the case for the center-related factors investigated here.

We agree with Dr. Deeren in that different interests might exist among authors from larger and smaller, academic and non-academic centers, respectively. Therefore, we took care that also authors from lower-volume centers and those that were not university hospitals were included. No authors from governmental agencies or health insurance institutions were included.

With regards to early referrals post transplantation, given that this is registry data, we have no information about referrals and therefore we could not include this question in our analysis. Empirically, however, transfer of post-transplant care to a referral center or a transplant center different from the center which has performed the transplantation is infrequent in Germany.

Dr. Deeren correctly states that assessment of the objective and reproducible assessment of performance status and comorbidities was not standardized. But this is a problem of every retrospective and even prospective study. Anyway, it does not seem to be crucial for our results or their interpretation.

As far as homogeneity within volume categories is con-

cerned, there is no doubt that low volume centers can also provide excellent clinical outcomes. In our study, also these centers were included in the analysis with the same weight as all others. The estimated effects are, therefore, the results of average values, and statistical analysis was aimed at adjusting for heterogeneity within categories. Nevertheless, center-specific benchmarking could be a complementary tool for transplant center selection. With regards to the implications and implementation of our conclusions, alternative approaches over-ruling the need for selecting large volume centers could be only those that neutralize its effect in the multivariable models. For the time being, it is unclear which center-specific approaches could make center experience and center routine practice unnecessary. At least JACIE accreditation did not substitute for center experience and center volume in our sample; in fact, it did not even show any additional benefit, although its effect had been demonstrated in an earlier study.³

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Disclosures

No conflicts of interest to disclose.

Contributions

WB and PD contributed equally to this work on behalf of the German Working Group for Hematopoietic Stem Cell Transplantation

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References

1. Deeren D. 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. *Haematologica*. 2026;111(2):770-771.
2. 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.
3. Gratwohl A, Brand R, McGrath E, et al. Use of the quality management system “JACIE” and outcome after hematopoietic stem cell transplantation. *Haematologica*. 2014;99(5):908-915.