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ORIGINAL ARTICLE

HLA-mismatched stem cell microtransplantation compared to matched-sibling donor transplantation for intermediate/high-risk acute myeloid leukemia

Limin Liu[1,2,3] · Xingxia Zhang[4] · Huiying Qiu[1,2,3] · Xiaowen Tang[1,2,3] · Yue Han[1,2,3] · Chengcheng Fu[1,2,3] · Zhengming Jin[1,2,3] · Mingqing Zhu[1,2,3] · Miao Miao[1,2,3] · Depei Wu[1,2,3]

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Abstract

HLA-mismatched stem cell microtransplantation is a new form of transplantation reported in recent years. We compared 59 patients undergoing microtransplantation to 66 patients undergoing HLA-matched sibling donor (MSD) transplantation at the same period from April 2012 to December 2016, who all suffered from intermediate/high-risk acute myelogenous leukemia (AML) in first complete remission (CR1). The estimated overall survival (OS) at 2 years was 74.1% ± 6.2% and 34.3% ± 7.9% in MSD and microtransplantation group, respectively ($P = 0.001$). The estimated leukemia-free survival (LFS) at 2 years was 73.3% ± 6.1% in the MSD group and 31.6% ± 7.6% in the microtransplantation group ($P = 0.000$). The 2-year cumulative incidence of relapse was 17.6% and 62.3% in the MSD and microtransplantation groups, respectively ($P < 0.0001$). The 2-year cumulative incidence of nonrelapse mortality was 10.9% in MSD group and 4.2% in the microtransplantation group ($P = 0.251$). Hematopoietic recovery time was shorter in the microtransplantation group than in the MSD group ($P < 0.05$). The infection rate was higher in the MSD group than in the microtransplantation group ($P = 0.012$). The preliminary results suggested that OS and LFS of microtransplantation were inferior to MSD transplantation for intermediate/high-risk AML in CR1.

Keywords Microtransplantation · Matched-sibling donor transplantation · Acute myelogenous leukemia

Introduction

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is an established treatment for acute myelogenous leukemia (AML) [1]. HLA-matched sibling donor (MSD) allo-HSCT is recommended as a first-line postremission treatment in intermediate- and high-risk AML patients [2–6]. However, only about 60% of patients who require allo-HSCT have MSDs or matched unrelated donors (MUD) [7]. Hence, it is very important for patients who have no HLA-matched donor to have allo-HSCT with an alternative donor. Wang et al. reported that haploidentical HSCT achieves 3-year disease-free survival (DFS) and OS rates similar to those of MSD-HSCT for AML patients in first complete remission (CR1) [8]. Ciurea et al. investigated comparable OS after haploidentical donor (HID) and MUD transplantation for AML [9].

In recent years, HLA-mismatched stem cell microtransplantation has been reported, and results have shown that de novo AML patients who underwent microtransplantation achieved significantly higher complete

Limin Liu and Xingxia Zhang contributed equally to this work.

✉ Miao Miao
mm85124@sina.com

✉ Depei Wu
wudepei@suda.edu.cn

[1] Jiangsu Institute of Hematology, Key Laboratory of Thrombosis and Hemostasis of Ministry of Health, The First Affiliated Hospital of Soochow University, 188 Shizi Street, Suzhou 215006, Jiangsu Province, People's Republic of China

[2] Institute of Blood and Marrow Transplantation, Collaborative Innovation Center of Hematology, Soochow University, Suzhou, People's Republic of China

[3] Key Laboratory of Stem Cells and Biomedical Materials of Jiangsu Province and Chinese Ministry of Science and Technology, Suzhou, Jiangsu Province 215006, People's Republic of China

[4] Department of Hematology, Huai'an Hospital Affiliated to Xuzhou Medical College, Huai'an Second People's Hospital, Huai'an 223002, Jiangsu Province, People's Republic of China

remission and 2-year probability of DFS rates than those who received chemotherapy alone [10]. One study reported that low- or intermediate-risk AML patients in CR1 were treated with HLA-mismatched stem cell microtransplantation, for which the 6-year leukemia-free survival (LFS) and OS rates were 84.4% and 89.5%, respectively [11]. These works have shown the excellent outcome of microtransplantation in patients with low- or intermediate-risk AML.

