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POSTER ABSTRACTS

721.ALLOGENEIC TRANSPLANTATION: CONDITIONING REGIMENS, ENGRAFTMENT AND ACUTE TOXICITIES

Impact of Conditioning Intensity and Regimen on Outcomes after Unrelated Cord Blood Transplantation for Patients with Myelodysplastic Syndrome

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Introduction

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) provides curative outcomes in patients with myelodysplastic syndromes (MDS). Unrelated cord blood transplantation (CBT) is an alternative donor option in MDS patients who lack an HLA-matched donor, and the increased availability of CBT expand indications for allo-HSCT in MDS patients.
Because concerns have been expressed regarding decreased hematopoietic recovery and increased relapse after CBT, many studies have been conducted to develop the conditioning regimen in CBT. The optimal intensity of conditioning regimen needs to be addressed based on patient- and disease-related factors. However, the optimal intensity of conditioning regimen in CBT for MDS remains unclear. We here conducted a nationwide retrospective study to clarify the optimal conditioning intensity for MDS in CBT.

Methods

This study included patients diagnosed with *de novo* MDS according to the WHO classification. The clinical data of 856 *de novo* MDS patients (i) who were 16-69 years old and (ii) who underwent their initial single-unit CBT between 2001 and 2020 were collected from the Japanese Data Center for Hematopoietic Cell Transplantation. Cox proportional hazards regression models were used to evaluate variables potentially affecting overall survival (OS), chronic graft-versus-host disease (GVHD)- and relapse-free survival (CRFS), and GVHD- and relapse-free survival (GRFS). Fine and Gray proportional hazards models were used to evaluate variables potentially affecting cumulative incidences of relapse (CIR) and non-relapse mortality (NRM), using cumulative incidence curves to accommodate competing events.

Results

In this study, 501 and 355 patients received myeloablative conditioning (MAC) and reduced-intensity conditioning (RIC), respectively. The median age at CBT was 53 (range,17-69) and 62 years (range,18-69) in MAC and RIC groups, respectively. The most frequently used MAC regimen consisted of total body irradiation >8 Gy-based regimen (n=209, 41.7%), followed by fludarabine (Flu) with myeloablative doses of busulfan (Bu 9.6 to 12.8 mg/kg)-based regimen (n=93, 18.6%). The most frequently used RIC regimen consisted of Flu with reduced doses (80 to 120 mg/m ^{2}) of melphalan-based regimen (n=245, 96.1%), followed by Flu with reduced doses of Bu (6.4 mg/kg)-based regimen (n=63, 17.7%).

The 3-year OS were 44.3 % and 48.8 % in MAC and RIC groups, respectively; the 3-year CRFS were 33.8 and 37.2%; the 3-year GRFS were 19.2 % and 26.9%; the 3-year CIR were 27.1% and 30.0%; and the 3-year NRM were 18.6% and 18.2 %. The univariate analysis revealed that RIC group tended to correlate with higher GRFS than MAC group (Hazard ratio (HR) 0.86 [95% confidential interval 0.74-1.00]; P=0.057), but there was no significant difference of OS (HR 0.95 [0.79-1.13]; P=0.552), CRFS (HR 0.95 [0.80-1.12]; P=0.522), CIR (HR 1.11 [0.87-1.41]; P=0.401) and NRM (HR 0.96 [0.77-1.20]; P=0.735) between MAC and RIC groups. The multivariate analyses confirmed the better GRFS in RIC group than MAC group (HR, 0.73 [0.61-0.89]; P=0.001). Apart from the conditioning intensity, the following six factors were associated with worse overall mortality: patient's age (40-60 years; P=0.039 and >60 years; P<0.001), patient's sex (male; P=0.038), performance status (PS) at CBT (PS 2-4; P=0.033), hematopoietic cell transplantation-specific comorbidity index (HCT-CI) (HCT-CI ≥3; P=0.035), high number of platelet transfusion before HSCT (≥20 times; P<0.001) , and cytogenetic risk group (poor risk; P=0.001).

We next performed the subgroup analysis stratified by the patient's characteristic affecting OS, such as age, sex, PS, HCT-CI, the number of platelet transfusion, and cytogenetic risks. The subgroup analysis showed the better OS (HR, 0.74 [0.59-0.92]; P<0.007), CRFS (HR 0.74, [0.60-0.94]; P=0.012), and GRFS (HR 0.62, [0.50-0.78]; P<0.001) of RIC group than MAC group among patients with patients aged >60 years, but no significant impact on CIR and NRM.

Conclusion

This study showed no significant difference of OS, CRFS, CIR and NRM between MAC and RIC groups, but RIC group correlated with better GRFS in the entire population. Furthermore, the subgroup analysis showed that RIC regimen may be preferable for patient aged >60 years. These findings would improve the management for CBT candidates with MDS.

Disclosures Miyazaki: *Nipponshinnyaku:* Honoraria; *Chugai:* Honoraria; *Celgene:* Honoraria; *Novartis:* Honoraria; *Dainippon-Sumitomo:* Honoraria; *Otsuka:* Honoraria; *Astellas:* Honoraria; *Kyowa-Kirin:* Honoraria. **Takahashi:** *Daiichi Sankyo RD Novare, Otsuka Pharmaceutical:* Research Funding; *Nippon Sinyaku:* Honoraria; *Novartis:* Honoraria; *Chugai Pharmaceutical:* Honoraria; *Asahi Kasei Pharma:* Honoraria; *AstraZeneca:* Honoraria; *Terumo:* Honoraria; *Kyowa Kirin:* Honoraria; *JCR pharma:* Honoraria. **Tanaka:** *Otsuka Pharmaceutical:* Speakers Bureau; *MSD:* Speakers Bureau; *Kyowa-Kirin:* Speakers Bureau; *Daiichi Sankyo:* Speakers Bureau; *Chugai Pharmaceutical:* Speakers Bureau; *Astellas Phrama:* Speakers Bureau; *Asahi Kasei Pharma:* Speakers Bureau; *Abbvie:* Speakers Bureau; *Pfizer:* Speakers Bureau; *Sumitomo Pharma:* Speakers Bureau. **Kanda:** *Amgen:* Ended employment in the past 24 months, Honoraria; *Janssen Pharmaceutical K.K.:* Honoraria; *Novartis Pharma K.K.:* Honoraria; *Sanofi K.K.:* Honoraria; *AbbVie Pharma:* Honoraria; *Megakaryon Co.:* Honoraria; *Eisai Co.:* Research Funding. **Atsuta:** *Novartis Pharma KK:* Speakers Bureau; *Otsuka Pharmaceutical Co., Ltd:* Speakers Bureau; *CHUGAI PHARMACEUTICAL CO., LTD.:* Speakers Bureau; *Meiji Seika Pharma Co, Ltd.:* Honoraria; *JCR Pharmaceuticals Co., Ltd.:* Consultancy.

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