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Reduced-intensity conditioning versus myeloablative conditioning allogeneic stem cell transplantation for patients with myelofibrosis

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Background
Allogeneic hematopoietic stem cell transplantation (alloSCT) is the sole curative option for myelofibrosis (MF). However, it is unknown as to which of the two, myeloablative conditioning (MAC) or reduced-intensity conditioning (RIC), is a better preconditioning regimen.

Methods
Twenty-five patients with MF were treated with alloSCT, 12 of whom underwent RIC. Baseline characteristics, response to alloSCT, adverse events, including graft-versus-host disease (GVHD), and survival outcomes were reviewed.

Results
There was no difference in the neutrophil engraftment rate and time to engraftment between MAC vs. RIC. The time to platelet engraftment was significantly longer in the MAC group (median, 112.8 vs. 28.8 days for MAC vs. RIC, respectively, P=0.049). RIC was more advantageous in terms of achieving complete chimerism (38.5% vs. 83.3%, P=0.041). The incidence of acute GVHD was 84.6% (11 of 13) and 58.3% (7 of 12) in the MAC and RIC groups, respectively. The cumulative incidence of grade III–IV acute GVHD was significantly higher in the MAC group than in the RIC group (P=0.03). No significant differences were observed in progression-free and overall survival. The 17-month probability of progression-free survival was 38.4% [95% confidence interval (CI), 19.3–76.5] vs. 47.6% (95% CI, 25.7–88.2) (P=0.21), and that of overall survival was 53.8% (95% CI, 32.5–89.1) vs. 48.6% (95% CI, 26.8–88.3) (P=0.85) for MAC vs. RIC, respectively.

Conclusion
RIC offers a significant advantage over MAC, even in younger patients with MF undergoing alloSCT, in terms of cell engraftment, rate of complete chimerism achievement, and incidence of acute GVHD.

Key Words Myelofibrosis, Hematopoietic stem cell transplantation, Reduced intensity, Myeloablative

INTRODUCTION

Myelofibrosis (MF) is a subtype of chronic myeloproliferative neoplasm (MPN) caused by the clonal proliferation of multipotent hematopoietic stem cells, leading to the secretion of diverse cytokines and eventually fibrosis of the bone marrow. Because of extensive scarring of the bone marrow, the cardinal features of MF include extramedullary hematopoiesis, splenomegaly, and anemia [1, 2]. MF can present as primary or secondary, evolving from previous polycythemia vera or essential thrombocythemia [3]. MF has various clinical courses but is generally associated with a poor prognosis [4].

Despite recent major advances in understanding the pathogenesis of MF and the development of novel therapeutic agents, including Janus-activated kinase (JAK) inhibitors, allogeneic hematopoietic stem cell transplantation (alloSCT)

remains the sole curative option for higher-risk diseases [5, 6]. The art of alloSCT depends on the conditioning intensity; traditionally, myeloablative conditioning (MAC) has been widely used with some success, considering the biology of the disease [7]. Historically, busulfan + cyclophosphamide and total body irradiation-based regimens have been used as MAC in MF [8], and the outcomes were somewhat encouraging, with some studies reporting a 5-year survival rate of over 60%. However, as reported by Kerbauy *et al.* [7], a high risk of grade II–IV acute graft-versus-host disease (GVHD) (64%) and chronic GVHD (84%) is worrisome. As MF is a disease of older adults, with a median age at diagnosis of 63.7 years in Korea, most patients are not fit for MAC due to advanced age and/or comorbidities [9]. Therefore, there has been increasing interest in reduced-intensity conditioning (RIC). Fludarabine with busulfan and fludarabine with melphalan are commonly used RIC regimens, and recent data have shown that older patients undergoing RIC can achieve similar overall survival (OS) to those undergoing MAC with a relatively low risk of acute and chronic GVHD [10, 11].

Unfortunately, no prospective studies have directly compared MAC versus RIC in patients with MF, especially in younger patients. In addition, even in several retrospective studies, there are few consistent conclusions in terms of transplant prognosis such as GVHD and OS [10, 12]. Therefore, we conducted this retrospective study to provide clues for the adaptive individualization of conditioning regimens.

MATERIALS AND METHODS

Patients and study design

This was a single-center retrospective longitudinal cohort study of patients with MF undergoing alloSCT between January 2005 and June 2021. Patients with both primary and secondary MF were included. Initially, 32 patients were included. After excluding 1 patient who underwent alloSCT in the accelerated phase and 6 patients who underwent alloSCT in the blast phase, a total of 25 patients were deemed eligible for analysis (Fig. 1). Their medical records were reviewed for demographics, baseline disease characteristics, alloSCT-related factors, response to alloSCT, adverse events, and survival outcomes. This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Seoul National University Hospital (IRB no. H-2207-083-1339).