However, there has yet been no report about HLA-mismatched stem cell microtransplantation for patients at high-risk of AML; we do not know the efficacy of HLA-mismatched stem cell microtransplantation for high-risk AML. Currently, no studies have compared the efficacy of HLA-mismatched stem cell microtransplantation and MSD transplantation for AML. In this study, we compared 59 patients undergoing HLA-mismatched stem cell microtransplantation and 66 patients undergoing MSD transplantation at the same period in our centers from April 2012 to December 2016. All participating patients suffered from intermediate- or high-risk acute myelogenous leukemia (AML) in CR1.

Patients and methods

Study environment and participants

In our centers, HLA-MSD was the first-choice treatment. Where HLA-MSD was unavailable, we chose HLA-MUD. Patients without a suitable HLA-MUD (> 8 of 10 matching HLA-A, B, C, DR, and DQ loci) after two cycles of consolidation chemotherapy were eligible for HLA-haplotype transplantation. HLA-mismatched stem cell microtransplantation was selected for patients who declined to HLA-haplotype transplantation. Between April 2012 and December 2016, 661 eligible patients who suffered from intermediate- or high-risk AML in CR1 with no contraindications to HSCT from the First Affiliated Hospital of Soochow University and Huai'an Hospital Affiliated to Xuzhou Medical College were enrolled in this retrospective control study. Consecutive patients receiving MSD ($n = 215$), MUD ($n = 115$), HID ($n = 272$), and HLA-mismatched stem cell microtransplantation ($n = 59$) were analyzed during the study period (Fig. 1). The inclusion criteria included the following: patients had intermediate- or high-risk AML (except APL) in CR1; underwent MSD-HSCT or HLA-mismatched stem cell microtransplantation; voluntary participation in HSCT; and the absence of uncontrolled infection or hepatocirrhosis, hepatic fibrosis, active viral hepatitis type B, abnormality of liver, renal, lung, or heart function, myocardial infarction, and severe liver, renal, lung, or heart disease. The exclusion criteria included the following: patients refused to undergo HSCT and patients unable to tolerate HSCT. Because the

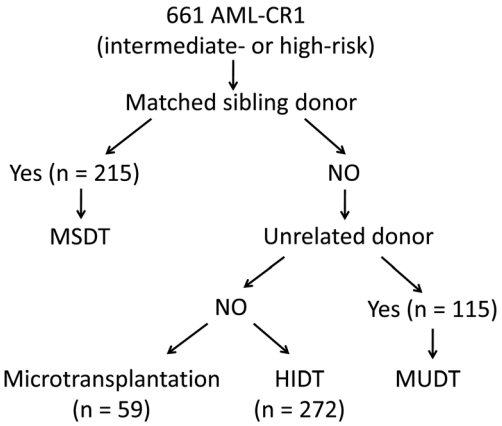

Fig. 1 Flow chart for donor selection strategy. MSDT, matched-sibling donor transplantation; MUDT, matched unrelated donor transplantation; HIDT, haploidentical donor transplantation

median age of microtransplantation group was 56 years (range 19–65), we selected patients with peripheral blood stem cells (PBSC) transplantation aged ≥ 45 years ($n = 66$; median age, 53 years [range 45–62]) for the MSD group and compared them to the microtransplantation group.

Diagnosis was confirmed according to the WHO and French-American-British classification criteria. A standard banding technique was used to perform the cytogenetic experiments on pretreated bone marrow samples [11]. The recommendations of the International System for Human Cytogenetic Nomenclature were used as the criteria to describe a cytogenetic clone and karyotype [12]. Cytogenetic analysis was performed to define risk groups as follows: favorable, t(8;21) without del(9q) or complex abnormalities, inv(16)/t(16;16)/del(16q) without any other abnormality; intermediate, + 8, −Y, + 6, del(12p), normal karyotype; and adverse, −5/del(5q), −7/del(7q), t(8;21) with del(9q) or complex abnormalities, inv(3q), 11q, 20q, or 21q abnormality, del(9q), t(6;9), t(9;22), 17p abnormality, complex abnormalities (≥ 3 unrelated abnormalities) [12]. Patients with t(8; 21), *ETO*, and/or *NPM1* without *FLT3-ITD* were defined as low risk, and initial leukocytes over 100×10^9/L, complex karyotypes, unfavorable cytogenetics, *FLT3-ITD* gene expression, and secondary AML were defined as high risk. The other patients were classified as intermediate risk [11, 13–15]. All donors and recipients provided written informed consent for the protocol. This study was approved by the First Affiliated Hospital of Soochow University and Huai'an Hospital Affiliated to Xuzhou Medical College Ethics Committee.

