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Optimal Practices in Unrelated Donor Cord Blood Transplantation for Hematologic Malignancies

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A B S T R A C T

Unrelated donor cord blood transplantation (CBT) results in disease-free survival comparable to that of unrelated adult donor transplantation in patients with hematologic malignancies. Extension of allograft access to racial and ethnic minorities, rapid graft availability, flexibility of transplantation date, and low risks of disabling chronic graft-versus-host disease (GVHD) and relapse are significant advantages of CBT, and multiple series have reported a low risk of late transplantation-related mortality (TRM) post-transplantation. Nonetheless, early post-transplantation morbidity and TRM and the requirement for intensive early post-transplantation management have slowed the adoption of CBT. Targeted care strategies in CBT recipients can mitigate early transplantation complications and reduce transplantation costs. Herein we provide a practical "how to" guide to CBT for hematologic malignancies on behalf of the National Marrow Donor Program and the American Society of Blood and Marrow Transplantation's Cord Blood Special Interest Group. It shares the best practices of 6 experienced US transplantation centers with a special interest in the use of cord blood as a hematopoietic stem cell source. We address donor search and unit selection, unit thaw and infusion, conditioning regimens, immune suppression, management of GVHD, opportunistic infections, and other factors in supportive care appropriate for CBT. Meticulous attention to such details has improved CBT outcomes and will facilitate the success of CBT as a platform for future graft manipulations.

INTRODUCTION

Unrelated donor (URD) cord blood (CB) is well established as an allogeneic hematopoietic stem cell (HSC) source that extends allograft access. Volunteer donor searches are much less likely to identify a matched URD in patients of non-European and mixed descent, owing to diverse HLA haplotypes, lower representation in URD registries, and an increased risk of poor donor availability. A recent National Marrow Donor Program (NMDP) study has demonstrated that whereas approximately 75% of white European patients are likely to identify an 8/8 HLA-matched URD, the rate is much lower in minority patients with availability for donation, further compromising access [1]. In the absence of a suitable URD, CB and haploidentical related donor transplants are alternative options.

Owing to the less-stringent HLA matching requirement, CB transplantation (CBT) has been shown to extend access to the majority of adults in all ancestry groups [1,2]. A further advantage of CB is its rapid availability, permitting flexibility of scheduling for transplantation. This greatly facilitates the care of patients with high-risk malignancies and avoids the adverse effects of delayed transplantation [3].

Multiple retrospective studies have demonstrated that CBT performed in experienced centers can achieve disease-free survival (DFS) rates comparable to those of the gold standard of HLA-matched URD transplantation in patients with hematologic

