INTRODUCTION

Other vulnerable populations that need special consideration include older age patients. Because of toxicity and nonrelapse mortality (NRM), allografting with conventional myeloablative conditioning is rarely performed in patients older than 50 years of age, and autografting in patients over the age of 65 years is performed in only a few centers. Both single-institution and registry analyses show that older age is associated with a higher incidence of graft-versus-host disease (GVHD) and NRM [1-3]. The biologic basis underlying the increased incidence of NRM in older patients is not well understood, although most studies show a relationship of acute GVHD (aGVHD) with age [4].

Improvements in supportive care and the use of peripheral blood stem cells (PBSC), together with improved HLA typing technology, have improved transplant outcomes in younger patients [5]. Although some centers have shown that conventional allografting can be successful in patients over the age of 55 years, the number of patients over 55 years who had until recently undergone allografting was extremely small [6,7]. The change in age distribution of transplant recipients over the last 20 years is summarized in Figure 1A and B.

Transplanting older patients has unique challenges; not only are comorbidities more common, but in some instances the risk-benefit ratios favor a more conservative approach when compared to younger patients with the same disease. What is surprising, however, is the number of instances in which aggressive therapy is actually indicated and appropriate for older patients. In this section, we will review some of the current studies regarding stem cell transplant (SCT) in older patients. In the last section we will discuss the comorbidity index and its applicability to high-risk patients.

Current Results with Reduced-Intensity Conditioning (RIC) Regimens for Older Patients with Acute Myelogenous Leukemia (AML)

The potency of the immune-mediated graft-versus-leukemia (GVL) effect as demonstrated by the ability of donor lymphocyte infusions (DLIs) to reinduce remissions in patients who have relapsed after an allogeneic progenitor cell transplant has led to the exploration of RIC regimens in older and medically debilitated patients [8-12]. Since the advent of RIC, the fraction of patients over the age of 55 years who are undergoing allogeneic transplantation has increased significantly and represents 1 of the largest areas of growth for this procedure, as can be seen in Table 1. Notwithstanding, most allografted patients are still <70 years of age, with only 54 patients reported to the registry >70 years of age [13]. Kiss et al. [14] recently reviewed the results of allografting for older patients with AML undergoing RIC allografting. In general, 2- to 3-year NRM rates between 10% and 30% are reported with 3-year event-free survival (EFS) rates between 30% and 50% for patients undergoing RIC allografting for AML/myelodysplastic syndromes (MDS) in remission [15-22]. Unfortunately, as demonstrated by Estey et al. [22], only a minority of patients achieving a complete remission actually undergo this procedure. There is a significant difference in dose intensity among the different RIC and minimally ablative regimens that are currently used [14]. Although dose intensity has been reported to be important for disease control after allografting in AML/MDS [16], none of the retrospective studies have demonstrated a benefit of 1 conditioning over another.

Timing of SCT in the Elderly AML/MDS Patients

Considering that the outcome for elderly patients with AML/MDS is so poor, one would think that most patients should be transplanted as soon as the diagnosis is made. The logistics of finding a donor, plus the poor performance status of many elderly patients with AML/MDS makes this difficult. Even in patients achieving a complete remission, the number of patients undergoing allografting is <15% [22]. The emerging data regarding the safety and efficacy of
this procedure should allow more patients and physicians to consider this as a valid option. However, patients with high comorbidity scores (see next section) and poor performance status continue to have a high rate of treatment-related complications and mortality (TRM) rates of 40% at 3 years, and the risk benefit ratio needs to be addressed with patients and family members before embarking on this procedure [23]. The lack of a related sibling donor or a suitable 10/10 unrelated donor also should not be considered an absolute barrier to proceed to allografting in elderly AML/MDS patients, because recent reports from the University of Minnesota have shown the feasibility and efficacy of unrelated donor cord blood transplantation using RIC regimens in older patients; however, this approach should still be limited to well-designed clinical trials [24].

Older patients with other hematologic malignancies have also been treated with allogeneic SCT. These series include a variety of both acute and chronic lymphogenous and myelogenous malignancies, and firm conclusions regarding the role of allografting in older patients with these disorders cannot be made. Notwithstanding, the preliminary analysis in patients with low-grade non-Hodgkin lymphoma (NHL) and chronic lymphocytic leukemia (CLL) are encouraging.

CONCLUSION

The development of RIC regimens has allowed physicians and patients to explore the option of long-term disease control. The risk-benefit ratio for this procedure will depend on the disease state, and the performance status of the patient. Better risk stratification through the use of the comorbidity index, which is discussed below, may also help in patient assessment and the choice of conditioning regimens. Current results underscore that age by itself should no longer be a contraindication for allogeneic transplant with curative intent in these patients, and long-term disease control with good quality of life is possible and can be expected. Future trials combining novel therapies as well as novel transplant technologies should allow more elderly patients with AML or MDS to achieve long and productive lives.

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REFERENCES


Figure 1. (A) Trends in allogeneic bone marrow transplant (1984-2002). (B) Trends in autologous transplantation (1990-2002).