Treatment protocol

MSD group was treated with a myeloablative BU/CY-based regimen that consisted of the following: methyl chloride hexamethylene urea nitrate (Me-CCNU): 250 mg/m^2/day,

orally once on day − 9; hydroxycarbamide: 80 mg/kg/day orally on day − 9; cytarabine (Ara-C): 2 g/m^2/day i.v. on days − 8 and − 7; busulfan (BU): 3.2 mg/kg/day i.v. on days − 6 to − 4; cyclophosphamide (CY): 1.8 g/m^2/day i.v. on days − 3 and − 2. Granulocyte colony–stimulating factor (G-CSF, 10 μg/kg/day from day − 4) was used to mobilize the stem cells. Bone marrow (BM) or peripheral blood (PB) stem cells were infused into the recipient on the day of collection. Cyclosporin (CsA) and short-term methotrexate (MTX) were administered for acute graft-versus-host disease (aGVHD) prophylaxis. CsA was administered at 3 mg/kg/day and was given by continuous infusion over 24 h from day − 1 until patients could switch to oral intake (PO), with a whole-blood trough level of 200–300 ng/ml during the first 40 days and then tapered, taking about 60 days to be fully discontinued in high-risk patients. MTX was given at 15 mg/kg/day on day + 1 and 10 mg/kg/day on days + 3 and + 6. Trimethoprim/sulfamethoxazole (four tablets daily twice a week) was given for the prevention of *Pneumocystis carinii* infection. Prophylactic antibiotic, antifungal (voriconazole 200 mg/12 h PO or micafungin 150 mg/day i.v.), and antiviral agents (acyclovir 200 mg/8 h PO) agents were administered during the conditioning and immunosuppressive periods according to institutional guidelines.

The microtransplantation consisted of three cycles of high-dose Ara-C chemotherapy (Ara-C, 2.0 g/m^2/12 h i.v. on days − 4 to − 2) followed by infusion of G-CSF-mobilized donor PB stem cells. The interval between the cycles was 3 months. For patients over 55 years old, the chemotherapy dose was decreased to Ara-C, 1.5 g/m^2/12 h i.v. on days − 4 to − 2. G-CSF (10 μg/kg/day from day − 4) was used to mobilize the PB. A portion of the fresh donor PB stem cells was infused into the recipient on the day of collection and the rest were aliquoted and cryopreserved in liquid nitrogen. Therapies such as prophylaxis of GVHD, *P. carinii*, and cytomegalovirus were not used at any point in the process.

Definitions

After HSCT, the first time that absolute neutrophil count (ANC) exceeded 0.5 × 10^9/L for 3 consecutive days was defined as neutrophil recovery. First time platelet counts > 20 × 10^9/L without blood transfusion for 7 consecutive days was defined as platelet recovery. Responses were determined according to the revised recommendations of the International Working Group for Diagnosis, Standardization of Response Criteria, Treatment Outcomes, and Reporting Standards for Therapeutic Trials in Acute Myeloid Leukemia [11, 15, 16]. Relapse was defined as recurrence of BM blasts > 5%, reappearance of blasts in PB, or presence of evidence of extramedullary infiltration at any site.

Death without leukemia progression was defined as transplantation-related mortality (TRM). Early mortality was defined as death within 60 days since HSCT. Nonrelapse mortality (NRM) was defined as death from any cause within 28 days post-HSCT or death without leukemia recurrence after 28 days [8]. Acute GVHD was scored according to the criteria proposed by the 1994 Consensus Conference on Acute GVHD Grading [17]. Chronic GVHD was scored according to the NIH Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: Diagnosis and Staging Working Report [18]. Leukemia-free survival (LFS) was defined as the length of time from CR to relapse. The duration of overall survival (OS) was calculated from the beginning of CR to the date of last follow-up or death, from any cause.

Statistical analysis

Statistical analyses were conducted on the basis of data available from the date of treatment to the date of final patient follow-up on April 30, 2017. Comparisons of patient characteristics between the MSD and microtransplantation groups were performed using the Mann–Whitney *U* test for continuous variable and chi-square test for categorical data. The probabilities of OS and LFS were estimated from the time of treatment using the Kaplan–Meier method. The log-rank test was used to compare these variables between the two groups. The Cox logistic analysis was applied to identify significantly independent factors for OS and LFS. Statistical analyses were performed with SPSS version 16.0 (SPSS, Chicago, IL, USA). All *P* values were two sided, and results were considered statistically significant when $P < 0.05$.