Definitions

From 2005 to 2007, MPN was diagnosed according to the 2001 World Health Organization (WHO) classification. From 2008 to 2015, MPN was diagnosed according to the 2008 WHO classification system. From 2016 to 2021, MPN was diagnosed according to the revised 2016 WHO classification.

The Glucksberg standard criteria have been used to grade acute GVHD [13]. Chronic GVHD was classified as mild, moderate, or severe, according to the 2014 National Institutes of Health consensus criteria [14]. OS was defined as the time from stem cell infusion to death due to any cause. Progression free survival (PFS) was defined as the time from stem cell infusion to relapse or death due to any cause. Both clinical relapse or molecular relapse were counted as relapse events: clinical relapse was defined as relapse of MF or transformation to other hematologic malignancies such as AML, while molecular relapse was defined as loss of complete chimerism or an increase in the recipient proportion in mixed chimerism. Non-relapse mortality (NRM) was defined as death without progression of the underlying disease. The causes of death were evaluated as disease recurrence or progression, graft failure, GVHD, infection, and others based on a report by Copelan *et al.* [15].

Neutrophil engraftment was defined as an absolute neutrophil count $>0.5\times10^9$/L for 3 consecutive measurements. Platelet engraftment was defined as seven consecutive measurements of $>20\times10^9$/L without transfusion.

Conditioning regimen

For the MAC regimens, BuCy (busulfan 4 mg/kg for 4 days, cyclophosphamide 60 mg/kg for 2 days), BuFlu (busulfan 4 mg/kg for 4 days, fludarabine 30 mg/m^2 for 4 days), FluMel (melphalan 70 mg/m^2 for 2 days, fludarabine 30 mg/m^2 for 5 days), and CyTLI (cyclophosphamide 50 mg/kg for 4 days, total lymphoid irradiation 750 cGy) were used. For RIC regimens, BuFlu (busulfan 3.2 mg/kg for 2 days, fludarabine 30 mg/m^2 for 6 days) was used. The choice of calcineurin inhibitor (cyclosporine vs. tacrolimus) was left to the attending physician's preference. Cyclosporine was started at 3 mg/kg 48 h before stem cell infusion, with adjustments made to achieve the target serum trough level of 250–400 ng/mL. Tacrolimus was started at 0.04 mg/kg/day 48 h before stem cell infusion, with adjustments to achieve

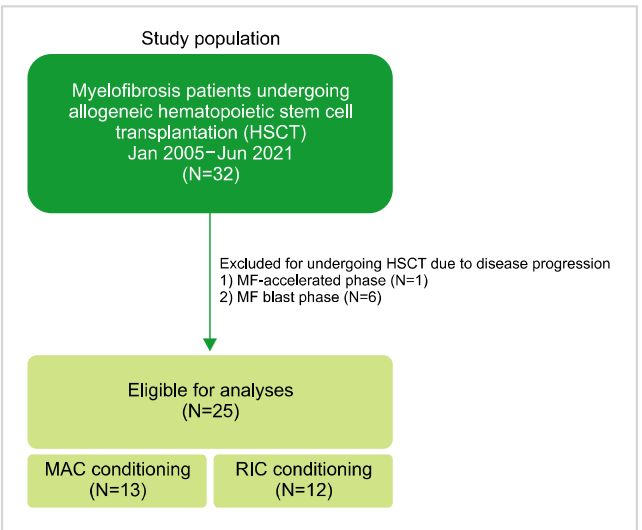

Fig. 1. Patient flow chart diagram.
Abbreviations: MAC, myeloablative conditioning; MF, myelofibrosis; RIC, reduced intensity conditioning.

the target serum trough level of 10–20 ng/mL. Serum cytomegalovirus antigen levels were monitored weekly, and intravenous immunoglobulin was administered for 9 months after alloSCT.

Statistical analysis

Differences between groups were assessed using Student's t-test or Wilcoxon rank-sum test for continuous variables, and Fisher's exact test or Pearson chi-square test for categorical variables, as indicated.

PFS and OS curves were estimated using the Kaplan–Meier

Table 1. Baseline characteristics.

