




aGvHD

Lower pre-transplant serum citrulline level as predictive marker for acute graft-versus-host disease

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Armin Rashidi and colleagues from the University of Minnesota, Minneapolis, MN, USA, evaluated serum biomarkers of gut barrier as predictors of allogeneic hematopoietic stem cell transplantation (allo-HSCT) outcomes. Three biomarkers (citrulline, regenerating islet-derived protein 3 alpha [Reg3a], and intestinal fatty acid binding protein [I-FABP]) were assessed pre-transplant on day -7, and then post-transplant on days 7 and 28 in consecutive patients undergoing allo-HSCT. The results of the study were published ahead of print in Biology of Blood and Marrow Transplantation on 6 July 2018.

Patients and methods:

- Allo-HSCT recipients: n = 95, median age = 58 years (range, 48–65)
- Controls were healthy donors: n = 16, median age = 51 years (range, 37–56)
- Assessed biomarkers:
 - Citrulline: total functional enterocyte mass
 - Reg3a: antibacterial activity of the gut
 - I-FABP: enterocyte turnover

Key findings:

Biomarkers

- Pre-HSCT biomarker levels were significantly different in patients vs controls:
 - Citrulline: 1.88 (1.23–3.31) vs 10.8 (9.05–11.9) ng/mL, $P < 0.01$
 - Reg3a: 7.07 (4.81–11.30) vs 4.70 (3.46–7.40) ng/mL, $P = 0.006$
 - I-FABP: 1.36 (0.78–1.83) vs 0.93 (0.74–1.18) ng/mL, $P = 0.03$
- Intensity of the most recent preconditioning management, underlying disease, or HSCT-CI did not show correlation with pre-HSCT biomarkers
- I-FABP and Reg3a showed a weak correlation: $r = 0.23$ (95% CI, 0.03–0.42)

Transplant outcomes and acute graft-versus-host disease (aGvHD)

- Median follow-up = 12 months
- 1-year non-relapse mortality (NRM): 13%, respectively

- Higher Reg3a at day +7 predicted higher non-relapse mortality: 11.51 (9.43–19.99) vs 4.20 (2.76–6.42) ng/mL, $P < 0.001$
- 6-month aGvHD grade II-IV: 51%, respectively
- Lower pre-HSCT citrulline correlated with higher risk of aGvHD grades II–IV: 1.64 (0.99–2.30) vs 2.70 (1.50–4.41) ng/mL, $P < 0.01$
- Lower pre-HSCT citrulline level independently associated with a higher risk of aGVHD grade II-IV: HR = 1.32 (95%CI, 1.03–1.69), $P = 0.02$

Rashidi and colleagues concluded that these findings support that pre-HSCT serum citrulline level can serve as a predictive marker for patients with high risk for developing acute graft-versus-host disease. They further added that their results “suggest that pre-HSCT interventions to augment the gut barrier may decrease the risk of aGvHD.”

References

1. Rashidi A. et al. Pre-transplant serum citrulline predicts acute graft-versus-host disease. *Biology of Blood and Marrow Transplantation*. 2018 July 06. DOI: [1016/j.bbmt.2018.06.036](https://doi.org/10.1016/j.bbmt.2018.06.036).

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