

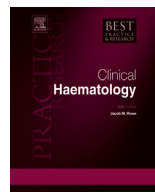


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Unrelated donor transplantation: Peripheral blood or bone marrow – Does it matter?



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Over the past decade, the use of peripheral blood progenitor cells (PBPC) has increased and now accounts for 70%–75% of grafts used for unrelated donor transplantation in adults with hematologic malignancy. It is important to recognize the shift in clinical practice from transplantation of bone marrow (BM) to PBPC occurred largely without adequate clinical data to support the change. It is presumed the change in clinical practice is attributed to results of randomized clinical trials in the setting of HLA-matched sibling transplantations. The results of these trials showed better engraftment but increased risk of acute graft-versus-host disease (GVHD) with PBPC and possibly better survival for advanced leukemia. However, the results of HLA-matched sibling transplants may differ from that after unrelated donor transplants. There is greater genetic diversity between unrelated adult donors and their recipients and therefore greater risks of GVHD even if the donor and recipient are fully HLA-matched. This review explores the relative merits of transplantation of PBPC relative to BM for myeloablative and reduced-intensity conditioning unrelated donor transplantation for hematologic cancers in adults.

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Introduction

Randomized trials have shown that the transplantation of peripheral blood progenitor cells (PBPC) from HLA-matched siblings results in faster hematopoietic recovery but increases the risk of acute and

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chronic graft-versus-host disease (GVHD) as compared to transplantation of bone marrow (BM) for hematologic malignancy [1,2]. Although these studies support a survival advantage for patients transplanted for advanced leukemia, a convincing survival advantage for those in first or second complete remission is not documented. Further, in good-risk patients, chronic myeloid leukemia in first chronic phase, mortality risks were higher after transplantation of PBPC compared to BM [3].

Over the past decade, use of PBPC for unrelated donor transplantation has increased and now accounts for 70%–75% of transplants from unrelated donors for adults with hematologic malignancy in the United States. A decade ago, the Blood and Marrow Transplant Clinical Trials Network (BMTCTN) in the United States initiated a phase 3, open labeled, multicenter randomized trial to study 2-year overall survival after transplantation of PBPC and BM from HLA-matched or mismatched adult unrelated donors (BMTCTN 0201) [4]. BMTCTN 0201 was limited to myeloablative transplantations. Yet, increasing numbers of allogeneic transplantation in adults older than 45 years utilize transplant conditioning regimens that are not myeloablative and PBPC, the predominant graft for these transplantations. This report reviews the merits of PBPC relative to BM for recipients of unrelated donor allogeneic transplantation for adults with hematologic malignancy.

Myeloablative transplantation

The BMTCTN 0201 enrolled 551 patients with acute and chronic leukemia or myelodysplastic syndromes over 5.5 years [4]. Patients were randomly assigned in a 1:1 ratio to PBPC or BM and the primary endpoint of the trial was 2-year overall survival. There were no significant differences in 2-year survival between PBPC and BM transplantation, 51% (95% confidence interval [CI] 45–57) and 46% (95% CI 40–52), respectively ($P = 0.29$). The overall incidence of graft failure was significantly lower after transplantation of PBPC (3%, 95% CI 1–5) compared to BM (9%, 95% CI 6–13), $P = 0.002$, and the 2-year overall incidence of chronic GVHD was significantly higher after transplantation of PBPC (53%, 95% CI 45–61) compared to BM (41%, 95% CI 34–48), $P = 0.01$. There were no significant differences between the two treatment groups in the incidence of acute GVHD or relapse. In conclusion, although rate of survival was similar with PBPC and BM grafts from unrelated donors, the rate of overall chronic GVHD was higher with PBPC.

Published reports have also shown long-term overall mortality is higher for patients with GVHD compared to those without GVHD. The treatment for GVHD is additional immunosuppression, which increases the risk of infection and consequently mortality in patients who are considered cured of their hematologic malignancy. The randomized clinical trial that compared PBPC with BM from unrelated donors reported 2-year outcomes as specified in that trial and the median follow-up of surviving patients was 36 months (range, 30–37). As the deleterious effects of GVHD on survival tend to occur well beyond 2–3 years after transplantation, using data reported to the Center for International Blood and Marrow Transplant Research, longer-term survival rates after transplantation of PBPC were compared to that after BM.

Patients with acute leukemia (acute myeloid or lymphocytic leukemia), chronic myeloid leukemia or myelodysplastic syndrome, aged 18 years and older and transplanted in the United States between 2000 and 2008 were studied. The choice of graft type (PBPC or BM) was at the discretion of the treating physician. Donors were matched to recipients at the allele-level at HLA-A, -B, -C and -DRB1 or mismatched at a single HLA-locus. Transplants that were either ex vivo T-cell depleted or CD34 selected were excluded. Conditioning regimens were limited to total body irradiation (≥ 1000 cGy) with cyclophosphamide or other chemotherapeutic agents, busulfan with cyclophosphamide or fludarabine. GVHD prophylaxis included a calcineurin inhibitor (cyclosporine or tacrolimus) either alone or with methotrexate or mycophenolate. The characteristics of PBPC and BM recipients were similar except PBPC recipients were slightly older, less likely to report performance scores of 90 or 100, and less likely to receive non-irradiation transplant conditioning regimens. PBPC transplantations were more recent with over half of transplants being performed after 2004. The median follow-up of surviving patients after PBPC transplantation was 5 years and after BM transplantation, 6 years.

Table 1 shows the 5-year probabilities of overall survival for acute leukemia, chronic myeloid leukemia, and myelodysplastic syndrome by disease, disease status, and graft type. The probability estimates are adjusted for factors that were associated with the above overall survival and included age,

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