

Do high-volume centers really save more lives? A call for scientific rigor and transparency. 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

by Wolfgang Bethge and Peter Dreger.

Collaborative Groups: German Working Group for Hematopoietic Stem Cell Transplantation and Cellular Therapy e.V. (DAG-HSzt), German Registry for Hematopoietic Stem Cell Transplantation and Cell Therapy (DRST)

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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**

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On behalf of the authors of 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

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And on behalf of the German Working Group for Hematopoietic Stem Cell
Transplantation and Cellular Therapy e.V. (DAG-HSZT) and the German Registry for
Hematopoietic Stem Cell Transplantation and Cell Therapy (DRST)

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Conflict of interest: none

To the Editor,

We thank Dr. Deeren¹ for his interest in our work² and his comments and questions.

We would like to reply as follows:

Ad 1. Causality versus correlation

Our study was a retrospective registry-based analysis and can as such 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 case of center volume that small sizes do not harm), there is no good reason not to consider those factors. In particular if a direct causal correlation is very plausible, as it is the case for the center-related factors investigated here.

Ad 2. Disclosure of conflicts of interest

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

Ad 3. Early referrals post-transplantation

Given this is registry data we have no information about referral 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.

Ad 4. Objective and reproducible assessment of performance status and comorbidities
Dr. Deeren correctly states that assessment of these items 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.

Ad 5. Homogeneity within volume categories

There is no doubt that low volume centers can also provide excellent clinical outcomes. In our study, these centers also 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 to adjust for heterogeneity within categories. Nevertheless, center specific benchmarking, could be a complementary tool for transplant center selection.

Ad 6. Implications and implementation

Alternative approaches overruling 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 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 study³.

Yours sincerely,

Wolfgang Bethge and Peter Dreger for the authors

Reference

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