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Case Study
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# Relationship between Transfusion and Mortality in Adult Patients Undergoing Single Unit Umbilical Cord Blood Transplantation

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## Case Study

The influence of blood product transfusion on mortality in the Hematopoietic Stem Cell Transplantation (HSCT) setting remains a controversial issue. Recent studies support the negative impact of Red Blood Cell (RBC) and platelet transfusions in mortality of patients undergoing HSCT from different sources [1,2]. Konuma et al. [2] analyzed influence of RBC transfusion burden on mortality in 278 adult patients after single Unit Cord Blood Transplantation (UCBT). These authors conclude that RBC transfusion >18 units by day 30 of UCBT are significantly associated with higher mortality. Previous reports have associated RBC transfusion to infectious and non infectious complications in different subsets of patients [3,4]. We previously reviewed data from 318 patients who underwent single unit UCBT for a 15-year period and analyzed RBC and platelet transfusion requirements at 30, 90, 120 and 365 days after UCBT [5]. Packed RBCs were transfused if the hemoglobin level of patients was <80 g/dl and prophylactic pooled platelets were transfused at platelets counts <20 × $10^9$/L. We also analyzed the risk factors for receiving more than 10 RBC transfusions at 90 days after UCBT. Presence of acute Graft Versus Host Disease (aGVHD) and more days until neutrophils engraftment (neutrophils ≥ 1 × $10^9$/L) significantly increased RBC transfusion requirements. We have recently performed a survival analysis in a sub cohort of 253 patients who underwent myeloablative UCBT, 156 male, 97 female, and median of age 35 years. Other characteristics of patients have been previously published [5]. Computer software SPSS (version 15, SPSS Inc., Chicago, IL) and EZR, a graphic user interface for R-2.13.0 were used to perform the statistical analysis. Univariable analysis for overall survival was first performed using the Kaplan Meyer and log rank test. Variables that showed statistical significance were included in the Cox proportional Hazard model. P-values <0.05 were considered to be significant. The following factors were included in the univariable analysis: Age (≤ 35 *vs*. >35), sex matching, diagnosis (acute myeloid leukemia *vs*. others), years of transplantation (2000 to 2007 *vs*. 2008 to 2018), disease (AML *vs*. others), TNC (<2.5 × $10^7$/Kg *vs*. ≥ 2.5 × $10^7$/Kg ), CD34+ cells × $10^5$/Kg, GVHD (≤ 2 *vs*. > 2), HLA mismatched (≤ 2 *vs*. >2), ABO group incompatibility (identical and minor *vs*. major), recipient CMV (positive *vs*. negative), RBC unit transfusions by day 30 (total and ≤ 10 *vs*. >10 units) and PLT transfusions by day 30 (total and ≤ 20 *vs*. >20 concentrates). Results are shown in the Table 1. There was statistical correlation between RBC and platelet transfusion at 30 days after UCBT (rho=0.731, p<0.001) and also at 90 days after UCBT (rho=0.839, p<0.001). In the univariable analysis, total RBC and PLT transfusions by 30 days of UCBT showed the strongest statistical significance as performed by log rank test (p<0.01). Figure 1 shows the survival according if patients received ≤ 10 RBC or >10

**Table 1:** Factors influencing overall mortality: results of multivariable analysis.

| Variables | Hazard Ratio | 95% CI | | p |
|---|---|---|---|---|
| | | Lower | Upper | |
| ABO major incompatibility | 2.038 | 1.194 | 3.478 | 0.009 |
| ≥ 10 RBC transfusions by day 30 of UCBT | 0.982 | 0.922 | 1.045 | 0.569 |
| ≥ 20 Platelet pool transfusions by day 30 of UCBT | 1.034 | 0.991 | 1.078 | 0.120 |
| aGVHD > grade 2 | 1.925 | 1.005 | 3.688 | 0.048 |
| TNC >2.5 x $10e^7$/Kg | 0.412 | 0.156 | 1.090 | 0.074 |
| HLA mismatched >2 | 0.591 | 0.298 | 1.175 | 0.134 |



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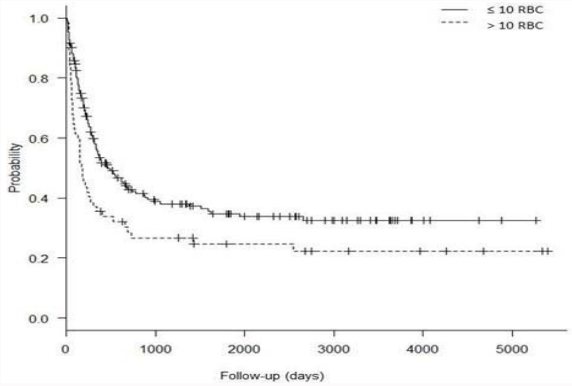


**Figure 1:** Probability of overall survival according if patients received ≤ 10 RBC or >10 RBC units, P=0.007.

RBC units. However, this effect was not confirmed in multivariable analysis in which only major ABO incompatibility and aGVHD were significantly associated to increased mortality risk. Presence of aGVHD more than grade 2 has also shown statistical influence on mortality in our subset of patients. Patients who suffered more than grade 2 aGVHD received a median of 11 RBC units (range 2 to 28), while patients with aGVHD grade 2 or less received a median of 6 RBC units (range 0 to 28), p<0.001. Therefore, if RBC and platelet transfusions play any role in mortality in the HSCT and specifically in UCBT setting remains unclear and controversial. Use of different protocols for transfusion, conditioning regimen, cell content of grafts, among other aspects, could explain the differences between centers. In summary, our analysis shows no influence of RBC or PLT transfusion on mortality in patients undergoing myeloablative single-unit UCBT. More studies are needed to provide consistent conclusions.

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