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Role of Uric Acid Levels as a Prognostic Indicator in Allogeneic Hematopoietic Stem Cell Transplantation: Insights from a Single-Center Study

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ABSTRACT

Uric acid (UA) acts as a richly available water-soluble antioxidant, contributing to approximately two-thirds of the overall free-radical-scavenging activity in human serum. It is discharged from damaged cells during the preparation for allogeneic hematopoietic stem cell transplantation (allo-HSCT). This study assessed how pretransplantation uric acid levels influence survival and mortality in allo-HSCT patients. In a retrospective analysis of 267 patients with hematologic diseases who underwent allo-HSCT, uric acid levels were documented on the day of allo-HSCT (day 0). Patients were divided into two cohorts based on their pretransplant uric acid levels: those at or below 4.4 mg/dL and those above 4.4 mg/dL. Among them, 153 (57.3%) were male, and 114 (42.7%) were female, with a median age of 31 years (ranging from 13 to 66). Those with serum uric acid levels of 4.4 mg/dL or lower exhibited notably poorer overall survival (OS) and disease-free survival (DFS) compared to those surpassing 4.4 mg/dL (p=0.032 and p=0.045, respectively). Our findings indicate an interrelation between low pretransplant serum uric acid levels and reduced survival rates in allo-HSCT patients. Further exploration into potential mechanisms, such as compromised antioxidative capacity in hypouricemia, may establish uric acid as a promising prognostic marker in allo-HSCT.

Keywords: Uric acid, Allogeneic Hematopoietic Stem Cell Transplantation, Survival, Prognosis

Allojenik Hematopoetik Kök Hücre Nakli' nde Ürik Asit Seviyesinin Prognostik Bir Belirteç Olarak Rolü: Tek Merkez Deneyimi

Araştırma Makalesi

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ÖZET

Ürik asit (UA) suda çözünebilen zengin bir antioksidan olarak görevi görür ve insan serumundaki toplam serbest radikal süpürücü aktivitenin yaklaşık üçte ikisine katkıda bulunur. Allojeneik hematopoetik kök hücre nakli (allo-HKHN) için hazırlık sırasında hasarlı hücrelerden atılır. Bu çalışmada, allo-HKHN hastalarında nakil öncesi ürik asit düzeylerinin sağkalım ve mortaliteyi nasıl etkilediği değerlendirilmiştir. Hematolojik hastalığı olan ve allo-HKHN yapılan 267 hastanın retrospektif analizinde, ürik asit düzeyleri allo-HKHN gününde (0. gün) belgelenmiştir. Hastalar nakil öncesi ürik asit düzeylerine göre iki gruba ayrılmıştır: 4,4 mg/dL veya altında olanlar ve 4,4 mg/dL'nin üzerinde olanlar. Bunların 153 'ü (%57,3) erkek, 114' ü (%42,7) kadındı ve ortanca yaşları 31'di (13 ile 66 arasında değişiyordu). Serum ürik asit düzeyleri 4,4 mg/dL veya altında olanlar, 4,4 mg/dL'yi aşanlara kıyasla belirgin şekilde daha kötü genel sağkalım (OS) ve hastalıksız sağkalım (DFS) sergilemiştir (sırasıyla p=0,032 ve p=0,045). Bulgularımız, allo-HKHN hastalarında düşük pretransplant serum ürik asit düzeyleri ile azalmış sağkalım oranları arasında bir ilişki olduğunu göstermektedir. Hipoürisemide bozulmuş antioksidatif kapasite gibi potansiyel mekanizmaların daha fazla araştırılması, ürik asidin allo-HKHN' nde umut verici bir prognostik belirteç olmasını sağlayabilir.

