Outcomes of autologous versus allogeneic hematopoietic stem cell transplantation for peripheral T-cell lymphomas: A multicenter retrospective study in china.

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Abstract

To date, there is no consensus on choosing autologous hematopoietic stem cell transplantation (auto-HSCT) or allogenic HSCT (allo-HSCT) for peripheral T-cell lymphomas (PTCLs). This study aimed to compare the relative efficacy of auto-HSCT versus allo-HSCT for patients with PTCLs. We conducted a multicenter retrospective study about 128 patients who underwent auto-HSCT (n=72) or allo-HSCT (n=56) at 8 medical centers across China between July, 2007 and June, 2017. With a median follow-up of 30 (2-143) months, outcomes of patients receiving auto-HSCT were better than those in allo-HSCT (3-year OS: 70% versus 46%, P = 0.003; 3-year PFS: 59% versus 44%, P = 0.002). Three-year non relapse rate (NRM) in auto-HSCT recipients was 6%, compared with 27% for allo-HSCT recipients (P =0.004). There was no difference in relapse rate between these two groups (34% in auto-HSCT versus 29% in allo-HSCT, P =0.84). Specifically, patients with low PIT score who received auto-HSCT group in upfront setting had better outcome than patients with high PIT score (3-year OS: 85% versus 40%, P = 0.003). Regarding remission status before transplantation, patients with CR undergoing auto-HSCT had the best outcome (3-year OS: 88% versus 48% in allo-HSCT; P =0.008). For patients less than CR, the outcome of patients undergoing auto-HSCT was similar to that in allo-HSCT (3-year OS:51% versus 46%; P =0.30). When further checking patients in PD or SD, the survival curve of patients in the allo-HSCT group was better than that in the auto-HSCT group. It is plausible to choose auto-HSCT versus allo-HSCT according PIT score and remission status before transplantation.

Introduction

Peripheral T-cell lymphomas (PTCLs) are a group of biologically and clinically heterogeneous malignancies with generally poor outcome. With geographical variations, PTCLs represent less than 15% of all non-Hodgkin's lymphomas (NHL) in Western countries(1), with high percentage approximately 25–30% in East Asia where NK/T-cell lymphomas are more frequent(2, 3). Peripheral T-cell lymphoma not otherwise specified (PTCL-NOS), NK/T-cell lymphoma (NK/TCL), Anaplastic lymphoma kinase (ALK) positive or negative anaplastic large cell lymphoma (ALCL), and angioimmunoblastic T-cell lymphoma (AITL) account for more than 90% of PTCLs in East Asia. Less frequent subtypes include Hepatosplenic γ/δ lymphoma (HSL), enteropathy-type T-cell lymphoma, and subcutaneous-like T-cell lymphoma.

The prognosis of PTCLs were generally unsatisfactory both in newly diagnosed setting and in refractory/relapsed settings except for ALK-positive ALCL(4–6). Despite the rapid progress in the knowledge of (epi)genetic changes about PTCLs and availability of these new drugs, none of them were incorporated into standard first-line treatment(7, 8). CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisolone) or CHOP-like regimens remains standard first-line therapy. Currently, there were no consensus for subsequent consolidations. Autologous hematopoietic stem cell transplantation (auto-HSCT) had been exploited as consolidation in first remission and refractory/relapsed settings(9–12). Allogeneic HSCT (allo-HSCT) were mainly tried in relapsed and refractory patients and showed promising results(13–15). Key questions about the relative efficacy of auto-HSCT versus allo-HSCT, identification of their optimal candidates, and optimal HSCT timing remained uncertain. We conducted a multi-center

retrospective study of 128 patients with PTCLs who underwent HSCT in 8 hospitals across China between July, 2007 and June, 2017.

Patients And Methods

Study design and population

A multicenter retrospective study was conducted to investigate the clinical outcomes of 128 consecutive patients with PTCLs who received auto-HSCT or allo-HSCT from 8 tertiary hospitals across China between July, 2007 and June, 2017. All diagnoses were confirmed and classified by pathologists at each institution according to the 2016 edition of the WHO classification of lymphoid neoplasms. When there was difficulty in diagnosis, central consensus pathology review was also applied. The eligibility criteria were Eastern Cooperative Oncology Group performance status of < 2, enough cardiac, hepatic, and renal function to undergo transplantation, and the absence of second or third transplantations. The decision of patients to receive auto-HSCT or allo-HSCT depending physicians' judgement based on the availability of donors and unfavorable prognostic factors. Our study was approved by the Medical Ethics Review Boards at each center.

Baseline characteristics of patients were collected regarding age, gender, histological subtype, 'B' symptoms, stage, IPI score, extranodal involvement at diagnosis, date of transplantation, the number of lines of chemotherapies before HSCT, time from diagnosis to HSCT, disease status at transplantation, donor type, conditioning regimens, graft-versus-host disease (GVHD) prophylaxis, engraftment, and information on acute GVHD (aGVHD) and chronic GVHD (cGVHD), complications, response to transplantation, duration of response, last follow-up, date and causes of death and other outcomes after HSCT.

Transplantation Procedures

For auto-HSCT, Patients were mobilized with high dose chemotherapy and rhG-CSF. BEAM (carmustine, etoposide, cytarabine, melphalan) and CBV (cyclophosphamide, etoposide, and BCNU) were the most common conditioning regimens. All allo-HSCT included in our study were myeloablative. Three myeloablative conditioning regimens were mainly used(16): 1) modified BuCy regimen: 2) modified FB regimen: substitution of cyclophosphamide in BuCy with fludarabine; 3) TBI + Cy regimen. Patients received allografts from HLA-matched donors, HLA-matched unrelated donors, or HLA-haploidentical donors. GVHD prophylaxis was cyclosporine A (CsA), methotrexate (MTX) based and mycophenolate mofetil (MMF) or in combination with ATG (Thymoglobulin) in haploidenical or unrelated donor transplantation setting.