Results

Patient characteristics

A total of 125 patients were enrolled in this study, 66 (52.8%) of whom were in the MSD group, and 59 (47.2%) in the microtransplantation group. Patient characteristics are shown in Table 1. The two groups were well matched, except the donor–recipient relationship.

Hematopoietic recovery

In the MSD group, the median (range) mononuclear cells (MNC) dose and CD34$^+$ cell dose of grafts were higher than that in microtransplantation group (MNC, 8.5 (3.3–25.4) × 10^8/kg vs 2.4 (0.4–8.2) × 10^8/kg, $P = 1.853E\text{-}10$; CD34$^+$, 3.2 (1.2–7.7) × 10^6/kg vs 1.6 (0.5–6.4) × 10^6/kg, $P = 4.164E\text{-}6$). Hematopoietic recovery time was shorter in the

Table 1 Patient and graft characteristics

Characteristics	Identical sibling ($N = 66$)	Microtransplantation ($N = 59$)	P
Age, years, median (range)	53 (45–62)	56 (19–65)	0.284
Gender, *n* (%)			0.097
Male	40 (60.6)	27 (45.8)	
Female	26 (39.4)	32 (54.2)	
FAB subtype, *n* (%)			
M0	2 (3.0)	0 (0)	0.498
M1	4 (6.1)	7 (11.9)	0.253
M2	22 (33.3)	22 (37.3)	0.644
M4	10 (15.2)	8 (13.6)	0.800
M5	22 (33.3)	15 (25.4)	0.334
M6	2 (3.0)	3 (5.1)	0.898
Undetermined	3 (4.5)	3 (5.1)	1.000
Secondary	1 (1.5)	1 (1.7)	1.000
WBC count at diagnosis, *n* (%)			
$> 10 \times 10^9$/L	31 (47.0)	25 (42.4)	0.606
$> 50 \times 10^9$/L	8 (12.1)	9 (15.3)	0.610
Duration from diagnosis to transplant, months, median (range)	3.5 (2–25)	3 (2–24)	0.423
Risk group, *n* (%)			0.317
Intermediate	35 (53.0)	26 (44.1)	
High	31 (47.0)	33 (55.9)	
Cytogenetic risk, *n* (%)			
Intermediate	53 (80.3)	48 (81.4)	0.881
High	8 (12.1)	7 (11.9)	0.965
FLT3 mutation, *n* (%)	11 (16.7)	11 (18.6)	0.772
DNMT3A mutation, *n* (%)	4 (6.1)	5 (8.5)	0.861
c-kit mutation, *n* (%)	8 (12.1)	5 (8.5)	0.505
Courses required achieving remission, *n* (%)			
1	48 (72.7)	39 (66.1)	0.421
2	18 (27.3)	17 (28.8)	0.848
3	2 (3.0)	3 (5.1)	0.898
Donor–recipient sex match, *n* (%)			
Male–male	22 (33.3)	18 (30.5)	0.735
Male–female	13 (19.7)	20 (33.9)	0.072
Female–male	19 (28.8)	10 (16.9)	0.117
Female–female	12 (18.2)	11 (18.6)	0.947
Donor–recipient relationship, *n* (%)			
Sibling donor	66 (100.0)	7 (11.9)	1.860E-23
Father donor	0 (0)	5 (8.5)	0.050
Mother donor	0 (0)	1 (1.7)	0.472
Children donor	0 (0)	46 (78.0)	1.825E-19

FAB, French-American-British; *WBC*, white blood cell

microtransplantation group than in the MSD group (median (range) time to neutrophil recovery, 10 (7–21) days vs 12 (10–17) days, $P = 3.457E\text{-}4$; median (range) time to platelet recovery, 11 (7–30) days vs 13 (9–40) days, $P = 1.784E\text{-}4$) (Table 2).