Anahtar Kelimeler: Ürik asit, Allojenik Hematopoietik Kök Hücre Nakli, Sağkalım, Prognoz

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Introduction

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a well-established therapeutic approach for various hematological malignancies and non-neoplastic genetic disorders.[1,2] The treatment result of allo-HSCT depended on two primary variables: transplant-related morbidity or mortality (TRM) and disease recurrence.[3,4] Despite advancements in recent decades, infectious complications and graft-versus-host disease (GVHD) continue to be significant contributors to transplant-related morbidity or mortality (TRM).[5,6] Efforts have focused on identifying prognostic markers for allo-HSCT recipients, with UA emerging as a potential predictive marker for survival. However, the prognostic significance of UA in determining post-transplantation outcomes remains uncertain. UA is the end product of the purine metabolic pathway.[7] Humans do not possess urate oxidase or uricase, enzymes necessary to convert UA into the more soluble compound allantoin.[8]

Consequently, humans tend to have higher serum UA concentrations than most other mammals. However, the increased UA levels in humans have been considered beneficial, especially during increased oxidative stress.[9] UA can bind iron and inhibit iron-dependent ascorbate oxidation, protecting against oxidative stress-induced injuries. Consequently, a decrease in UA concentration may result in heightened oxidative stress.[10]

Oxidative stress, marked by heightened free radical activity, is considered a significant factor in conditions such as cancer, heart disease, and aging. UA is the principal natural antioxidant in peripheral blood, contributing to approximately 60% of the capacity for scavenging free radicals.[9] Moreover, the suggested antioxidant properties of heightened UA levels in humans are believed to provide neuroprotection against a range of neurodegenerative and neuroinflammatory disorders.[11-15]

The antioxidant impact of UA has not been sufficiently documented in patients undergoing allo-HSCT. Numerous studies present conflicting findings regarding the association between UA levels and overall survival among patients undergoing allogeneic hematopoietic stem cell transplantation (allo-HSCT). While one previous retrospective study indicates no significant association between UA levels prior to transplantation and mortality following allo-HSCT,[16] another study suggests a negative association between UA levels and mortality. The antioxidant effect of UA has not yet been adequately reported in patients undergoing allo-HSCT.[17] Therefore, we aimed to evaluate the prognostic significance of pretransplant UA levels for survival outcomes in patients undergoing allogeneic hematopoietic stem cell transplantation (allo-HSCT).

Methods

Patient Cohort

Three hundred patients who underwent transplantation at Erciyes University Hematology Transplant Center between 2007 and 2016 were included for retrospective data analysis. After excluding individuals with missing UA levels on the day of hematopoietic stem cell transplantation (HSCT) (day 0) (n=33), the final dataset consisted of 267 patients. These patients were divided into two groups based on their pretransplant UA levels: those with serum UA levels of 4.4 mg/dL or lower (≤4.4 mg/dL) and those with levels exceeding 4.4 mg/dL (>4.4 mg/dL). The study was approved by the local ethics committee of Erciyes University (Approval number: 2021/338).

Transplantation Procedures and Prophylaxis Strategy

HSCT procedures followed standard protocols. Myeloablative conditioning (MAC) regimens included either cyclophosphamide/total body irradiation (TBI) or cyclophosphamide/busulfan. Non-myeloablative conditioning (NMA) was primarily administered to patients with aplastic anemia, with cyclophosphamide being the primary conditioning agent. Reduced-intensity conditioning (RIC) comprised fludarabine/busulfan, fludarabine/melphalan, or fludarabine/low-dose TBI. Prophylaxis against GVHD consisted of methotrexate plus cyclosporine A, with or without anti-thymocyte globulin (ATG).

Within the first four weeks following transplantation, patients were prescribed prophylactic antibacterial (moxifloxacin 1×400 mg/day) and antiviral (valacyclovir 1×500 mg/day) treatments. Antifungal prophylaxis consisted of fluconazole 2×200 mg/day until the 75th day post-transplantation. After engraftment, trimethoprim and sulfamethoxazole were administered twice daily, twice weekly, for pneumocystis jirovecii prophylaxis until day 180. Patients were scheduled for weekly visits during the initial month and biweekly visits for the subsequent three months.