	All patients (N=25)	MAC group (N=13)	RIC group (N=12)	*P*
Age, years, median (range)	49.9 (27–64)	45.0 (27–64)	55.2 (48–63)	0.028
Sex, male, N (%)	14 (56)	5 (38.5)	9 (75)	0.151
Secondary MF	6 (24)	3 (23.1)	3 (25)	1.000
Splenomegaly at diagnosis	21 (84)	11 (84.6)	10 (83.3)	1.000
Spleen status at HSCT				
Splenomegaly	17 (68)	7 (53.8)	10 (83.3)	0.250
Splenectomy prior to HSCT	4 (16)	3 (23.1)	1 (8.3)	0.647
RT to spleen prior to HSCT	1 (4)	0 (0)	1 (8.3)	0.967
Ruxolitinib before HSCT	10 (40)	0 (0)	10 (83.3)	0.000
Mutation status (positive/tested)				
Not assessed	6	6	0	
JAK2 V617F	10/19	2/7	8/12	0.259
JAK2 exon 12	0/2	0/1	0/1	
CALR	0/4	0/2	0/2	
MPL	0/4	0/2	0/2	
Triple negative				
Cytogenetics				0.360
Normal	15 (68.2)	6 (54.5)	9 (81.8)	
Abnormal	7 (31.8)	5 (45.5)	2 (18.2)	
D-IPSS at diagnosis				
Low	5 (20)	2 (15.4)	3 (25)	0.920
Intermediate-1	9 (36)	5 (38.5)	4 (33.3)	1.000
Intermediate-2	9 (36)	5 (38.5)	4 (33.3)	1.000
High	2 (8)	1 (7.7)	1 (8.3)	1.000
D-IPSS at HSCT				
Low	0	0	0	
Intermediate-1	0	0	0	
Intermediate-2	18 (72)	12 (92.3)	6 (50)	0.056
High	7 (28)	1 (7.7)	6 (50)	0.056
Time to HSCT from diagnosis, months (range)	30.9 (2.9–118.3)	18.7 (2.9–114.5)	44.1 (8.8–118.3)	0.087
Donor type				
Matched related	16 (64)	8 (61.5)	8 (66.7)	1.000
Matched unrelated	3 (12)	2 (15.4)	1 (8.3)	1.000
Mismatched unrelated	3 (12)	2 (15.4)	1 (8.3)	1.000
Haplo-identical	3 (12)	1 (7.7)	2 (16.7)	0.941
CD34+, $\times 10^6$/kg, median (range)	5.7 (2.12–12.23)	6.2 (2.12–10.34)	5.1 (3.39–12.23)	0.426
Calcineurin inhibitor, N (%)				
Cyclosporine	25 (100)	13 (100)	12 (100)	
Tacrolimus	0	0	0	
Methotrexate, N (%)	12 (48)	6 (46.2)	6 (50)	1.000
ATG, N (%)	21 (84)	9 (69.2)	12 (100)	0.121
pre-HSCT CBC, median (range)				
WBC count (10^3μL)	10.7 (0.52–38.9)	8.81 (1.08–34.4)	12.75 (0.52–38.9)	0.414
Hemoglobin (g/dL)	7.9 (5–14.6)	7.5 (5.5–14)	8.4 (5–14.6)	0.453
Platelet count (10^3/μL)	137.4 (14–543)	114.8 (14–543)	161.9 (17–384)	0.408
Blast (%)	0.6 (0–6)	0.07 (0–1)	1.2 (0–6)	0.201

Abbreviations: ATG, antithymocyte globulin; *CALR*, calreticulin; CBC, complete blood count; D-IPSS, Dynamic International Prognostic Scoring System; HSCT, hematopoietic stem cell transplantation; *JAK2*, janus kinase 2; MAC, myeloablative conditioning; MF, myelofibrosis; *MPL*, myeloproliferative leukemia virus; RIC, reduced intensity conditioning; RT, radiotherapy; WBC, white blood cell.

method. If a patient survived without death or progression, survival was censored at the latest follow-up data when no death or progression was confirmed.

Cumulative incidence curves were used in the competing-risk setting to calculate the probabilities of acute and chronic GVHD and NRM. For GVHD, death without an event was considered as the competing event. For NRM, relapse was considered as the competing event. For all statistical analyses, the statistical software 'R' version 4.1.3 (www.r-project.org) was used. *P*-values <0.05 were considered statistically significant.

RESULTS

Baseline characteristics

Thirteen patients underwent MAC and 12 underwent RIC. Of the 25 patients, 13 (52%) underwent transplantation before 2015 and 11 (84.6%) were in the MAC group. Baseline characteristics are listed in Table 1. The median age for the whole group was 50 years (range, 27–64 yr), which can be considered relatively young. As expected, patients in the MAC group were significantly younger than those in the RIC group (*P*=0.028); however, other than age there were no significant differences between the two groups with regards to MF disease characteristics and factors related to alloSCT, including donor type and time from MF diagnosis to alloSCT.

Interestingly, no patients in the MAC group were exposed to ruxolitinib prior to alloSCT, whereas most patients in the RIC group had a history of ruxolitinib use. However, there were no differences in spleen size between the two groups prior to alloSCT.

Outcomes of alloSCT

Of the 25 patients undergoing alloSCT, the response could not be evaluated in three patients because of death within 1 month of alloSCT. The causes of death were acute GVHD and sepsis in the MAC group, and veno-occlusive disease in the RIC group.