Endpoints And Definitions

The primary endpoints of this study were overall survival (OS) and progression free survival (PFS). OS was calculated from the day of transplantation to the day of death from any cause, or last follow-up for survivors. PFS was defined as the date of transplantation for CR patients at transplantation or the date achieved CR after transplantation for non-CR patients at transplantation to the date of disease relapse, progression, or death, or last follow-up for survivors without evidence of disease. Secondary endpoints were non-relapse mortality (NRM) and relapse (progression). NRM was defined as death from any cause related to transplantation without evidence of lymphoma progression. Time to relapse and time to NRM were calculated from the date of transplantation. Neutrophil engraftment was calculated from the day of transplantation to the first day of 3 consecutive days with the neutrophil count in blood above 0.5×10^9/L. Platelet engraftment was defined as the number of days from transplantation to the first day of 7 consecutive days with platelet count was higher than 20×10^9/L, unsupported by platelet transfusion. The development of aGVHD and cGVHD (limited or extensive) were graded according to international criteria(17, 18).

Responses to treatment were evaluated according to the International Workshop non-Hodgkin's lymphomas criteria(19). Patients were evaluated computed tomography (CT) scan, positron emission tomography computed tomography (PET-CT), or bone marrow aspiration or biopsy before and + 3 months, + 6 months, + 9 months, + 12 months after allo-PBSCT, and thereafter semi-annually until 5 years after transplantation unless otherwise clinically indicated. The definitions of sensitivity to chemotherapy were as follows: primary sensitive was defined as CR or partial remission (PR) after first-line chemotherapy; primary refractory, never reached CR or PR with first-line chemotherapy; relapse sensitive, achieved CR or partial remission (PR) again after salvage chemotherapy; relapse resistant, once getting CR or partial remission (PR) with primary chemotherapy but never achieved any CR or PR after progression or relapse with salvage chemotherapy.

Statistical Analysis

Statistical descriptive analyses were used for baseline and transplantation characteristics. The probability of survival (OS and PFS) was estimated with the Kaplan-Meier method with 95% confidence intervals (CIs) and statistical significance was compared by the log rank test. Cumulative incidences of NRM, Relapse and GVHD were calculated with competing-risk analysis and compared with Gray's test. All analysis was performed with R software, version 2.12.

Results

Patient characteristics

A total of 128 patients with PTCLs were included in this study. 72 patients received auto-HSCT, and 56 patients underwent allo-HSCT. Patient characteristics are shown in Table 1. As summarized in Table 1, NK/T cell lymphoma (n = 37), ALK-positive ALCL (n = 24), PTCL-NOS (n = 23), AITL (n = 19) were dominant histological subtypes. Other subtypes (n = 16) include subcutaneous panniculitis-like T-cell lymphoma

(SPTCL) (n = 5), enteropathy-associated T-cell lymphoma (EATL) (n = 2) in the auto-HSCT group (n = 7), and hepatosplenic γ/δ T-cell lymphoma (HSTCL) (n = 4), SPTCL(n = 3), cutaneous γ/δ T-cell lymphoma (n = 1), and CD8-positive epidermotropic cytotoxic T-cell lymphoma (n = 1) in the allo-HSCT group (n = 9). There were no significant differences between auto-HSCT group and allo-HSCT group in terms of sex distribution, median age, proportion of different histological subtypes, proportion of patients with B symptoms at diagnosis, CNS and extranodal involvement at diagnosis, prognostic index (aaIPI and PIT score), lines of prior therapy and interval between diagnosis and HSCT. Nevertheless, there were more unfavorable variables in the allo-HSCT group. Allo-HSCT recipients were more likely to be diagnosed with stage III or IV disease and bone marrow involvement, and less likely to be diagnosed with ALK-positive ALCL.

Treatment- and transplantation-related characteristics are listed in table 2. The proportion of patients with PD in the allo-HSCT group was higher than that in the auto-HSCT group (32% vs 4.2%, P□0.001). And allo-HSCT recipients were more likely to be with chemotherapy-resistant disease at the time of HSCT (41% vs 8.4%, P = 0.001). Conditioning regimens in the auto-HSCT group consisted of BEAM, CBV, and TBI/Cy based regimens in 88.7% of all patients. All the conditioning regimens in the allo-HSCT group were myeloablative. TBI/Cy and Bu/Cy based regimens accounted for more than 80% of all patients. Peripheral blood was the sole graft source for all patients. 32 (57%) of the 56 allo-HSCT recipients received their grafts from HLA-matched siblings, 20 patients (35.7%) from HLA haploidentical siblings, and 4 patients (7.2%) HLA-matched unrelated donors.

General Clinical Outcomes

The median follow-up period for survivors was 30 months (range, 2-143 months). After excluding 11 patients who were lost to follow-up, clinical outcomes about the remaining 117 patients were finally analyzed. As expected, the engraftment of neutrophil and platelets in the auto-HSCT were both shorter than those in the allo-HSCT group (neutrophil engraftment: 10 days (range, 9 to 19 days) in auto-HSCT vs 13 days (range, 9 to 27 days) in allo-HSCT, P□0.001; platelets engraftment: 12 days (range, 6 to 46 days) in auto-HSCT vs 15 days (range, 9 to 38 days) in allo-HSCT, P = 0.009). For the allo-HSCT group, the cumulative incidence of grade □-□ acute GVHD at 100-day was 35.29% (95% confidence interval [CI], 22–48%) (Supplemental Fig. 1A). The cumulative incidence of limited and extensive chronic GVHD at 2 years was 40% (95% CI, 26–52%) (Supplemental Fig. 1B).