Donor chimerism

Patients underwent weekly chimerism evaluations following transplant of whole blood for the first month after transplantation by amplification and analysis of STR polymorphisms

Table 2 Clinical outcomes after HSCT

Variable	Identical sibling ($N = 66$)	Microtransplantation ($N = 59$)	P
Median mononuclear cells, $\times 10^8$/kg (range)	8.5 (3.3–25.4)	2.4 (0.4–8.2)	1.853E-10
Median $CD34^+$ cells, $\times 10^6$/kg (range)	3.2 (1.2–7.7)	1.6 (0.5–6.4)	4.164E-6
Median $CD3^+$ cells, $\times 10^8$/kg (range)	1.5 (1.2–2.8)	0.8 (0.2–2.2)	2.353E-4
Median neutrophil engraftment, days (range)	12 (10–17)	10 (7–21)	3.457E-4
Median platelet engraftment, days (range)	13 (9–40)	11 (7–30)	1.784E-4
Early mortality	0 (0%)	1 (1.7%)	0.472
Infection, *n* (%)	61 (92.4)	45 (76.3)	0.012
Febrile neutropenia	23 (34.8)	23 (39.0)	
Pulmonary infections	9 (13.6)	4 (6.8)	
Septicemia	9 (13.6)	10 (16.9)	
Urinary infection	3 (4.5)	2 (3.4)	
Mucositis/stomatitis	8 (12.1)	3 (5.1)	
Anal infection	4 (6.1)	2 (3.4)	
Viremia	3 (4.5)	0 (0)	
Upper airway	2 (3.0)	1 (1.7)	
Causes of death, *n* (%)			
Relapse	10 (15.2)	27 (45.8)	1.820E-4
GVHD	5 (7.6)	0 (0)	0.089
Infection	3 (4.5)	3 (5.1)	1.000
Median follow-up time among living patients, months (range)	25 (4–61)	20 (4–42)	0.131

HSCT, hematopoietic stem cell transplantation; *GVHD*, graft-versus-host disease

using multiplex amplification of STR loci. In the MSD group, all patients achieved donor chimerism > 95.0%. In the microtransplantation group, no full or mixed donor chimerism was found.

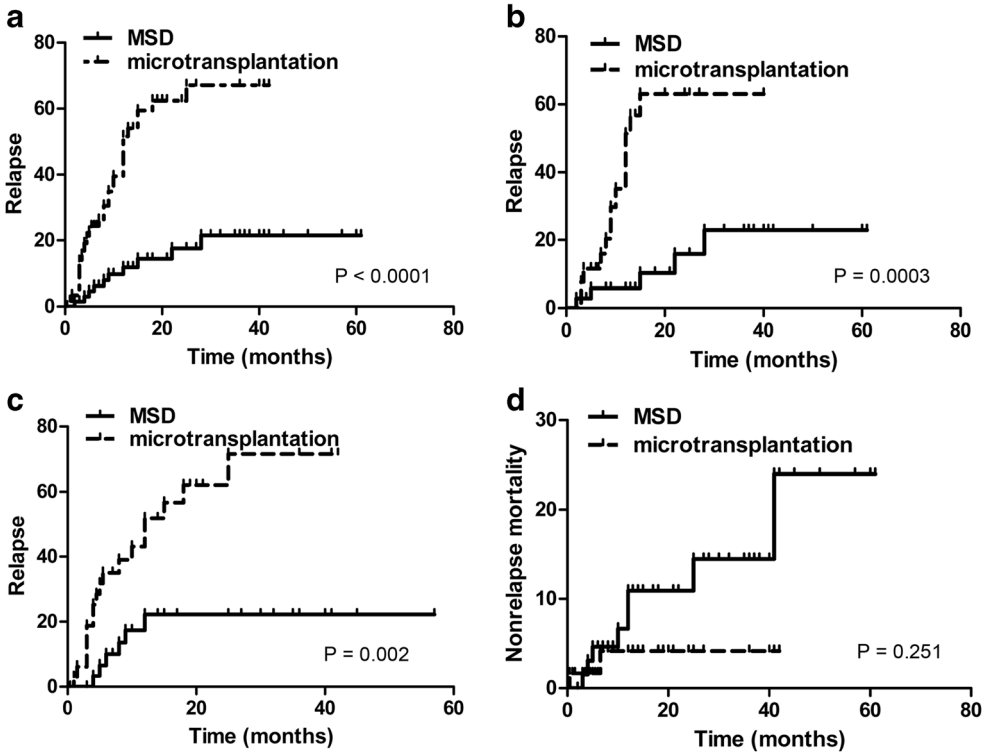

Fig. 2 Relapse and nonrelapse mortality. **a** The 2-year cumulative incidence of relapse in microtransplantation group was higher than in MSD group (62.3% vs 17.6%, $P < 0.0001$). **b** The 2-year cumulative incidences of relapse of intermediate-risk patients were 15.9% and 60.9% among MSD and microtransplantation groups ($P = 0.0003$). **c** The 2-year cumulative incidence of relapse of high-risk patients in microtransplantation group was higher than in the MSD group (71.6% vs 22.2%, $P = 0.002$). **d** There was no statistically significant difference of 2-year nonrelapse mortality between MSD group and microtransplantation group (10.9% vs 4.2%, $P = 0.251$)