The outcomes of transplantation are shown in Table 2. The remaining 22 patients showed neutrophil engraftment with a median time to engraftment of 16 days (range, 8–23 days). There was no difference in neutrophil engraftment rate and time to engraftment between the MAC and RIC groups. In contrast, 18 of the 22 patients showed platelet engraftment, with the median time to engraftment being 71 days (range, 16–317 days). There was no difference in rate of platelet engraftment between the two groups; however, the time to platelet engraftment was significantly longer in the MAC group (median, 112.8 days vs. 28.8 days for MAC vs. RIC, respectively, *P*=0.049).

Initially, complete chimerism was achieved in 5 patients (20%). Fifteen patients (60%) achieved complete chimerism at least once during the follow-up period. The rate of complete chimerism was significantly higher after RIC (38.5% in the MAC group vs. 83.3% in the RIC group, *P*=0.041). Two patients in the MAC group experienced delayed engraftment failure: one underwent a second alloSCT, and the other received supportive care only.

Table 2. Transplantation outcomes.

	MAC group	RIC group	*P*
Neutrophil engraftment	11 (84.6)	12 (100)	0.497
Time to engraftment, days (median, range)	15.9 (8–23)	15.8 (11–22)	0.964
Platelet engraftment, N (%)	9 (69.2)	9 (75)	1.000
Time to engraftment, days (median, range)	112.8 (22–317)	28.7 (16–74)	0.049
Acute GVHD, any, N (%)	11 (84.6)	7 (58.3)	0.201
Grade III–IV acute GVHD	7 (53.8)	2 (16.7)	0.096
Chronic GVHD, any, N (%)	5 (38.5)	4 (33.3)	1.000
Moderate to severe chronic GVHD	4 (30.8)	2 (16.7)	0.644
Death, N (%)	10 (76.9)	6 (50)	0.325
NRM, N (%)	8 (61.5)	3 (25.0)	0.151
Causes of death, N (%)			0.345
Disease recurrence or progression	2 (20.0)	3 (50.0)	0.486
Graft failure	2 (20.0)	0 (0.0)	0.696
GVHD	1 (10.0)	1 (16.7)	1.000
Infection	3 (30.0)	0 (0.0)	0.408
Others	2 (20.0)	2 (33.3)	1.000
Complete chimerism achievement, N (%)			
At initial post-transplantation evaluation	1 (7.7)	4 (33.3)	0.271
During follow-up	5 (38.5)	10 (83.3)	0.041

Abbreviations: GVHD, graft-versus-host disease; MAC, myeloablative conditioning; NRM, non-relapse mortality; RIC, reduced intensity conditioning.

Survival outcomes

The 17-month probabilities of OS and PFS for all 25 patients were 51.4% [95% confidence interval (CI), 35–75.6%] and 43.1% (95% CI, 27.2–68.1%), respectively (Fig. 2A, B). The OS and PFS for patients in the MAC and RIC groups are shown in Fig. 2A, B. The difference in OS between the MAC and RIC groups was not significant (P=0.85). The cumulative incidence of NRM was higher in the MAC group; however, the difference was not significant (Fig. 2C, P=0.28).

A total of 10 patients relapsed during the follow-up: five patients relapsed with myeloid malignancy and were treated with induction chemotherapy but all died; the other five patients showed increased recipient chimerism and were treated with donor lymphocyte infusion and ruxolitinib but three died due to progressive disease. Of the 13 patients in the MAC group, three patients were alive at the last follow-up, while 6 of 12 patients in the RIC group were alive at the last follow-up.