The clinical characteristics in the allo-HSCT group were more unfavorable than those in the auto-HSCT group. The estimated 3-year OS in the allo-HSCT group was much lower than that in the auto-HSCT group (46% (95% CI, 34–63%) vs 70% (95% CI, 58–85%), P = 0.003, Fig. 1A). The 3-year PFS in the allo-HSCT group was also lower than that in the auto-HSCT group (44% (95% CI, 32–60%) vs 59% (95% CI, 47–76%), P = 0.02, Fig. 1B). 3-year NRM for allo-HSCT recipients was 27% (95% CI, 16–40%) compared with 6% (95% CI, 2–14%) for auto-HSCT recipients (P = 0.004, Fig. 1C). There was no difference in relapse rates between these two groups (29% (95% CI 17–42%) in allo-HSCT vs 34% (95% CI 20–48%) in auto-HSCT, P

= 0.84; Fig. 1D). As for causes of death (Supplemental Table S1), lymphoma was the most common reason in both groups. Causes other than lymphoma progression in the auto-HSCT group were infection (n = 4), cerebral hemorrhage (n = 1), and multi-organ dysfunction (n = 2). And 14 patients died of transplantation related causes in the allo-HSCT group (graft failure (n = 1), massive hemorrhage of gastrointestinal tract (n = 1), infection (n = 2), cerebral hemorrhage (n = 2), GVHD (n = 3), and multi-organ dysfunction (n = 5).

Outcomes In Different Subgroups

Subgroup analysis about patients with different Prognostic Index was firstly performed. For patients who received auto-HSCT group in upfront setting, the survival of patients with PIT 0 or 1 was significantly better than that of patients with PIT 2 or higher. (3-year OS: 85% vs 40%, P = 0.003; 3-year PFS:75% vs 36%, P = 0.006, Fig. 2A and B). For patients with PIT 2 or higher who received auto-HSCT or allo-HSCT in upfront settings, there was also no difference both in 3-year OS (40% vs 34%, P = 0.59, Fig. 2C) and PFS (36.4% vs 35.7%, P = 0.85, Fig. 2D). When specifically checking their baseline characteristics, patients who received up-front allo-HSCT had more patients with stage IV disease (92.9% (13/14) versus 70.6% (12/17)) in patients who received upfront auto-HSCT), more patients in PD/SD (35.7% (5/14) vs 5.9% (1/17)) in patients who received upfront auto-HSCT), and more bone marrow involvement (78.6% (11/14) versus 35.3% (6/17)) in patients receiving upfront auto-HSCT) (data not shown).

According to disease status before transplantation, patients in CR undergoing auto-HSCT had the best 3-year OS (88% v 48% in allo-HSCT; P = 0.008, Fig. 3A). But there was no significant difference in PFS (73% v 54%; P = 0.15, Fig. 3B). It may be because of the small number of patients (n = 7) in CR received allo-HSCT. After excluding patients with CR, 29 patients received auto-HSCT, and 47 patients received allo-HSCT. There was no difference both in 3-year OS (51% v 46%; P = 0.304, Fig. 3C) and PFS (46% v 42%; P = 0.49, Fig. 3D) between this two groups. Also, there was no difference in 3-year NRM (10% v 27%; P = 0.11, Supplemental Fig. 2A) and relapse ((44% v 31%; P = 0.48, Supplemental Fig. 2B) rate.

Further analysis about patients less than CR before transplantation were also performed. For patients with PR, there was no difference in 3-year OS (59% v 48%; P = 0.40, Fig. 4A) and PFS (51% v 41%; P = 0.39, Fig. 4B) between auto-HSCT and allo-HSCT group. For patients with PD or SD, there was still no difference in OS (43% v 22%; P = 0.85, Fig. 4C) and PFS (43% v 25%; P = 0.59, Fig. 4D) between these two groups. But the survival curve of patients with PD or SD in the auto-HSCT group did not plateau, compared with the curve of patients with PD or SD in the allo-HSCT group. We'd like to point out here that there were only 6 patients with PD or SD that received auto-HSCT. There were 23 patients with PD or SD in the allo-HSCT group. When specifically examining the clinical characteristics of patients less than CR, allo-HSCT recipients had more patients with advanced stages ((85% with stage III-IV disease compared with 48% in the auto-HSCT group), more bone marrow involvement (40% vs 17% in the allo-HSCT group) (data not shown).

According to the different histology of patients between these two groups, subgroup analyses were also performed. Given the good prognosis of ALK-positive ALCL and that there were more ALK-positive ALCL in the auto-HSCT group, we firstly excluded ALK-positive ALCL patients in both groups. Patients in the auto-HSCT group (n = 50) still had better 3-year OS (71% vs 50%, P = 0.01, Supplemental Fig. 3A) than that in the allo-HSCT group (n = 49), with no difference in PFS (56% vs 46%, P = 0.08, Supplemental Fig. 3B). For patients with PTCL-NOS, patients in the auto-HSCT group had better 3-year PFS (57% vs 32% in allo-HSCT, P = 0.047, Supplemental Fig. 4B), with no difference in OS (71% in auto-HSCT VS 42% in allo-HSCT, P = 0.06, Supplemental Fig. 4A). There were also no differences both in 3-year OS (56% in auto-HSCT vs 57% in allo-HSCT, P = 0.98, Supplemental Fig. 4C) and PFS (34% in auto-HSCT vs 57% in allo-HSCT, P = 0.45, Supplemental Fig. 4D) for patients with AITL. For patients with NK/TCL, patients in the auto-HSCT had better 3-year OS (82% vs 41% in the allo-HSCT, P = 0.03, Supplemental Fig. 4E), with no difference in PFS (65% in auto-HSCT VS 46% in allo-HSCT, P = 0.11, Supplemental Fig. 4F).

Discussion

The outcome of first-line chemotherapy is far from optimal until today for most PTCLs subtypes. HSCT is a valuable option to achieve longer survival or cure this disease. In this study, we reported the outcomes of a multi-center retrospective study of 128 patients who underwent HSCT in 8 hospitals across China. To the best of our knowledge, this is the largest report in China. In general, the survival of patients in the auto-HSCT group was better than that in the allo-HSCT group. NRM was as expected lower in the auto-HSCT group. Relapse rates were similar between these two groups. It was difficult to draw definite conclusions because of the differences in baseline characteristics between these two groups. Compared with patients in the auto-HSCT group, patients undergoing allo-HSCT were more likely to be diagnosed with ALK-negative ALCL, advanced stage, bone marrow involvement, or relapsed/refractory disease status before transplantation. We further compared the survival of patients in different subgroups. Firstly, we found that patients with low PIT score who received auto-HSCT group in upfront setting had better outcome than patients with high PIT score. Secondly, patients with CR undergoing auto-HSCT had the best outcome (3-year OS: 88% vs 46% in the allo-HSCT group). For patients with PR, their survival was similar (3-year OS: 59% in auto-HSCT vs 48% in allo-HSCT). The survival curve of patients with PD or SD undergoing allo-HSCT was better than that of auto-HSCT recipients. Our results suggested that it was plausible to choose auto-HSCT versus allo-HSCT according PIT score and remission status before transplantation.