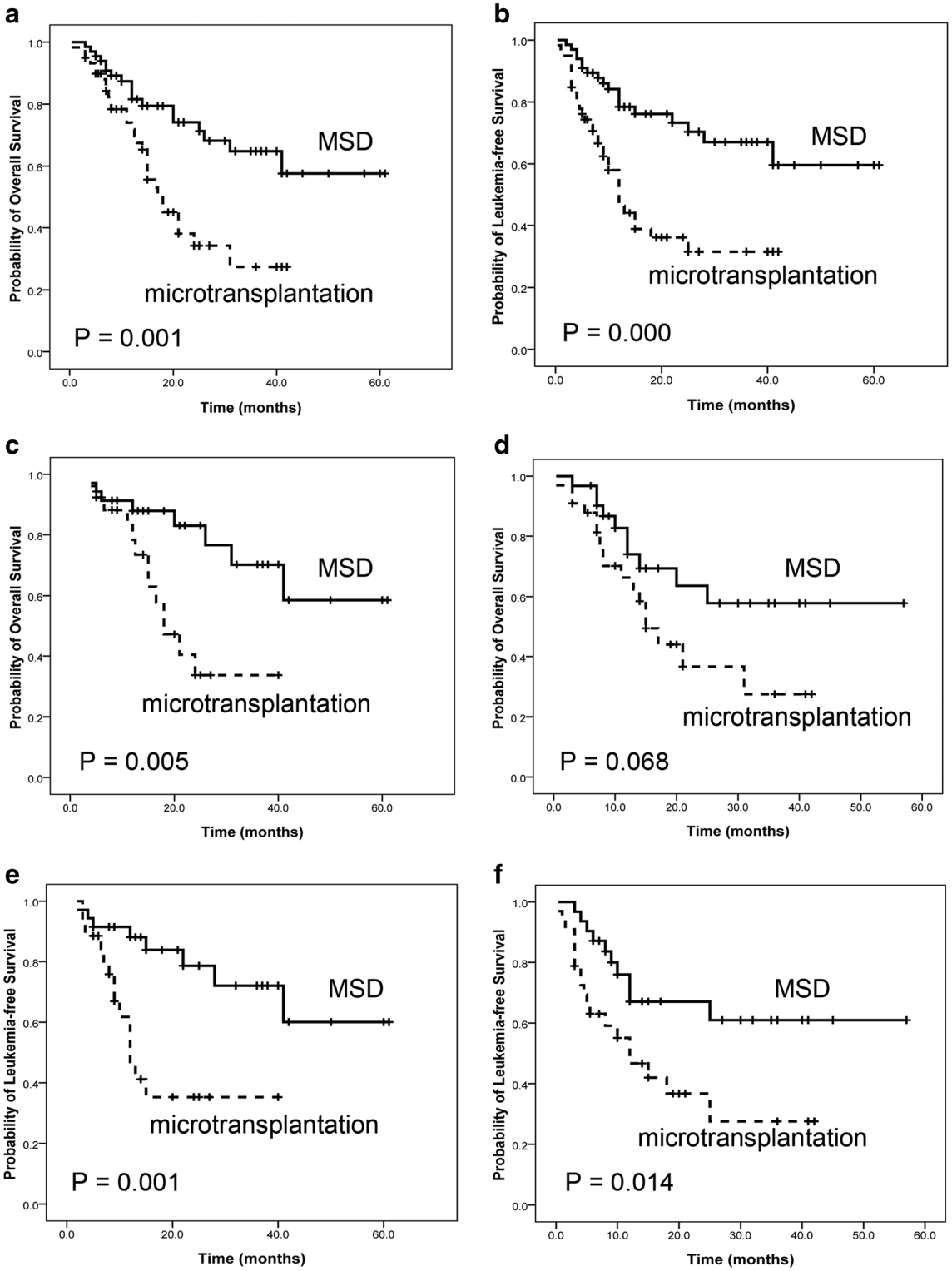

Fig. 3 Patient overall survival (OS) and leukemia-free survival (LFS) for MSD transplant and microtransplantation as assessed using the Kaplan–Meier analysis. **a** The estimated OS at 2-year of microtransplantation was lower than MSD transplantation (34.3% ± 7.9% vs 74.1% ± 6.2%, P = 0.001). **b** The estimated LFS at 2 years in the MSD group was higher than in microtransplantation group (73.3% ± 6.1% vs 31.6% ± 7.6%, P = 0.000). **c** The estimated OS at 2 years in intermediate-risk patients in the MSD group was higher than in the microtransplantation group (83.0% ± 7.2% vs 33.7% ± 11.3%, P = 0.005). **d** A trend toward the estimated OS at 2 years in high-risk patients in microtransplantation was lower than in the MSD transplantation group, but there was no statistically significant difference (63.6% ± 10.1% vs 36.7% ± 10.8%, P = 0.068). **e** The estimated LFS at 2 years in intermediate-risk patients in the MSD group was higher than in the microtransplantation group (78.6% ± 8.1% vs 35.3% ± 10.7%, P = 0.001). **f** The estimated LFS at 2 years in high-risk patients in the MSD group was higher than in the microtransplantation group (60.9% ± 10.2% vs 27.6% ± 10.8%, P = 0.014)

GVHD and infections

In the MSD group, the cumulative incidences of grades 2 to 4 and grades 3 to 4 acute GVHD within 100 days were 18.6% and 7.0%, respectively; the cumulative incidences of chronic GVHD and severe chronic GVHD at 1 year were 23.3% and 7.0%, respectively. In the microtransplantation group, no acute or chronic GVHD was observed at any point during the treatment or follow-up periods. Two patients developed a slight skin rash on the second day of the first course of therapy, but it disappeared no later than 12 h after antiallergic therapy.

In the MSD group, 61 (92.4%) patients experienced infection, while in microtransplantation group, the infection rate was 45 (76.3%), which showed significant statistical differences ($P = 0.012$) (Table 2).

Relapse and nonrelapse mortality