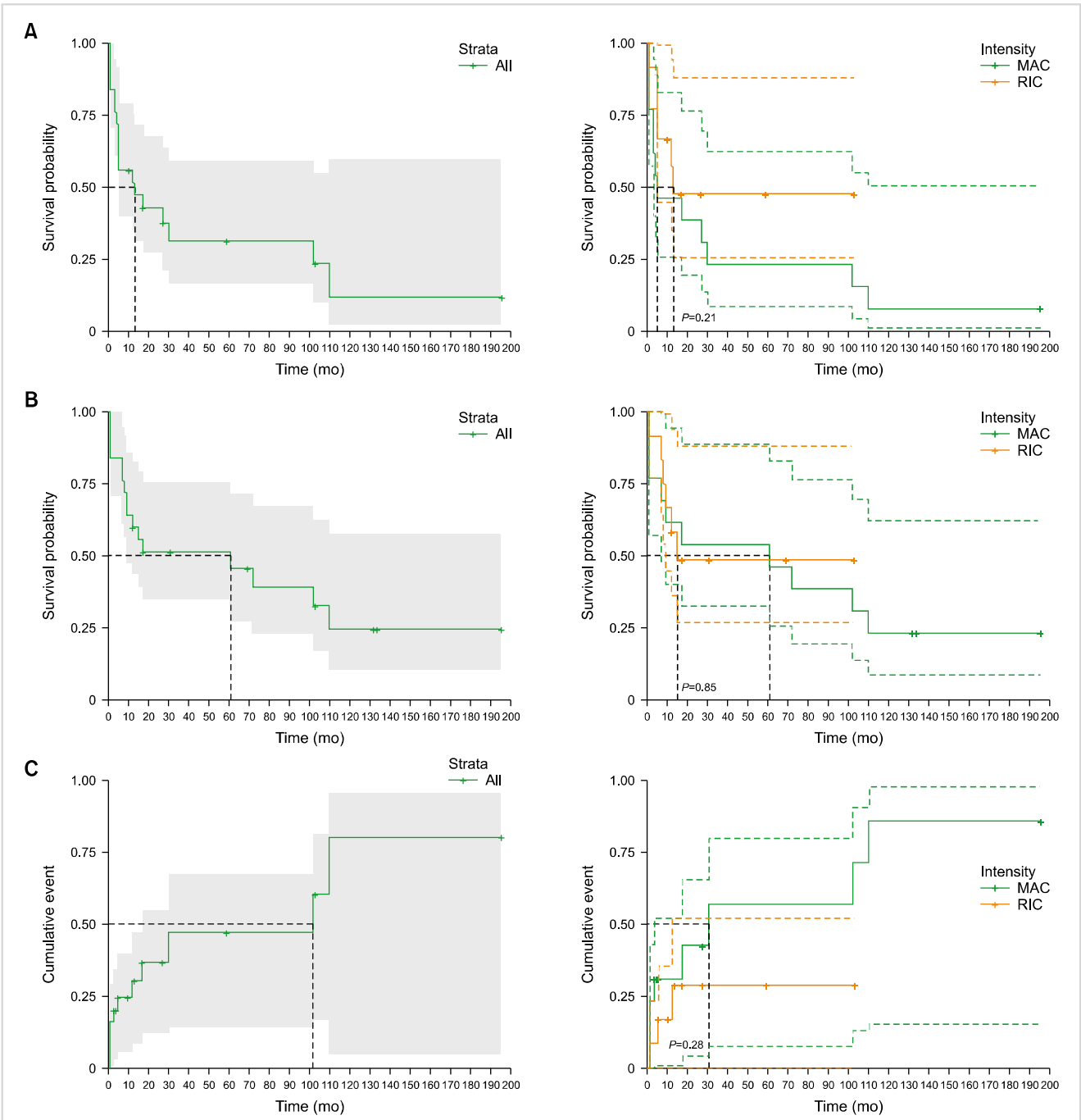

Fig. 2. Survival outcomes. **(A)** Kaplan–Meier curves of progression-free survival for all patients (left) according to conditioning intensity (right). **(B)** Kaplan–Meier curves of overall survival for all patients (left) according to conditioning intensity (right). **(C)** Cumulative incidence of non-relapse mortality in all patients (left) according to conditioning intensity (right).

GVHD and other complications

Overall, 18 (72%) patients developed acute GVHD (grade I in 5 patients, grade II in 4, grade III in 4, grade IV in 5). Numerically, the incidence of acute GVHD was 84.6% (11 of 13 patients) in the MAC group versus 58.3% (7 of 12 patients) in the RIC group. The cumulative incidence of grade III–IV acute GVHD was significantly higher in the MAC group than that in the RIC group (Fig. 3B, P=0.03). Chronic GVHD occurred in nine (36%) patients (mild in 3 patients, moderate in 1, and severe in 5). There were no differences in the cumulative incidence of chronic GVHD between the two groups (Fig. 4A, any chronic GVHD, P=0.28; Fig. 4B, moderate to severe chronic GVHD, P=0.11).

DISCUSSION

Through this study, we found that 1) RIC is more advantageous in terms of cell engraftment and rate of complete chimerism achievement after alloSCT compared to MAC, and 2) RIC is associated with less acute GVHD and overall mortality. In line with previous data advocating RIC over MAC for patients with MF, the importance of our study lies in the fact that we present data from East Asians who are often under-represented, and our patients represent a relatively younger end of the spectrum of patients with MF.

Because the pathophysiology of MF lies in the constitutive activity of JAK signaling, ruxolitinib, a potent JAK 1/2 tyrosine kinase inhibitor, has been shown to improve constitutional symptoms and reduce splenomegaly in patients with MF [16-18]. As a result, ruxolitinib has been approved for MF, and the treatment options for MF have expanded [19]. Several previous studies have reported that splenomegaly is associated with a delay in hematological engraftment, a high risk of graft failure, and even lower survival [20-22]. Although there was a difference in the rate of use of pre-transplant ruxolitinib between the two groups, the effect of pre-transplant ruxolitinib could be partially leveled out considering that there was no difference in spleen size prior to transplantation between the two groups. The possible additive role of pre-transplant ruxolitinib in modulating the course of disease other than spleen size requires further exploration [10].