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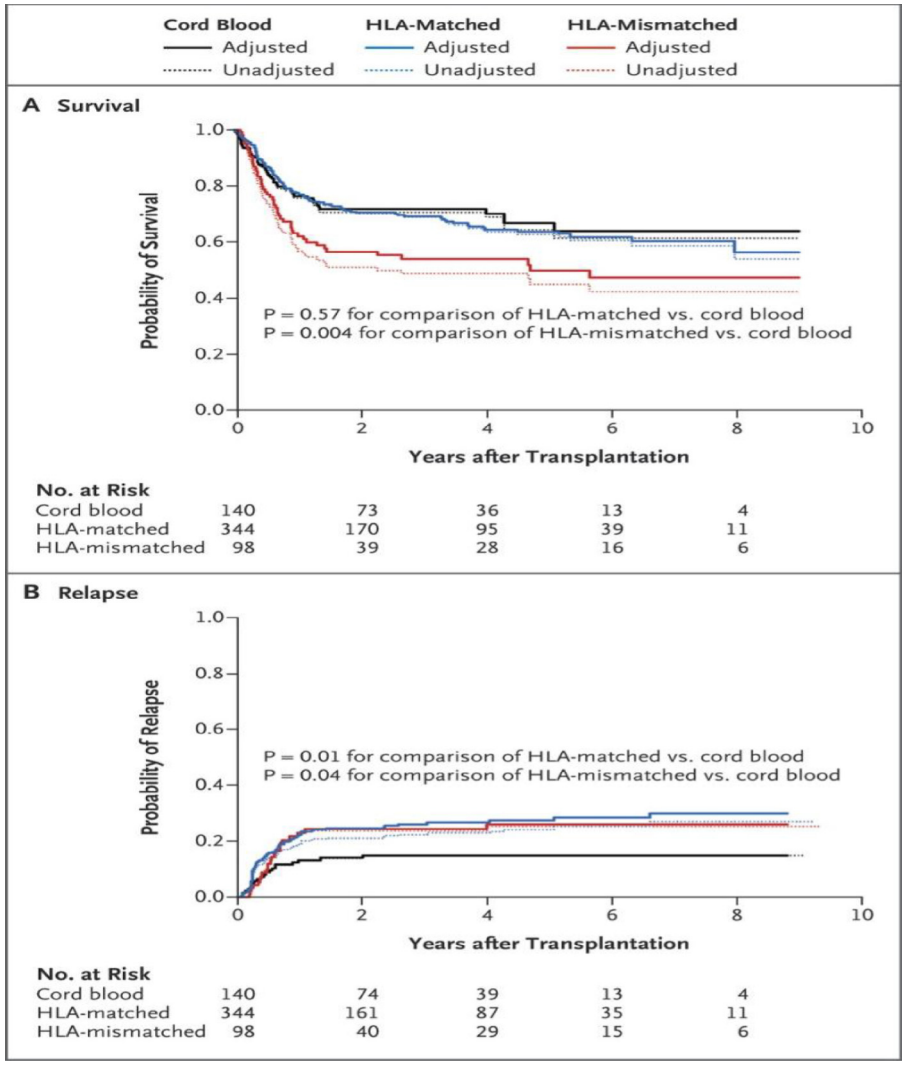

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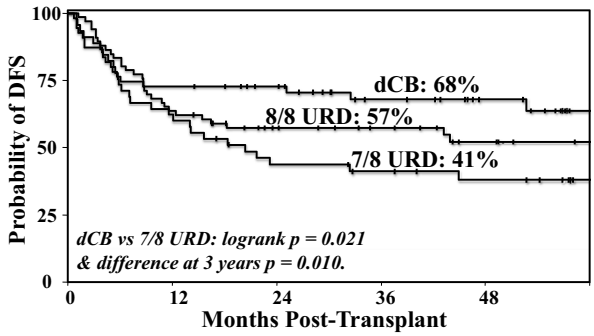

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Figure 1. Comparison of survival in CBT recipients and URD transplant recipients. (A) Acute leukemia/myelodysplasia syndrome survival at FHCRC after unmodified adult donor allografts and CBT [8]. The hazard ratio (HR) for death in HLA-matched versus CBT recipients was 1.12 (95% CI, .77 to 1.63; $P = .57$), and the HR in HLA-mismatched versus CBT recipients was 1.91 (95% CI, 1.23 to 2.98; $P = .004$). The HR for relapse in HLA-matched versus CBT recipients was 1.95 (95% CI, 1.16 to 3.27; $P = .01$), and the HR in the HLA-mismatched versus CBT recipients was 1.97 (95% CI, 1.04-3.73; $P = .04$). (B) MSKCC analysis demonstrating DFS in adults with acute leukemia (dCBT compared with T cell–depleted URD allografts) [6]. In this analysis, CBT recipients had significantly higher DFS than HLA-mismatched URD recipients.

malignancies [4-8]. For example, the University of Minnesota (UMN)/Fred Hutchinson Cancer Research Center (FHCRC) reported comparable 5-year DFS after myeloablative matched related, matched URD, mismatched URD, and double-unit CB (dCB) transplantation [4]. Recent single-center comparisons have demonstrated comparable DFS in recipients of 8/8 HLA-matched URD and CB transplants (Figure 1 A,B) [6,8]. These analyses are notable for the low rates of relapse after CBT. Moreover, the recent FHCRC analysis has shown a markedly reduced relapse rate after CBT compared with URD transplantation in patients who undergo