Characterization of Transplant-Related Variables and Statistical Analysis

Patients diagnosed with acute leukemia in first or second complete remission (CR) or those with myelodysplastic syndrome (MDS) were categorized as standard risk for risk stratification associated with transplantation.[18]

Patients not falling into these categories were classified as high-risk. In instances of gender mismatch between donor and recipient, female donors matched with male recipients were considered high risk, while all other combinations were categorized as standard risk.[19] GVHD was evaluated according to established clinical criteria.[20,21]

The primary endpoints included overall survival (OS) and disease-free survival (DFS). OS was defined as the period from HSCT to death from any cause. DFS was delineated as the duration (in months) from the date of HSCT until disease recurrence was confirmed radiologically or histologically. Early transplant mortality referred to events occurring within the initial 30 days post-transplantation, while peritransplant mortality encompassed events within the first 100 days after transplantation.

We utilized the Mann-Whitney U test to compare continuous variables between the two groups. For

qualitative data comparison, we employed the Pearson Chi-Square and Fisher-Freeman Halton tests. Survival and mortality probabilities were estimated using the Kaplan-Meier method, with comparisons performed using the log-rank test. The optimal cut-off value for uric acid levels in predicting survival was determined through receiver operating characteristic (ROC) curve analyses. Furthermore, we conducted univariate and multivariate Cox regression analyses to identify the most significant risk factors affecting survival and mortality probabilities.

Variables that had a significance level of p<0.20 were included in the multiple models, and backward elimination was used to identify independent risk factors. Hazard ratios, along with 95% confidence intervals (CIs), were reported. A significance level of p<0.05 was considered statistically significant.

Results

Patients Attributes

A total of 267 patients participated in the study, with 153 (57.3%) being male and 114 (42.7%) female. Patient characteristics before transplantation are summarized in Table 1. The median age overall was 31 years (range 13-65). In terms of risk classification, 124 patients (46.4%) were categorized as high risk, while 143 (53.6%) were considered standard risk. Most patients underwent transplantation for acute leukemia (74.2%), while a smaller proportion received transplants for lymphoproliferative diseases (10.9%) or other conditions (15%). The median pretransplant uric acid (UA) level was 4.2 mg/dL (range 1.1-8.5 mg/dL). Among the patients, 198 (74.2%) underwent allo-HSCT within the first 12 months after diagnosis, while 69 patients (25.8%) underwent the procedure after completing the initial 12 months following diagnosis. In post-transplant evaluation, infections were identified as the primary complication, with 206 patients (77.2%) experiencing at least one episode of infectious events. GVHD emerged as the second most common complication during the post-transplant period.

Among the patients, 33 (12.4%) were diagnosed with acute GVHD, while chronic GVHD was observed in 98 (36.7%) cases. During the posttransplant follow-up, a total of 103 patients (38.6%) passed away. Within the initial 30 days after transplantation, 24 patients (9%) succumbed, while 12 patients (4.4%) passed away within the first 100 days post-transplantation. Fifty-five patients (20.6%) experienced relapse during the follow-up period. The OS and DFS were observed to be 90 months (range 52.3-105.7) and 98 months (range 78.2-115.4), respectively.

Establishing the Threshold for Low Serum UA Levels

The median serum UA value in the entire cohort was 4.2 mg/dl (range 1.1-8.5). Based on ROC analysis, the optimal cut-off value of UA to predict survival was determined to be 4.4 mg/dl. At this cut-off value, UA exhibited a sensitivity of 64.1%, a specificity of 51.2% (p=0.022), and an accuracy of 56.18% for predicting mortality. The area under the curve (AUC) was computed to be 0.583 (95% CI: 0.514-0.652; p<0.05).