One of the most obvious limitations of this study was the small number of enrolled patients. We could not identify prognostic factors related to alloSCT. However, it should

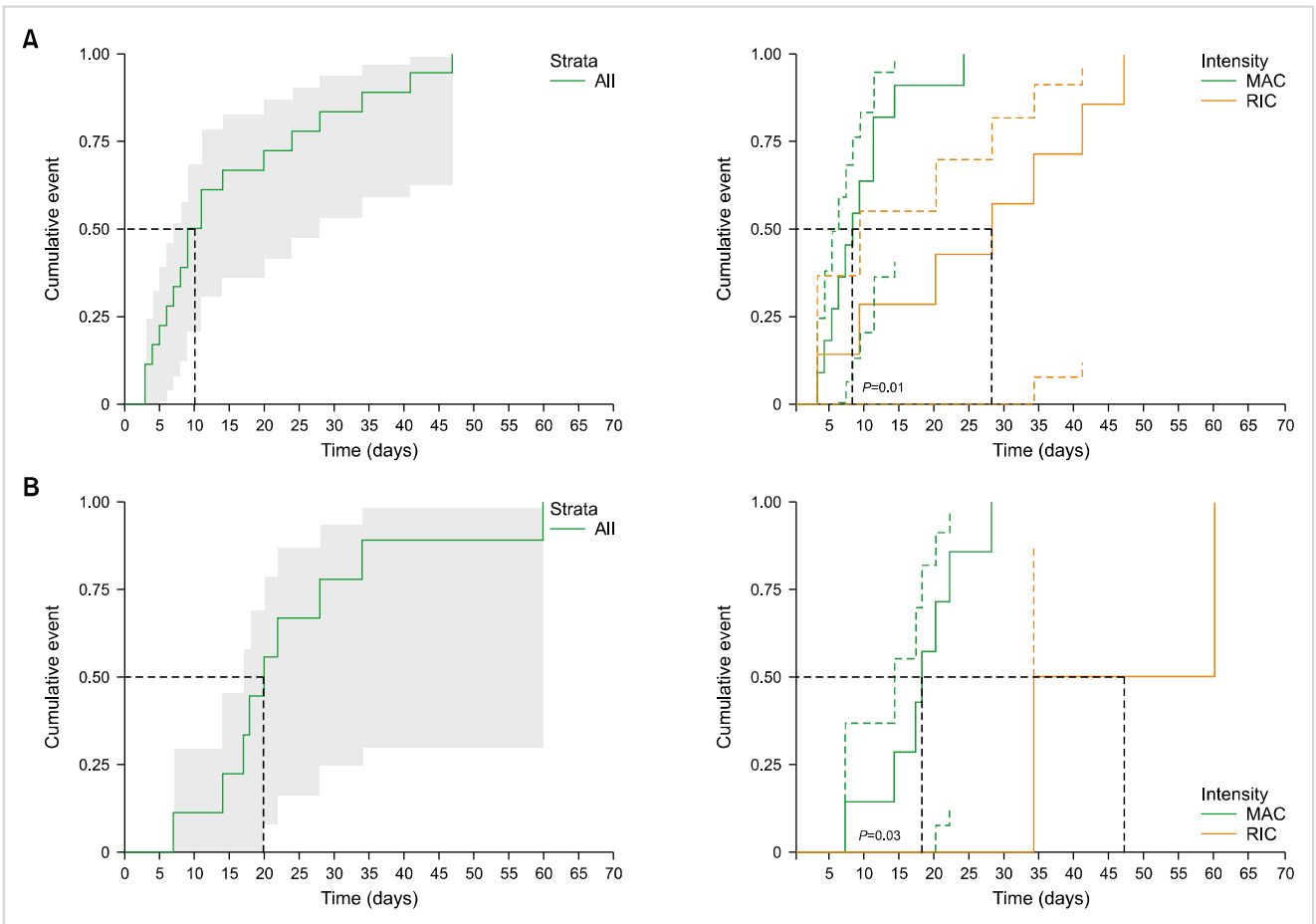

Fig. 3. Cumulative incidence of acute graft-versus-host disease (GVHD). **(A)** Cumulative incidence of acute GVHD in all patients (left) according to conditioning intensity (right). **(B)** Cumulative incidence of grade III–IV acute GVHD in all patients (left) according to conditioning intensity (right).