The efficacy of auto-HSCT had been evaluated both in retrospective and prospective studies, with reported three- to five-year OS raging from one third to more than two thirds(12, 20–23). The huge variability in survival rate was related to the heterogeneity in baseline characteristics of patients included in above studies. Among the baseline factors, remission status before HSCT was the most important factor affecting post-HSCT survival. The 3-year OS in our study was 70% (58–85%). This was higher than OS of 59% (49–68%) in the study by CIBMTR (Center for International Blood and Marrow Transplant Research), where 64 patients (56%) were in CR at transplantation(21). Also, the five-year OS was only 46% in the largest Asian study, which comprised of 104 (77%) patients in CR/PR(20). It can be partially

explained by three reasons. Firstly, over 90% of patients (66/72) undergoing auto-HSCT were in CR (37) or PR (29) at transplantation in our study. Secondly, the percentage of ALK-positive ALCL patients (19/72) was higher than that (12/135) in the Asian study. Thirdly, the median follow-up time was only 23 (4-143) months, which was shorter than that in the above studies.

Another question was which part of patients can benefit from auto-HSCT. Prognostic Index attained at diagnosis wasn't so important for patients who received HSCT in relapsed settings. So, we only checked the role of PIT score in the upfront setting. We found that the prognosis of patients with PIT 2 or higher who received upfront auto-HSCT was very poor, which was consistent with Shigeo's study(24). We'd rather believe that it was reasonable to avoid auto-HSCT for patient with higher PIT score in the upfront setting.

Because of the fact that the vast majority of patients will eventually relapse after upfront chemotherapies, even when auto-HSCT were followed thereafter(25, 26), or remained refractory at the beginning, allo-HSCT was mostly performed in the relapsed or refractory setting. About one half of patients could achieved long-term survival through allo-HSCT, which was confirmed in large retrospective studies from CIBMTR(21),Europe(13), Asian(20). Likewise, there were also kinds of heterogeneity in histologic subtypes, stages, remission status at transplantation, intensity of conditioning regimens, donor types and GVHD prophylaxis among previous reports. In our study, over 90% of patients (52/56) in the allo-HSCT group were diagnosed with advanced stages. And more than 80% of patients (48/56) were non-CR at transplantation. The 3-year OS of allo-HSCT recipients was 46% (34–63%), which was similar with previous studies. In particular, all allo-HSCT in our study were myeloablative conditioning regimens. There were few studies that all patients received myeloablative conditioning regimens. With regarding the impact of regimens intensities on survival, there was two studies but failed to find significant difference either in toxicity and survival between myeloablative and reduced conditioning regimens(13, 21). With progress in supportive care, GVHD prophylaxis, and donor selection system, there were 20 patients in our study that receive HLA-haploidentical HSCT.

Because of the inherent toxicity of conditioning regimens and GVHD along with allo-HSCT, NRM in the allo-HSCT group was as expected higher than that (27% vs 6%) in the auto-HSCT group. But there was no difference in relapse rates (29% vs 34% in auto-HSCT). One possible explanation was that approximately 40% patients of patients (23/56) were at progressive status before transplantation. Allo-HSCT in our study, like most previous studies, often performed as salvage treatment, compromising the effectiveness of allo-HSCT. As for causes of death, lymphoma progression or relapse was the leading factor in both groups, which indicated that prevention of relapse was also very important in the allo-HSCT.

More practical issues for physicians were how to choose the type of HSCT, HSCT timing and identification of optimal populations. With huge heterogeneity in disease itself and results of previous studies, it was no consensus about these issues until today. Hopefully with evidence from both retrospective and prospective cohort studies, auto-HSCT was recommended as consolidation in most institutes for patients who achieved a CR or PR after first-line therapies(22, 27). Two recent prospective

studies also failed to demonstrate that allo-HSCT could achieve better survival than auto-HSCT for patients in first remission(28, 29). Allo-HSCT for patient in first remission still remained controversial until today. To further explore these issues, we assessed the survival of patients according to the disease status at transplantation in this study. Consistent with literature, patients with CR can benefit from auto-HSCT. For patients with PR, their survival was similar between auto-HSCT and allo-HSCT. Although no significant difference was noted, the survival curve of patients in progression underwent allo-HSCT was better than that in auto-HSCT. Based on the evidence and results above, we are proposing that it is advisable to choose auto-HSCT for patients with CR with previous treatments. And for patient with PR, either modality could be advised. For patients in progression disease, it was more plausible to proceed allo-HSCT. This was just our scenario. It was urgently to be confirmed in further prospective or randomized studies.

There were several limitations in this study. Firstly, the basal characteristics and prognosis of patients who were unable to undergo transplantation were not included in this study. It can't reflect the whole clinical picture of PTCLs. Secondly, due to the retrospective design and small size of this study, the conclusions should be interpreted with caution. Nevertheless, this study showed patients with PTCLs can benefit from both auto-HSCT and allo-HSCT. Specifically, for patients with high PIT score in upfront setting, it was wise to avoid auto-HSCT. For patients with CR with previous treatments, it is advisable to undergo auto-HSCT. For patient with PR, either modality works well. It was wise to proceed allo-HSCT for patients in progression disease. We concluded to choose auto-HSCT versus allo-HSCT according PIT score and remission status before transplantation.