The 2-year cumulative incidences of relapse were 17.6% and 62.3% in the MSD and microtransplantation groups, respectively ($P < 0.0001$) (Fig. 2a), which were 15.9% and 60.9% in intermediate-risk patients, respectively ($P = 0.0003$) (Fig. 2b), and 22.2% and 71.6% in high-risk patients, respectively ($P = 0.002$) (Fig. 2c). In the microtransplantation group, the cumulative incidence of relapse in high-risk patients was higher than in intermediate-risk patients, but there was no statistically significant difference ($P = 0.492$).

The 2-year cumulative incidence of nonrelapse, mortality was 10.9% in the MSD group and 4.2% in the microtransplantation group ($P = 0.251$) (Fig. 2d).

Survival

The estimated OS at 2 years was 74.1% ± 6.2% in MSD group and 34.3% ± 7.9% in microtransplantation group ($P = 0.001$) (Fig. 3a). The estimated LFS at 2 years was 73.3% ± 6.1% in MSD group and 31.6% ± 7.6% in microtransplantation group ($P = 0.000$) (Fig. 3b). For intermediate-risk patients, the estimated OS at 2 years was 83.0% ± 7.2% in MSD group and 33.7% ± 11.3% in microtransplantation group ($P = 0.005$) (Fig. 3c). For high-risk patients, the estimated OS at 2 years was 63.6% ± 10.1% in MSD group and 36.7% ± 10.8% in microtransplantation group ($P = 0.068$) (Fig. 3d). For intermediate-risk patients, the estimated LFS at 2 years was 78.6% ± 8.1% in MSD group and 35.3% ± 10.7% in microtransplantation group ($P = 0.001$) (Fig. 3e). For high-risk patients, the estimated LFS at 2 years was 60.9% ± 10.2% in the MSD group and 27.6% ± 10.8% in microtransplantation group ($P = 0.014$) (Fig. 3f). In microtransplantation group, there were no statistically significant differences in estimated OS and LFS at 2 years between high-risk patients and intermediate-risk patients ($P = 0.520$ and 0.514, respectively). Multivariate analysis (including relevant variables of HCT-CI comorbidity score, DRI disease risk index, CMV serostatus, and ABO match/mismatch) showed both OS and LFS for the entire population correlated significantly with therapy (MSD-HSCT or microtransplantation) did not correlate significantly with HCT-CI comorbidity score, disease risk index (DRI), CMV serostatus, and ABO match/mismatch (Table 3).