Table 1. Patient characteristics

Variables	Results, n (%)
Age, years (<40/≥40)	183 (68.5)/84 (31.5)
Gender (male/female)	153 (57.3)/114 (42.7)
Diagnosis	
Acute leukemia	198 (74.2)
Lymphoproliferative diseases	29 (10.9)
Other diseases	40 (15)
Sex mismatch (standard risk/high risk)	166 (62.2)/101 (37.8)
Risk group (standard risk/ high risk)	143 (53.6)/124 (46.4)
Time to transplant (<12 months/*≥12months)*	198(74.2)/69(25.8)
Conditioning regimen	
MAC	208 (77.9)
NonMAC	26 (9.7)
RIC	16 (6.0)
MISSING	17 (6.4)
HLA match	
Full match	219 (82)
Mismatch	45 (16.9)
Unreleated	3 (1.1)
CD 34^{+}count, 10^{6}/kg, median (range)	7.01 (2.7-19.2)
Uric acid at HSCT Median in mg/dl (range)	4.2 (1.1-8.5)
Infection (yes)	206 (77.2)
Acute GVHD (yes)	33 (12.4)
Chronic GVHD (yes)	98 (36.7)
GVHD (yes)	123 (46.1)
DFS, m, median (range)	98 (78.2-115.4)
OS, m, median (range)	90 (52.3-105.7)
Peri-transplant mortality	12 (4.5)
Early-transplant mortality	24 (9)

DFS: disease-freesurvival; GVHD: graft-versus-hostdisease; HLA: human leukocyte antigen; OS:overall survival; m: month; MAC: myeloablative; NonMAC: nonmyeloablative; RIC: reduced intensity conditioning; HR: hazard ratio; CI: confidence interval

The association of OS with low serum UA levels

The median OS for patients with serum UA levels ≤4.4 mg/dL was 73.8 months (range, 31.35-116.2), whereas it was 101 months (range, 79.9-127.3) for those with serum UA levels >4.4 mg/dL. Our analysis revealed a significantly poorer OS among patients with low serum UA levels (p=0.029, Figure 1).

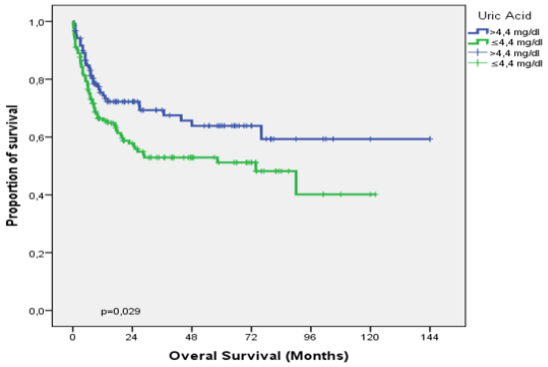

Figure 1. Patients with serum uric aci levels ≤4,4 mg/dl had significantly lower overall survival compared with those with serum uric acid levels >4,4 mg/dl (p=0,029)

Both univariate and multivariate analyses demonstrated that patients with serum UA levels ≤4.4 mg/dL exhibited significantly lower OS compared to those with levels >4.4 mg/dL (univariate hazard ratio [HR] for OS: 1.55, 95% CI: 1.04-2.33, p=0.031; multivariate HR: 1.57, 95% CI: 1.04-2.39, p=0.032), suggesting a heightened risk of mortality among patients with low serum UA levels ≤4.4 mg/dL. Detailed results of both multivariate and univariate analyses are presented in Table 2. In conclusion, low serum UA levels prior to allo-HSCT represent an independent risk factor for mortality.

Table 2. Univariate and multivariate analysis of parameters for overall survival (OS)

