Pulmonary Function and Pretransplant Evaluation of the Hematopoietic Cell Transplant Candidate

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KEYWORDS

• Pretransplant evaluation • Hematopoietic cell transplantation • Pulmonary function tests
• Pulmonary complications • Risk assessment • FEV_1 • DLCO

KEY POINTS

- Pretransplant pulmonary function tests establish lung function baseline and help detect pulmonary disease in hematopoietic cell transplant candidates.
- Pretransplant impairments in lung function are associated with an increase in posttransplant pulmonary complications and mortality.
- The use of formal risk assessment tools can aid in prognostication and clinical decision making before hematopoietic cell transplantation.

INTRODUCTION

Of all the organ-specific complications that can occur after allogeneic and autologous hematopoietic cell transplantation (HCT), pulmonary complications remain among the most significant in terms of incidence and impact on outcome of HCT recipients. Historically, pulmonary complications, infectious and noninfectious, affected up to 50% of HCT recipients and continues to be a primary cause of mortality in the early posttransplant period.[1] Early acute complications such as idiopathic pneumonia syndrome are less common in a contemporaneous era of transplantation; however, there remains significant use of the intensive care unit for respiratory failure in this population with an incidence of acute respiratory failure of up to 15% to 25% in allogeneic HCT recipients.[2] Patients who survive beyond 1 year and are cured of their original condition continue to experience pulmonary complications, which contribute to early mortality compared with the general population as well as other cancer patients.[3,4] The goal of this article is to update the practicing chest physician on current practices in HCT, discuss the impact of pulmonary dysfunction on the outcome of HCT recipients as well as the relevance of pretransplant pulmonary function evaluation, and provide recommendations for clinical practice.

RECENT DEVELOPMENTS IN HEMATOPOIETIC CELL TRANSPLANTATION

HCT has evolved from a salvage therapy for terminal malignancies to a widely accepted, life-saving procedure for a number of hematologic malignancies and nonmalignant conditions. As of December 2012, 1 million transplants have been

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performed,[5] and more than 50,000 transplants are performed annually worldwide.[6] The rate of allogeneic transplants continues to increase. Since the first infusion of isolated marrow cells into terminally ill cancer patients in 1957, the technology and indications for HCT have expanded dramatically, in part owing to improved HLA typing, allowing for unrelated donors, the use of peripheral blood stem cells, cord blood cells, and now the use of haploidentical donors.

Historically, HCT was limited to younger patients owing to the significant toxicities associated with myeloablative conditioning regimens, which involve supralethal doses of total body irradiation (TBI) and high doses of chemotherapeutic agents. TBI is a well-documented cause of interstitial pneumonitis and severe pulmonary toxicity.[7,8] Although intensification of conditioning regimens reduced relapse of disease, the degree of nonrelapse mortality was unacceptably high for older patients or those with significant comorbidities. Observations that patients who developed graft-versus-host disease had lower rates of relapse led to the recognition of the graft-versus-tumor effect, in which the immune effects of the donor cells eliminate the malignancy. As a consequence, the intensity of the conditioning regimens could be reduced, allowing the use of HCT in older, previously ineligible patients. The use of reduced intensity conditioning, which used smaller doses of chemoradiation to achieve marrow ablation, and nonmyeloablative conditioning regimens has contributed to the expansion of HCT for patients with lower risk disease and with medical comorbidities.[9,10]

Although survival after HCT has improved in recent years with reduction in regimen-related toxicities as well as improvements in infectious prophylaxis, prophylaxis for graft-versus-host disease, and supportive care, HCT remains a treatment modality with significant risks for morbidity and mortality.[11] Given the significant medical, personal, social, and financial resources required to undertake HCT, meticulous evaluation of potential candidates is of utmost importance. Because acute respiratory failure from infectious and noninfectious causes contributes significantly to early nonrelapse mortality, lung function continues to carry significant weight in the assessment of eligibility and selection of a suitable transplant regimen.

ROLE OF PULMONARY FUNCTION TESTING BEFORE HEMATOPOIETIC CELL TRANSPLANTATION

As with preoperative evaluation in nontransplant settings, the pretransplant evaluation is done to ensure that a patient has sufficient physiologic fitness to survive the significant physiologic stresses associated with conditioning and engraftment and includes evaluation of cardiac, renal, hepatic, as well as pulmonary function. Although the majority of patients who present for transplantation have normal lung function, pulmonary function tests (PFTs) will identify patients who have serious pulmonary comorbidities that would limit candidacy for transplant. Overall, the prevalence of abnormalities in PFTs is greater for nonmyeloablative regimens compared with myeloablative regimens owing to the more permissive eligibility requirements.[12]

Given the expanded options for less toxic conditioning regimens in contemporary practice, very few patients will be denied transplant based on lung function alone. Most HCT centers routinely perform PFTs before transplant to establish a baseline by which to reference post-HCT lung function in the event of respiratory insufficiency. Lung function abnormalities before transplantation may be a result of toxic chemoradiation therapy, the sequelae of suppurative lung infections brought on by neutropenia, or preexisting medical lung disease such as smoking-related chronic obstructive pulmonary disease. At the minimum, PFTs are performed just before transplant, at day 80 to 100 after transplant, and then at 1 year.[13] It is recommended that patients who are at higher risk for developing late noninfectious complications, such as those with chronic graft-versus-host disease, undergo PFT screening more frequently.[14] The diagnosis of bronchiolitis obliterans syndrome, a late noninfectious pulmonary complication, is contingent on recognizing new spirometric decline compared with an established pretransplant baseline.[15]

In addition to establishing baseline lung function, pretransplant PFTs can aid in the prognostication and identification of individuals at greater risk for posttransplant complications and mortality. However, the practical usefulness of lung function parameters for prognostication remains a matter of debate, because these predictive tools are based on data from single centers in which transplant protocols, including the extensive use of TBI in myeloablative regimens, may not reflect current practices. There continues to be controversy about which parameters and the degree to which these impairments contribute to pulmonary complications and nonrelapse mortality, and specifically respiratory-related mortality, although there is general agreement that pulmonary dysfunction contributes to worse outcomes.