Causes of death

During the follow-up period, in MSD group, patients died of relapse, GVHD, or infection; while in microtransplantation group, causes of death were relapse and infection (Table 2).

Discussion

Fewer than 30% of patients who require allo-HSCT can find MSDs [19], although MSD-HSCT is recommended as a first-line postremission treatment for intermediate- and high-risk AML patients. Recent progress in HID transplantation offers the benefits of near-universal donors. However, older patients cannot tolerate the myeloablative HSCT. HLA-mismatched

Table 3 Multivariate Cox logistic analysis of factors relating to overall survival and leukemia-free survival

Variables	OS			LFS		
	P	Odds ratio	95% confidence interval	*P*	Odds ratio	95% confidence interval
Therapy (MSD-HSCT or microtransplantation)	0.013	0.434	0.226–0.836	0.002	0.373	0.197–0.704
HCT-CI comorbidity score	0.055	1.036	1.003–1.070	0.052	1.038	1.005–1.071
Disease risk index	0.377	1.300	0.726–2.328	0.393	1.278	0.728–2.245
CMV serostatus	0.822	1.071	0.589–1.946	0.889	1.042	0.587–1.850
ABO match/mismatch	0.928	1.028	0.565–1.869	0.959	1.015	0.573–1.797

OS, overall survival; *LFS*, leukemia-free survival; *MSD-HSCT*, matched-sibling donor hematopoietic stem cell transplantation; *HCT-CI*, hematopoietic stem cell transplantation comorbidity score

stem cell microtransplantation is a new kind of transplantation that has been reported in recent years. To our knowledge, this study is the first comparison of microtransplantation and MSD-HSCT among patients with intermediate- or high-risk AML in CR1. Data demonstrated that the 2-year cumulative incidence of relapse in microtransplantation group was higher than in the MSD group, whereas the nonrelapse mortality was similar between the two groups. The hematopoietic recovery time was shorter in microtransplantation group than in the MSD group. At 2 years, the estimated OS and LFS were higher in MSD group than in microtransplantation group.

Our results further indicated that, in high-risk patients, the cumulative incidence of relapse in microtransplantation group was higher than in the MSD group. The estimated OS and LFS at 2 years among high-risk patients were lower in microtransplantation group than in the MSD group. The cumulative incidence of relapse in intermediate-risk patients was higher in microtransplantation group than that in MSD group. The estimated OS and LFS at 2 years in intermediate-risk patients were also lower in the microtransplantation group than in the MSD group.

In this study, we found that hematologic recovery time to be shorter in the microtransplantation group than in the MSD group. We here speculate this may be linked to more intensive conditioning regimen in the MSD group (BU/CY) than in the microtransplantation group (high/intermediate-dose Ara-C). Another advantage of microtransplantation was the lower infection rate.

During the follow-up period, the major cause of death in microtransplantation group was relapse. Reducing the relapse rate for intermediate- and high-risk AML patients after microtransplantation is very important. Some studies have shown that microtransplantation can mediate specific antileukemia effects, including GVL effects and recipient-versus-leukemia effects [11, 20–24]. The mechanism of the antileukemia effect remains unclear. Both donor and recipient-derived T cells contribute to the antileukemic effect [25]. It has been known that infusion of allogeneic immune cells can mediate a direct or indirect cytotoxic effect [26]. Currently, we cannot draw a confirmed conclusion about why the relapse rate in the microtransplantation group was higher than in the MSD group. We can only speculate that this result may be linked to the lower intensity of conditioning regimen, the lower dose of T cells and stem cells in the graft and the inferior antileukemie response of microchimerism in microtransplantation. This result may be linked to the NK cells and other immune cells in the stem cell graft.

This study has some limitations. The patients in the two groups were not randomized because of ethical and practical reasons, the sample size was relatively small, and the follow-up period was short.

In summary, the preliminary study showed that the estimated 2-year OS and LFS values were higher in the MSD-HSCT group than in microtransplantation for patients with intermediate- or high-risk AML in CR1. The cumulative incidence of relapse was higher in the microtransplantation group than in the MSD-HSCT group. Further studies with larger samples and longer follow-up periods are needed to derive more conclusive findings.

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Compliance with ethical standards

The First Affiliated Hospital of Soochow University and Huai'an Hospital Affiliated to Xuzhou Medical College Ethics Committee approved this study; patients were recruited after obtaining informed consent.

Conflict of interest The authors declare that they have no conflict of interest.

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