Variables	OS			
	Univariate		Multiple	
	HR (95% CI)	p	HR (95% CI)	p
Age, years				
<40	1.00			
≥40	1.022 (0.67-1.54)	0.918	-	-
Gender				
Male	1.00			
Female	1.444 (0.98-2.13)	0.062	-	-
Diagnosis				
Other diseases	1.00			
Acute leukemia	1.064 (0.59-1.91)	0.836	-	-
Lymphoproliferative diseases	1.357 (0.63-2.93)	0.437	-	-
Sex mismatch				
Standard risk	1.00			
High risk	1.053 (0.71-1.56)		-	-
Disease status				
Standard risk	1.00			
High risk	1.229 (0.82-1.83)	0.316	-	-
Conditioning regimen				
RIC	1.00			
NonMAC	1.842 (0.57-5.98	0.310	-	-
MAC	1.814 (0.67-4.95	0.245	-	-
Time to transplant				
<12months	1.00			
≥12 months	1.686 (1.12-2.54)	0.012*	1.552 (1.03-2.34)	0.037*
HLA Match				
Full Match	1.00		1.00	
MisMatch	2.270 (1.45-3.55)	0.001**	2.366 (1.48-3.79)	0.000**
Unrelated	3.502 (0.86-14.35)	0.081	3.759(0.91-15.46)	0.066
Uric asid				
>4.4	1.00			
≤4.4	1.558 (1.04-2.33)	0.031*	1.577 (1.04-2.39)	0.032*
$CD34^+$ Count	1.019 (0.94-1.11)	0.659	-	-
Infection (yes/no)	1.353 (0.83-2.20)	0.225	-	-
Acute GVHD (yes)	1.670 (1.03-2.78)	0.048*	1.539 (0.91-2.59)	0.107
Chronic GVHD (yes)	0.601 (0.39-0.91)	0.017*	0.593 (0.38-0.91)	0.016*
GVHD (no)	0.831 (0.56-1.23)	0,349	-	-

GVHD: graft-versus-host disease; HLA: human leukocyte antigen; RIC: reduced intensity conditioning; HR: hazard ratio; CI: confidence interval; * p<0.05, **p<0.01

In the multivariate analysis, risk factors associated with OS included HLA mismatched donor (HR 2.36, 95% CI: 1.48-3.79, p=0.001), time to transplant interval (HR 1.55, 95% CI: 1.03-2.34, p=0.037), and the presence of chronic GVHD (HR 0.59, 95% CI: 0.38-0.91, p=0.032). Parameters such as age, gender, diagnosis, gender mismatch, disease status, conditioning regimens, presence of infection, and the number of total infused CD34+ cells did not show a significant effect on OS (p>0.05).

The association of DFS with low serum UA levels

The median DFS for patients who had serum UA levels of ≤4.4 mg/dl was 83.2 (range, 72.9-93.4) months versus 115.9 (range, 104.2-127.3) months for patients with serum uric acid levels >4.4 mg/dl.

The disease-free survival rate was significantly lower in patients with UA levels were ≤4.4 mg/dl than those with UA levels >4.4 mg/dl (figure 2, DFS univariate HR 1.72, 95% CI: 1.09-3.01, p=0.044; multivariate HR 1.68, 95% CI: 1.03-3.06, p=0.045).

Table 3. Univariate and multivariate analysis of parameters for disease-free survival (DFS)

Variables	DFS			
	Univariate		Multiple	
	HR (95% CI)	p	HR (95% CI)	p
Age, years				
<40	1.00		1.00	
≥40	0.462 (0.23-0.92)	0.027*	0.431 (0.21-0.87)	0.018*
Gender				
Male	1.00		1.00	
Female	1.667(0.98-2.83	0.059	1.932 (1.09-3.44)	0.025*
Diagnosis				
Other diseases	‡	0.956	-	-
Acute leukemia	0.63(0.29-1.23)	0.166	-	-
Lymphoproliferative diseases	1.00			
Sex mismatch				
Standard risk	1.00			
High risk	0.778 (0.44-1.39)	0.384	-	-
Disease status				
Standard risk	1.00			
High risk	1.145 (1.25-3.69)	0,006**	2.456 (1.35-4.47)	0,003**
Conditioning regimen				
RIC	1.00			
NonMAC	‡	0.967	-	-
MAC	1.330 (0.41-4.27)	0.632	-	-
Time to transplant				
<12months	1.00		1.00	
≥12 months	1.928 (1.11-3.34)	0,019*	1.921 (1.07-3.44)	0.028*
HLA Match				
Full Match	1.00		1.00	
MisMatch	2.189 (1.16-4.09)	0.014*	1.311 (0.59-2.88)	0.501
Unrelated	‡	0.977		0.977
Uric asid				
>4.4	1.00		1.00	
≤4.4	1.726 (1.09-3.01)	0.044*	1.686 (1.03-3.06)	0.045*
$CD34^+$ Count	1.087 (0.97-1.22)	0.145	-	-
Infection (yes/no)	1.065 (0.57-1.98)	0.843	-	-
Acute GVHD (yes)	1.731 (0.87-3.44)	0.118	-	-
Chronic GVHD (yes)	1.058 (0.62-1.80)	0.836	-	-
GVHD (no)	1.204 (0.71-2.05)	0.493	-	-