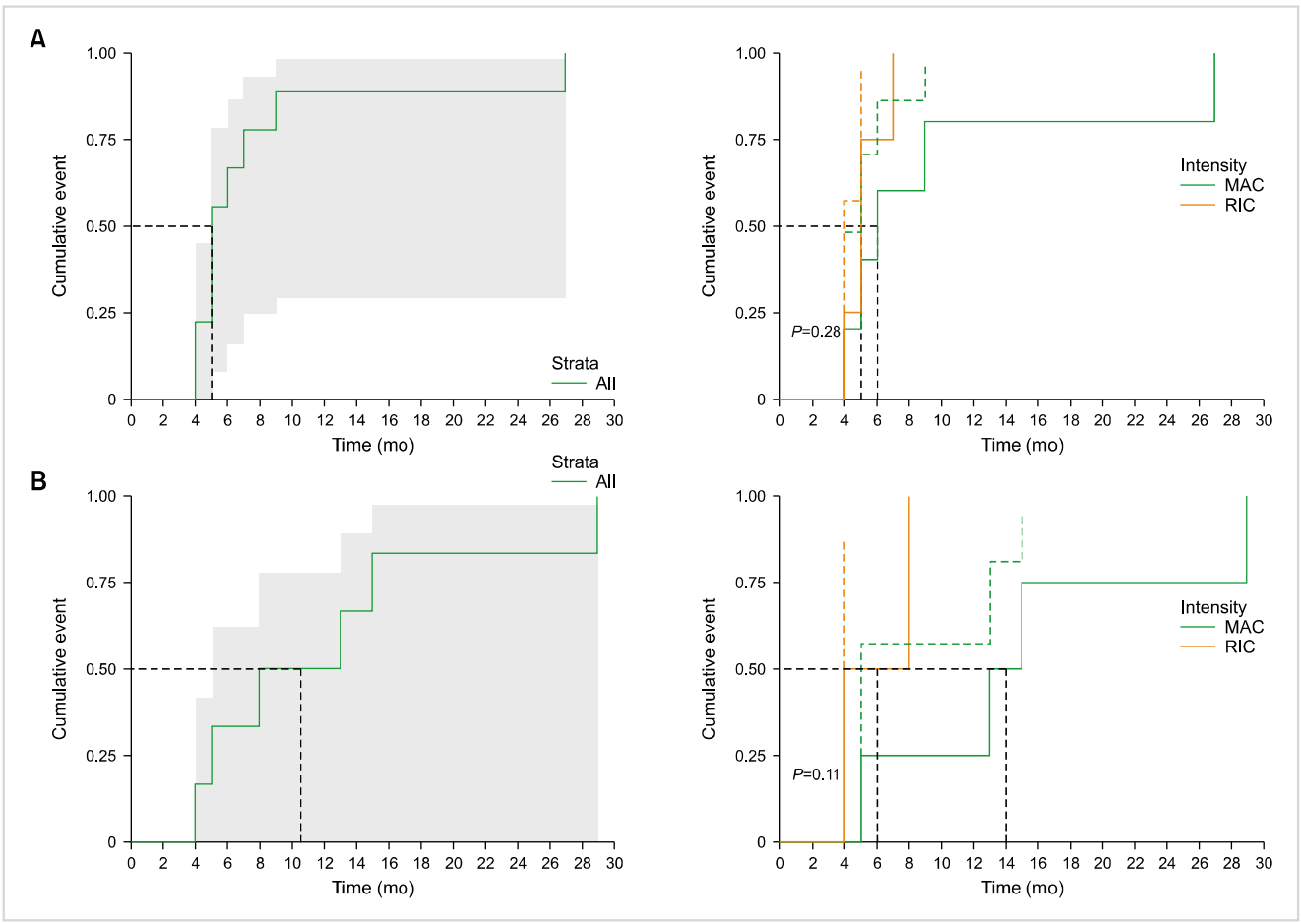

Fig. 4. Cumulative incidence of chronic graft-versus-host disease (GVHD). **(A)** Cumulative incidence of chronic GVHD in all patients (left) according to conditioning intensity (right). **(B)** Cumulative incidence of moderate to severe chronic GVHD in all patients (left) according to conditioning intensity (right).

be taken into consideration that conducting a study in this certain setting is not easy, as evident by paucity of previous data. As our study provides additional information to guide the nuanced decision in choosing the appropriate conditioning regimen in a rare population, we believe that the small number of patients does not diminish the importance of our study. In addition, the effects of the transplantation period could not be excluded. After the introduction of ruxolitinib in clinical practice, we tried to avoid alloSCT using ruxolitinib in patients with MF, which seems to be the reason for the difference in age, transplantation period, and use of pre-transplant ruxolitinib between the two groups. In addition, since all our patients in the RIC group underwent BuFlu conditioning, we were not able to determine the best RIC regimen. Jain *et al.* [23] recently reported FluMel to be superior to BuFlu, which warrants future studies.