Abbreviations

Auto-HSCT:autologous hematopoietic stem cell transplantation; Allo-HSCT:allogenic HSCT; PTCLs:peripheral T-cell lymphomas; OS:overall survival; PFS:progression free survival; NRM:non-relapse mortality; CR:complete remission; PR, partial remission; SD, stable disease; PD, progression disease; NHL:non-Hodgkin's lymphomas; PTCL-NOS:Peripheral T-cell lymphoma not otherwise specified; NK/TCL:NK/T-cell lymphoma; ALCL:Anaplastic lymphoma kinase (ALK) positive or negative anaplastic large cell lymphoma; AITL:angioimmunoblastic T-cell lymphoma; HSL:Hepatosplenic γ/δ lymphoma; CHOP:cyclophosphamide, doxorubicin, vincristine, and prednisolone; NA:not available; TBI/Cy:total body irradiation, cyclophosphamide; Bu/Cy:busulfan, cyclophosphamide; BEAM:semustine, carmustine, etoposide, cytarabine, melphalan; CBV:cyclophosphamide, etoposide, and BCNU; FB:fludarabine, busulfan; HLA:human leukocyte antigen; GVHD:graft-versus-host disease; CSA:cyclosporine; MTX:methotrexate; ATG:antithymocyte globulin; MMF:mycophenolate mofetil.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Medical Ethics Review Boards at each medical center. Since 2000, patients at all these 8 medical centers have provided informed consent authorizing the use of their personal information for research purposes.

Consent for publication

Not applicable.

Availability of data and materials

The dataset supporting the conclusions of this article are available in the clinical data (which were sorted from 8 above medical centers) repository of the First Medical Center of Chinese PLA General Hospital, Beijing 100853, China; Tel: +86-010-55499303. The datasets are available from the corresponding author on reasonable request.

Competing interests

All authors have no competing financial interests.

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Authors' contributions

Zhao wang, Liangding Hu, Wenrong Huang designed the study and initiated this work; Data was obtained by Zhenyang Gu, Yujun Dong, Xiaorui Fu，Nainong Li，Yao Liu，Xiaoxiong Wu，Yini Wang; Yuhang Li; Hanyun Ren，Mingzhi Zhang，Xiaofan Li，Maihong Wang，Yamei Wu; Daihong Liu. All statistical analyses were performed by Zhenyang Gu, Yujun Dong, Xiaorui Fu. Zhenyang Gu wrote the paper; all the authors were involved in the interpretation of the results; read, gave comments, and approved the final version of the manuscript; had full access to the data in the study; and take responsibility for the accuracy of the data analysis.

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Tables

Table 1. Main characteristics of All Patients.

Characteristics	Auto-HSCT No. (%)	Allo-HSCT No. (%)	P
No. of patients	72	56	
Sex			0.06
Male	44 (61.1)	43 (76.8)	
Female	28 (38.9)	13 (23.2)	
Median Age at HSCT (range)	35 (9-60)	34 (12-59)	0.81
Histology			0.09
PTCL-NOS	11 (15.3)	12 (21.4)	
AITL	12 (16.7)	7 (12.5)	
ALK-pos ALCL	19 (26.4)	5 (8.9)	
Alk-neg ALCL	6 (8.3)	3 (5.4)	
NK/T lymphoma	17 (23.6)	20 (35.7)	
other	7 (9.7)	9(16.1)	
B symptoms at diagnosis	42 (58.3)	38 (69.1)	0.21
BM involvement at diagnosis	11 (15.3)	23 (41.8)	0.001
CNS involvement at diagnosis	4 (5.8)	3 (5.6)	1.00
Extranodal involvement at diagnosis	54 (75.0)	40 (72.4)	0.65
aaIPI score≥2	41 (57.7)	31 (63.3)	0.54
PIT score≥2	25 (37.3)	17 (34.0)	0.85
Disease stage at diagnosis			
	13 (18.1)	3(5.5%)	0.03
	59 (81.9)	52(94.5)	
Unknown	0	1	
lines of therapy before HSCT			0.73
≤2	39 (54.2)	27 (57.4)	
2	33 (45.8)	20 (42.6)	
Median time from diagnosis to HSCT, months, (range)	9 (4-66)	6 (1-144)	0.28

Abbreviations: Auto-HSCT, autologous hematopoietic stem cell transplantation; Allo-HSCT, allogenic HSCT; PTCL-NOS, peripheral T-cell lymphoma, not otherwise specified; AITL, angioimmunoblastic T-cell lymphoma; ALK-pos ALCL, anaplastic lymphoma kinase positive anaplastic large cell lymphoma; ALK-neg ALCL, ALK-negative ALCL; BM, bone marrow; CNS, central nervous system; PIT, prognostic index for PTCLs.

Table 2. Treatment- and Transplantation-Related Characteristics

Characteristics	Auto-HSCT No. (%)	Allo-HSCT No. (%)	P
Disease status at HSCT			0.001
CR	37(51.4%)	8(17.8%)	
PR	29(40.3%)	25(46.3%)	
SD	3(4.2%)	5(8.9%)	
PD	3(4.2%)	18(32.1%)	
Chemosensitivity status at HSCT			0.001
Primary sensitive	54(75%)	25(44.6%)	
Primary resistant	3(4.2%)	14(25 %)	
Relapse sensitive	12(16.7%)	8(14.3%)	
Relapse resistant	3(4.2%)	9(16.1%)	
Conditioning regimens			0.001
TBI/Cy based	11(15.5%	33 60%	
BuCy based	2 2.8%	12 21.8%	
FB based	0	5 9.1%	
BEAM	37 52.1%	4 7.3%	
CBV	15 21.1%	0	
Others	6 8.5%	1(1.8%)	
Unknown	1	1	
Donor HLA match	NA		
HLA-identical sibling		32(57.1%)	
Haplo-identical sibling		20(35.7%)	
Matched unrelated		4(7.2%)	
GVHD prophylaxis	NA		
CSA+MTX		6 10.9%)	
ATG+ CSA+MTX		1(1.8%)	
CsA+MTX+MMF		26(47.3%)	
ATG+ CSA+MTX+MMF		17(30.9%)	
Other		5(9.1%)	
Unknown		1	
Follow-up of survivors, median (range), months	23 (4-143)	39 (2-112)	0.51

Abbreviations: Auto-HSCT, autologous hematopoietic stem cell transplantation; Allo-HSCT, allogenic HSCT; CR, complete remission; PR, patial remission; SD, stable disease; PD, progression disease; NA, not available; TBI/Cy, total body irradiation, cyclophosphamide; Bu/Cy, busulfan, cyclophosphamide; BEAM, semustine/carmustine, etoposide, cytarabine, melphalan; CBV, cyclophosphamide, etoposide, and BCNU; FB, fludarabine, busulfan; HLA, human leukocyte antigen; GVHD, graft-versus-host disease; CSA, cyclosporine; MTX, methotrexate; ATG, antithymocyte globulin; MMF, mycophenolate mofetil.