GVHD: graft-versus-hostdisease; HLA: human leukocyte antigen; OS:overall survival; MAC: myeloablative; NonMAC: nonmyeloablative; RIC: reduced intensity conditioning; HR: hazard ratio; CI: confidence interval; *<0.05; **<0.01; ‡: HR could not be computed because all cases were censored in this group

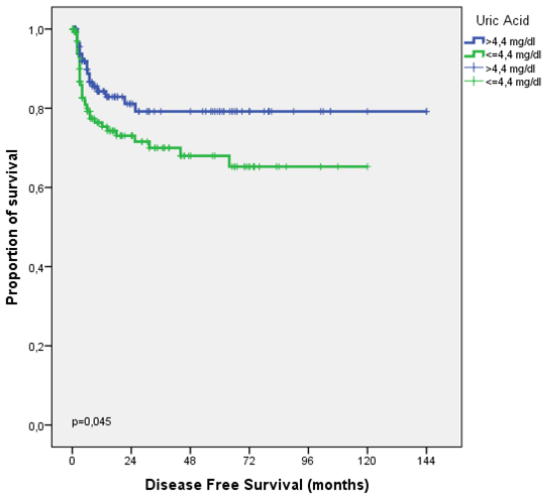

Figure 2. Patients with serum uric aci levels ≤4,4 mg/dl had significantly lower disease-free survival compared with those with serum uric acid levels >4,4 mg/dl (p=0,045)

Additional factors showing notable differences among groups were age, with patients older than 40 years having an increased risk compared to those younger than 40 years (HR 0.43, 95% CI 0.21-0.87; p=0.018); gender, where females faced a higher risk compared to males (HR 1.93, 95% CI 1.09-3.44; p=0.025); risk status, wherein patients with high transplantation-associated risk had significantly lower DFS compared to those with standard transplantation-associated risk (HR 2.45, 95% CI 1.35-4.47; p=0.003); and time to transplant interval, with patients undergoing allo-HSCT within 12 months from diagnosis (<12 months) having higher DFS compared to those undergoing allo-HSCT more than 12 months from diagnosis (≥12 months) (HR 1.92, 95% CI 1.09-3.44; p=0.028). The diagnostic parameters, gender mismatch, conditioning regimens, presence of infection, acute GVHD, chronic GVHD, and the total number of infused CD34+ cells did not exhibit a significant effect on OS (p>0.05). The multivariate and univariate analyses of variables for DFS are presented in Table 3.

Discussion

The attributes of both patients and donors before transplantation, along with factors occurring after transplantation, serve as crucial predictors of outcomes for allo-HSCT recipients. Many recipients remain in close proximity to the transplant center during the initial 90-100 days post-transplantation. Therefore, establishing prognostic factors is essential for identifying patients at high risk of poor outcomes. This study primarily focused on evaluating the predictive significance of pretransplantation low serum UA levels on the outcomes of patients who have undergone allo-HSCT during the post-transplant period. Recent research indicates that hypouricemia is associated with various inflammatory and degenerative diseases.[10,22-24] The link between hypouricemia and reduced antioxidative capacity has been noted. Toxicity induced by oxygen radicals initiates a chain reaction of lipid peroxidation, which in turn leads to damage to DNA, RNA, proteins, cellular membranes, and cellular organization.[9] In a study by Waring et al.[25], it was shown that elevated UA concentrations were linked to heightened serum antioxidant capacity and decreased oxidative stress during acute physical exercise in a group of twenty healthy subjects. UA is considered the predominant natural antioxidant in peripheral blood. Hence, our initial hypothesis primarily aimed to uncover any potential association between low serum UA levels and survival.

