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Commentary: The jury is out—expanding eligibility for lung transplantation after hematopoietic stem cell transplantation

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Over the last 30 years, early mortality after allogeneic hematopoietic stem cell transplantation (HSCT) has declined, with a consequent increase in long-term morbidity.¹ Among late post-HSCT complications are noninfectious pulmonary complications, including bronchiolitis obliterans, which typically occur within 2 years after HSCT and portend a 5-year survival probability of <15%.^{2,3} Medical management is of limited efficacy in this setting, and lung transplantation (LTx) has emerged as a potential therapy for select patients.³⁻⁵

Presently, only 1% of LTx are performed for bronchiolitis obliterans unrelated to previous LTx; of those, cases related to HSCT represent only a subset.^{5,6} To maximize the utility of a scarce resource, LTx is offered to patients at high risk of lung disease–related mortality, without comorbidities that may compromise posttransplantation survival.⁷ As HSCT recipients remain at risk of recurrence of their original malignancies, the International Society for Heart and Lung Transplantation lists hematologic malignancy within the past 2 years, and conservatively within the past 5 years, as a contraindication for LTx.⁷ Nevertheless, post-LTx recurrence seems to be rare, affecting 2% to 7% of HSCT recipients.^{5,8,9} As such, revisitation of eligibility for LTx after HSCT may be warranted to meet rising needs.

CENTRAL MESSAGE

Consideration of recurrence risk may facilitate lung transplantation after hematopoietic stem cell transplantation. Further study is needed before advocating for new lung transplantation criteria in this setting.

In this issue of the *Journal*, Noguchi and colleagues¹⁰ present novel eligibility criteria for LTx after HSCT, and outcomes among 40 patients transplanted under their protocol. At their institution, HSCT patients may undergo LTx if the risk of recurrence is considered to be <30%; for deceased donor LTx, transplantation may occur 2 years after HSCT, whereas living donor lobar LTx (LDLLT) is permitted within 2 years. As HSCT alters patients' ABO blood types to those of corresponding bone marrow donors, post-HSCT LTx is further facilitated by tolerance of major ABO incompatibility in the absence of antibodies to donor blood group antigens. Their results demonstrate comparable 5-year post-LTx survival among HSCT and non-HSCT patients, and among HSCT patients with disease-free interval >5 years or <5 years. No recurrences were documented during a median 4 years of follow-up.

These eligibility criteria for LTx after HSCT are intriguing for several reasons. First, compared with current guidelines, this protocol allows HSCT recipients to undergo LTx sooner, potentially mitigating severity of lung dysfunction at transplantation. Second, the use of ABO-incompatible donors may offer a novel means by which to expand the donor pool. However, wide applicability of their findings remains uncertain. In particular, 32 of 40 patients in their cohort underwent LDLLT owing to a paucity of deceased organ donors in Japan. In other countries, however, LDLLT represents the vast minority of LTx.¹¹ Although previous studies have shown comparable outcomes among HSCT and non-HSCT deceased donor LTx recipients,^{5,8}

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the utility and safety of new eligibility criteria for LTx require further investigation in this setting.

In conclusion, the jury is out on expanding eligibility for LTx to HSCT recipients, but Noguchi and colleagues offer a thoughtful new paradigm for evaluating the optimal provision of lung grafts in this population.

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