Figures

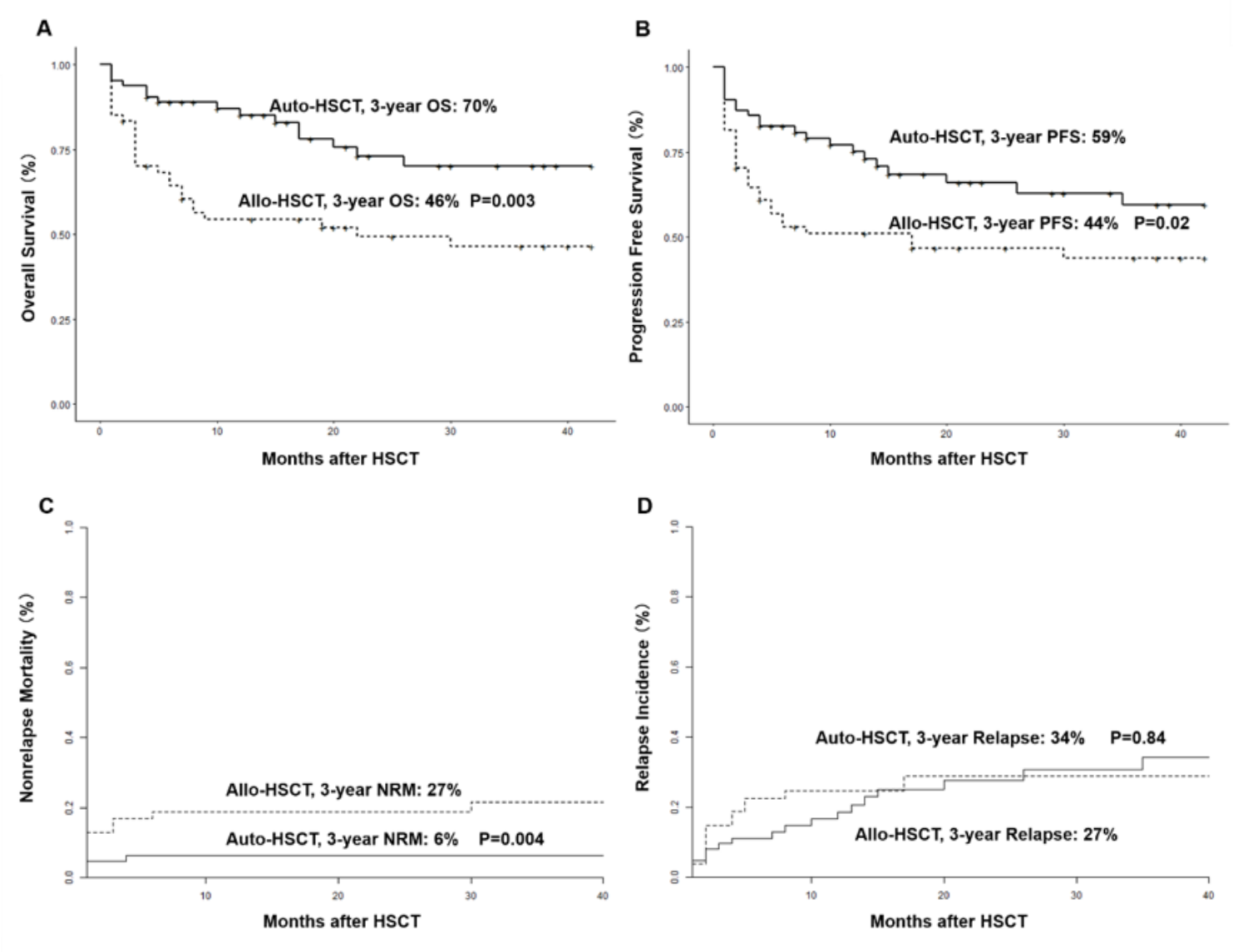

Figure 1

A. Adjusted 3-year overall survival (OS); B. Adjusted 3-year progression-free survival (PFS); C. Cumulative incidence of 3-year nonrelapse mortality (NRM); D. Cumulative incidence of relapse/progression.