In conclusion, RIC offers a significant advantage over MAC, even in younger patients with MF undergoing alloSCT, in terms of cell engraftment, rate of complete chimerism achievement, and acute GVHD.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

REFERENCES

1. Castro-Malaspina H, Moore MA. Pathophysiological mechanisms operating in the development of myelofibrosis: role of megakaryocytes. Nouv Rev Fr Hematol (1978) 1982;24:221-6.
2. Wolf BC, Neiman RS. Myelofibrosis with myeloid metaplasia: pathophysiologic implications of the correlation between bone marrow changes and progression of splenomegaly. Blood 1985; 65:803-9.
3. Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood 2016;127:2391-405.
4. O'Sullivan JM, Harrison CN. Myelofibrosis: clinicopathologic features, prognosis, and management. Clin Adv Hematol Oncol 2018;16:121-31.
5. Kröger NM, Deeg JH, Olavarria E, et al. Indication and

management of allogeneic stem cell transplantation in primary myelofibrosis: a consensus process by an EBMT/ELN international working group. Leukemia 2015;29:2126-33.
6. Gupta V, Hari P, Hoffman R. Allogeneic hematopoietic cell transplantation for myelofibrosis in the era of JAK inhibitors. Blood 2012;120:1367-79.
7. Kerbauy DM, Gooley TA, Sale GE, et al. Hematopoietic cell transplantation as curative therapy for idiopathic myelofibrosis, advanced polycythemia vera, and essential thrombocythemia. Biol Blood Marrow Transplant 2007;13:355-65.
8. Guardiola P, Anderson JE, Bandini G, et al. Allogeneic stem cell transplantation for agnogenic myeloid metaplasia: a European group for blood and marrow transplantation, Société Française de Greffe de Moelle, Gruppo Italiano per il Trapianto del Midollo Osseo, and Fred Hutchinson Cancer Research Center Collaborative Study. Blood 1999;93:2831-8.
9. Byun JM, Kim YJ, Youk T, Yang JJ, Yoo J, Park TS. Real world epidemiology of myeloproliferative neoplasms: a population based study in Korea 2004-2013. Ann Hematol 2017;96:373-81.
10. McLornan DP, Yakoub-Agha I, Robin M, Chalandon Y, Harrison CN, Kroger N. State-of-the-art review: allogeneic stem cell transplantation for myelofibrosis in 2019. Haematologica 2019; 104:659-68.
11. Robin M, Porcher R, Wolschke C, et al. Outcome after transplantation according to reduced-intensity conditioning regimen in patients undergoing transplantation for myelofibrosis. Biol Blood Marrow Transplant 2016;22:1206-11.
12. McLornan D, Szydlo R, Koster L, et al. Myeloablative and reduced-intensity conditioned allogeneic hematopoietic stem cell transplantation in myelofibrosis: a retrospective study by the Chronic Malignancies Working Party of the European Society for Blood and Marrow Transplantation. Biol Blood Marrow Transplant 2019;25:2167-71.
13. Glucksberg H, Storb R, Fefer A, et al. Clinical manifestations of graft-versus-host disease in human recipients of marrow from HL-A-matched sibling donors. Transplantation 1974;18:295-304.
14. Jagasia MH, Greinix HT, Arora M, et al. National Institutes of Health consensus development project on criteria for clinical trials in chronic graft-versus-host disease: I. The 2014 Diagnosis and Staging Working Group Report. Biol Blood Marrow Transplant 2015;21:389-401, e1.
15. Copelan E, Casper JT, Carter SL, et al. A scheme for defining cause of death and its application in the T cell depletion trial. Biol Blood Marrow Transplant 2007;13:1469-76.
16. Delhommeau F, Jeziorowska D, Marzac C, Casadevall N. Molecular aspects of myeloproliferative neoplasms. Int J Hematol 2010;91:165-73.
17. Verstovsek S, Mesa RA, Gotlib J, et al. A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis. N Engl J Med 2012;366:799-807.
18. Harrison C, Kiladjian JJ, Al-Ali HK, et al. JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis. N Engl J Med 2012;366:787-98.
19. Mascarenhas J, Hoffman R. Ruxolitinib: the first FDA approved therapy for the treatment of myelofibrosis. Clin Cancer Res 2012;18:3008-14.
20. Ciurea SO, Sadegi B, Wilbur A, et al. Effects of extensive splenomegaly in patients with myelofibrosis undergoing a reduced intensity allogeneic stem cell transplantation. Br J Haematol 2008;141:80-3.
21. Polverelli N, Mauff K, Kröger N, et al. Impact of spleen size and splenectomy on outcomes of allogeneic hematopoietic cell transplantation for myelofibrosis: a retrospective analysis by the Chronic Malignancies Working Party on behalf of European Society for Blood and Marrow Transplantation (EBMT). Am J Hematol 2021;96:69-79.
22. Akpek G, Pasquini MC, Logan B, et al. Effects of spleen status on early outcomes after hematopoietic cell transplantation. Bone Marrow Transplant 2013;48:825-31.
23. Jain T, Kunze KL, Temkit M, et al. Comparison of reduced intensity conditioning regimens used in patients undergoing hematopoietic stem cell transplantation for myelofibrosis. Bone Marrow Transplant 2019;54:204-11.