In our study, we conducted a retrospective analysis of data from 267 recipients of allo-HSCT to explore the relationship between serum UA levels and key transplant outcomes. We discovered that pretransplant low serum UA levels in allo-HSCT recipients were linked to inferior survival. This association could be explained by the reduced antioxidative capacity. Our findings align with those reported in the study by Ghasemi and colleagues.[17] The research findings indicated that serum UA levels falling below 3.4 mg/dl were linked to heightened mortality risk and diminished OS, with 3.4 mg/dl identified as the threshold value for serum UA level. Moreover, their findings revealed that patients exhibiting serum UA levels exceeding 3.4 mg/dl experienced a 37% reduced probability of developing GVHD, a significant factor contributing to transplant-related mortality (TRM).

Consistent with existing literature, our study also identified a higher mortality rate among patients who developed chronic GVHD following allo-HSCT (p=0.016).

In a separate study, Ostendorf et al.[16] demonstrated a notable correlation between low UA levels and the occurrence of acute GVHD. However, they did not find a significant association between low UA levels and OS or relapse. The lack of statistical significance regarding survival and serum UA levels in their study might be attributed to its single-center, retrospective design and inclusion of HLA-matched transplant recipients. The reduced antioxidative capacity attributed to hypouricemia may explain the inverse correlation observed between UA levels and GVHD in both studies (Ghasemi et al.[17] and Ostendorf et al.[16]), as well as the lower OS outcome reported in the former study.

Our results diverge from those reported in a prior prospective study by Penack et al.[26] Their research indicated that elevated UA levels prior to the commencement of conditioning correlated with increased mortality post-allo-HSCT. However, their study design varied as it was prospective and concentrated solely on allo-HSCT from HLA-identical sibling donors. Hence, they could not extrapolate conclusions from these results regarding the association between UA levels and outcomes in matched unrelated donor allo-HSCT or haploidentical allo-HSCT.

In our study, the time elapsed before transplantation emerged as a significant predictor for both OS and DFS. This could be attributed to some patients attaining remission earlier due to the efficacy of first or second-line chemotherapy regimens. It's important to note that patients resistant to chemotherapy underwent allo-HSCT at a later stage compared to those who achieved remission with first-line regimens. Particularly, patients transplanted within the early group (<12 months)

exhibited prolonged survival compared to those in the late group (≥12 months). This disparity was statistically significant for both OS and DFS (p=0.037 and p=0.028, respectively). Our study encountered several limitations: 1) It was conducted retrospectively at a single-center university hospital, making it challenging to ascertain the specific causes of death or infections. Therefore, additional multicenter studies may offer more comprehensive data concerning the relationship between serum UA levels and transplant outcomes. 2) Another limitation of our findings is that UA participates in complex reactions with various oxidants, potentially generating free radicals in diverse radical-forming systems. These radicals primarily target lipids (LDL and membranes) rather than other cellular components. Simultaneously, the hydrophobic environment created by lipids presents challenges to the antioxidant properties of UA. Furthermore, oxidized lipids may convert UA into an oxidant, contributing to cellular oxidative damage. The mechanisms underlying these reactions are intricate and not yet fully understood.[27] While a previous retrospective study demonstrated a positive correlation between UA levels before transplantation and mortality following allo-HSCT, our study revealed a negative association between UA levels and mortality. As a result, there remain unanswered questions regarding the potential involvement of UA in allo-HSCT, whether as an antioxidant or a regulator of allogeneic immune responses. Further research is warranted to elucidate and validate these observations. In conclusion, our study highlights that pretransplant serum low UA levels could potentially act as a predictive marker for outcomes among allo-HSCT recipients. Further investigation and verification of these results may warrant considering this parameter as a selection criterion for survival rate in future risk assessment tools for patients undergoing allo-HSCT.

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