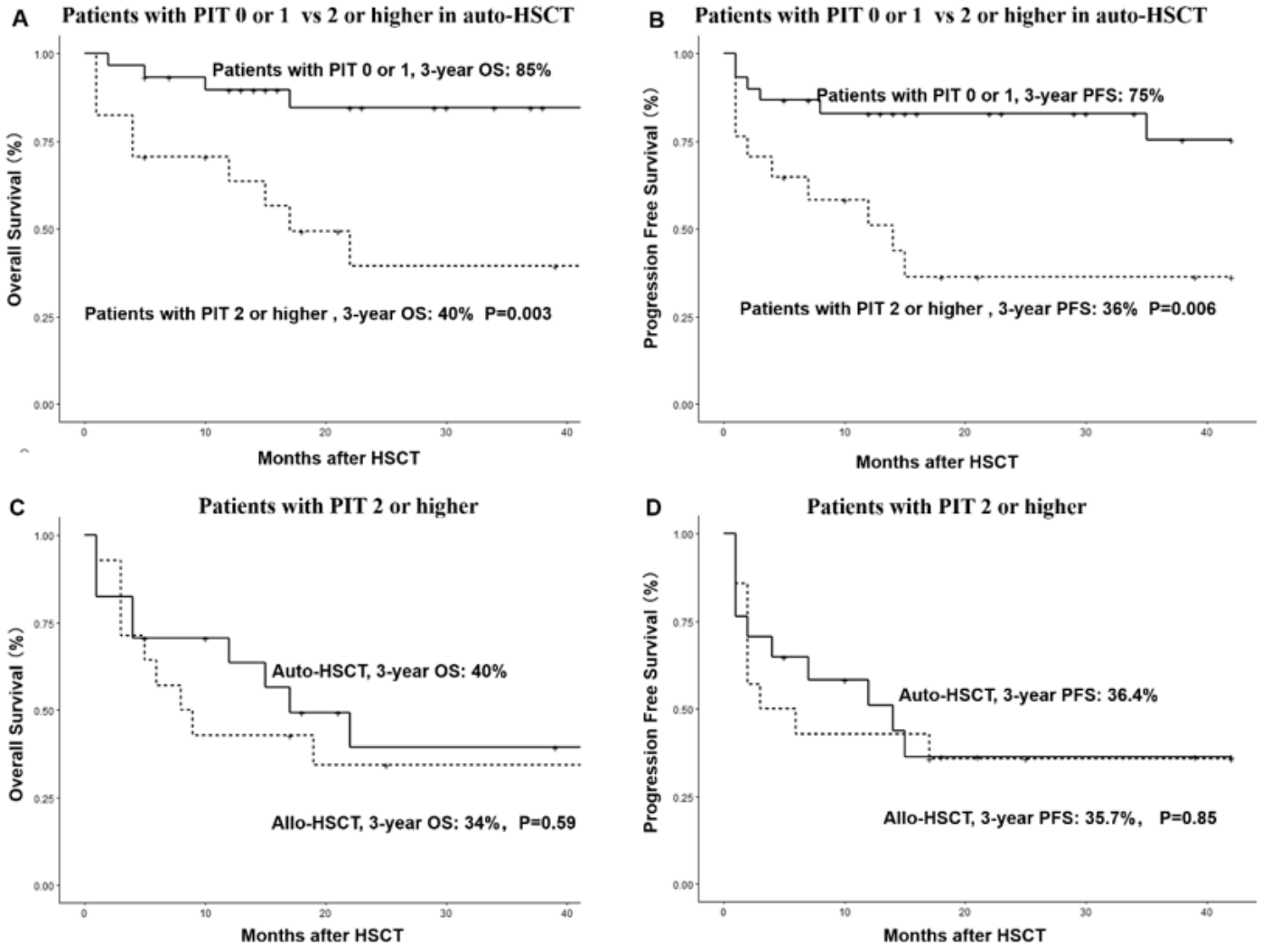

Figure 2

For patients who received auto-HSCT group in upfront setting, the survival of patients with PIT 0 or 1 was significantly better than that of patients with PIT 2 or higher. (3-year OS:85% (95% CI, 72–100%) vs 40% (95% CI, 20–77%), P= 0.003; 3-year PFS:75% (95% CI, 59–97%) vs 36% (95% CI, 19–71%), P= 0.006, A and B). For patients with PIT 2 or higher who received auto-HSCT or allo-HSCT in upfront settings, there was no difference both in 3-year OS (40% (95% CI, 20–77%) vs 34% (95% CI, 16–72%), P= 0.59, C) and PFS (36.4% (95% CI, 18.6–71.4%) vs 35.7% (95% CI, 17.7–70%), P= 0.85, D).

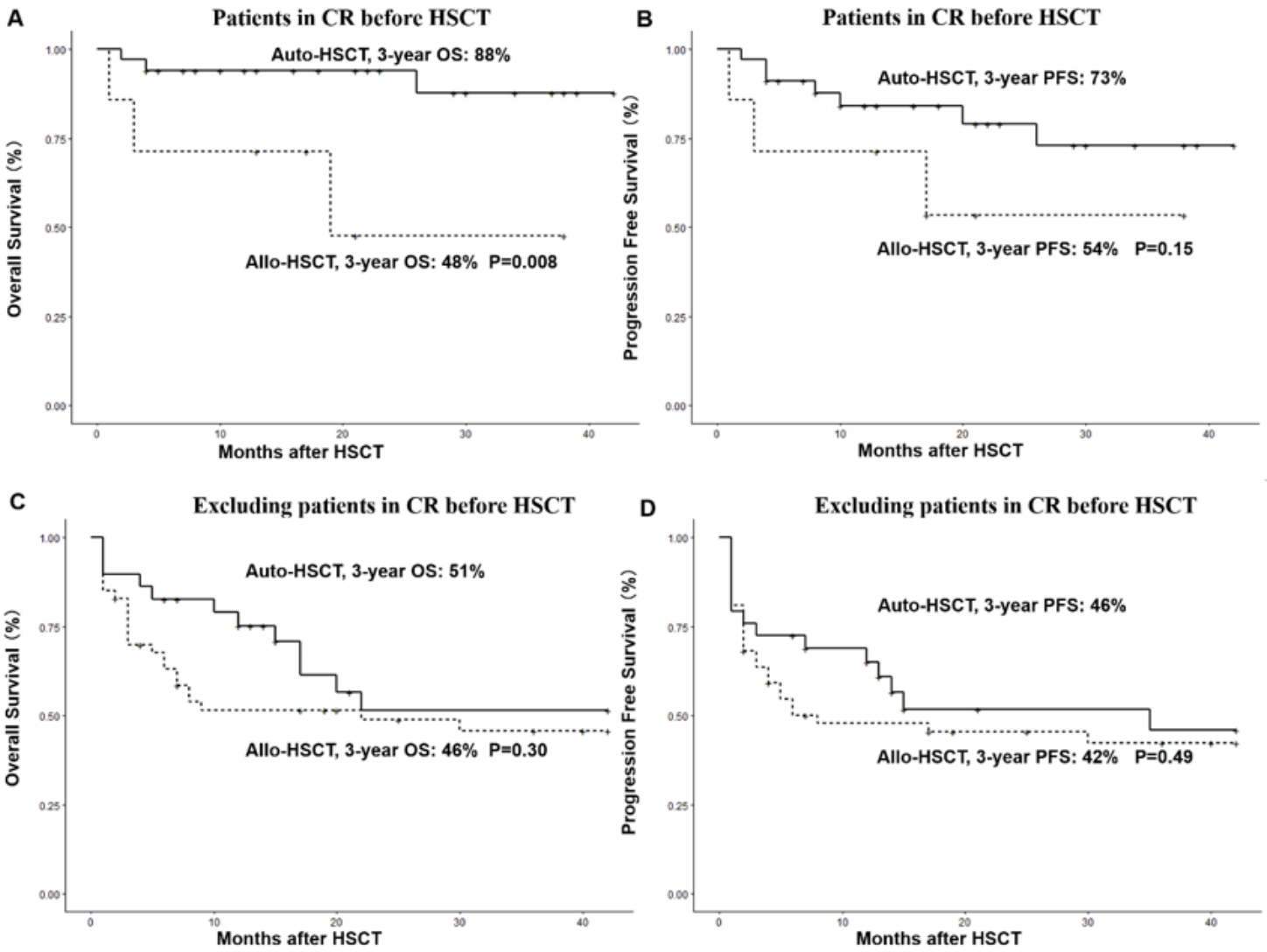

Figure 3

For patients in CR, the outcome of patients undergoing auto-HSCT had the best 3-year OS (88 %(95% CI, 75–100%) vs 48%(95% CI, 19–100%), P= 0.008,A); but there was no significant difference in PFS (73 % (95% CI, 57–94%) vs 54%(95% CI, 26–100%), P= 0.15, B). For patients excluding CR, There were no difference both in 3-year OS (51%(95% CI, 35–77%) vs 46%(95% CI, 33–64%), P= 0.30, C) and PFS (46% (95% CI, 30–71%) vs 42%(95% CI, 30–60%) P= 0.49, D) between this two groups.

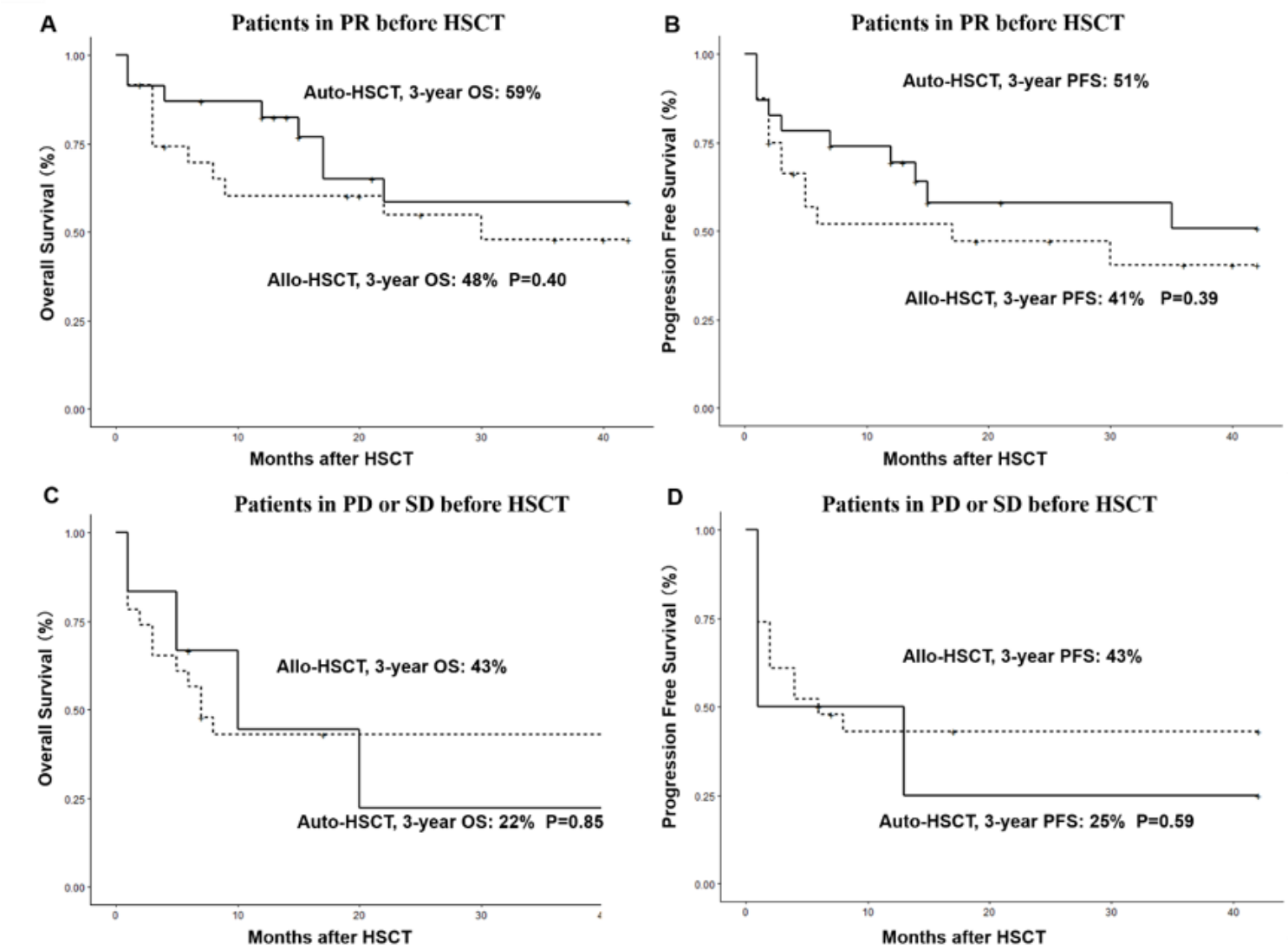

Figure 4

For patients with PR, there was no difference in 3-year OS (59%(95% CI, 40-86) vs 48%(95% CI, 30-76%); P=0.40, A) and PFS (51%(95% CI, 32-80) vs 41%(95% CI, 24-69%) , P=0.39, B) between auto-HSCT and allo-HSCT group. For patients with PD or SD, there was still no difference in OS (43%(95% CI, 27-69%) vs 22%(95% CI, 4-100), P=0.85, C) and PFS (43%(95% CI, 27-69%) vs 25%(95% CI, 5-100) ; P=0.59, D) between these two groups.

Supplementary Files

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