



Development and validation of a comorbidity index for predicting survival outcomes after allogeneic stem cell transplantation in adult patients with acute leukemia: a Korean nationwide cohort study

Sung-Soo Park¹, Hee-Je Kim^{1,2}, Tong Yoon Kim¹, Joon yeop Lee¹, Jong Hyuk Lee¹, Gi June Min¹, Silvia Park¹, Jae-Ho Yoon^{1,2}, Sung-Eun Lee^{1,2}, Byung-Sik Cho^{1,2}, Ki-Seong Eom^{1,2}, Yoo-Jin Kim^{1,2}, Seok Lee^{1,2}, Dong-Wook Kim^{1,2}

¹Department of Hematology, Catholic Hematology Hospital, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, ²Leukemia Research Institute, College of Medicine, The Catholic University of Korea, Seoul, Korea

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Background

Allogeneic hematopoietic stem cell transplantation (alloSCT) is a potentially curative treatment option for acute leukemia. We aimed to identify the comorbidity factors affecting survival outcomes after alloSCT and develop a new comorbidity index tool for predicting overall survival (OS).

Methods

A Korean nationwide cohort of 3,809 adults with acute leukemia treated with alloSCT between January 2002 and December 2018 was analyzed as the development cohort. A retrospective cohort comprising 313 consecutive adults with acute leukemia who underwent alloSCT between January 2019 and April 2020 was analyzed as the validation cohort.

Results

In the development cohort, advanced age, male sex, and comorbidities such as previous non-hematologic malignancy, hypertension, and coronary or cerebral vascular disease were significantly related to poor OS. Subsequently, a new comorbidity scoring system was developed, and risk groups were created, which included the low-risk (score ≤ 0.17), intermediate-risk ($0.17 < \text{score} \leq 0.4$), high-risk ($0.4 < \text{score} \leq 0.55$), and very high-risk (score > 0.55) groups. The 1-year OS rates were discriminatively estimated at 73.5%, 66.2%, 61.9%, and 50.9% in the low-risk, intermediate-risk, high-risk, and very high-risk groups in the development cohort, respectively ($P < 0.001$). The developed scoring system yielded discriminatively different 1-year OS rates and 1-year incidence of non-relapse mortality according to the risk group ($P = 0.085$ and $P = 0.018$, respectively). Furthermore, the developed model showed an acceptable performance for predicting 1-year non-relapse mortality with an area under the curve of 0.715.

Conclusion

The newly developed predictive scoring system could be a simple and reliable tool helping clinicians to assess risk of alloSCT in adults with acute leukemia.

Key Words Comorbidity, Allogeneic, Transplantation, Stem cell, Acute leukemia, Score

Correspondence to

Hee-Je Kim, M.D., Ph.D.
Department of Hematology, Catholic Hematology Hospital, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 222 Banpo-daero, Seocho-gu, Seoul 06591, Korea
E-mail: cumckim@catholic.ac.kr

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INTRODUCTION

Although novel therapies have recently been introduced [1, 2], allogeneic hematopoietic stem cell transplantation

(alloSCT) is still regarded as the only curative modality for acute leukemia [3-6]. However, a low overall survival (OS) related to relapse or treatment-related mortality is an important obstacle that compromises the efficacy of alloSCT [7]. Thus, a precise risk-adapted approach remains an unmet

need in clinical practice.

In addition to emerging biological factors (such as adverse cytogenetics, failure to achieve minimal residual disease, and intolerance to chemotherapeutic toxicities), the comorbidity of individuals could have tremendous impacts on the prognosis of alloSCT. In this regard, various models, including the hematopoietic cell transplantation-specific comorbidity index (HCT-CI) [8], comorbidity-age index [9], and Charlson comorbidity index [10], have been used for pre-transplant risk stratification prior to alloSCT based on the patient's comorbidities. These indices also provide a well-defined risk stratification for mortality. Nevertheless, these indices were not established in a nationwide cohort of patients with acute leukemia. Furthermore, the prognostic impact of commonly emphasized variables among the aforementioned comorbidity indices, such as diabetes, hypertension, cerebrovascular disease, pulmonary dysfunction, and prior non-hematologic malignancy, has not yet been validated in a Korean nationwide cohort.

In Korea, the Korean National Health Insurance Service (KNHIS) program is a mandatory public health insurance system that covers approximately 98% of the overall Korean population. The KNHIS database contains universal medical claims and mortality for the entire Korean population [11] and has been used in various epidemiological research studies on hematologic diseases, as described in detail elsewhere [12-15]. These strengths enable research on a nationwide cohort with the endpoint of identifying personal comorbidities related to patient prognosis after alloSCT.

Accordingly, this study aimed to verify whether well-known patient comorbidity-related prognostic factors, including age, sex, previous non-hematologic malignancy, hypertension, diabetes, dyslipidemia, chronic obstructive pulmonary disease (COPD), cerebrovascular or cardiovascular disease (CVA), anxiety disorder, and depression, have prognostic impacts on outcomes of alloSCT using KNHIS data. We were also interested in the development of a prognostic scoring system based on identified individual comorbidities, followed by external validation of the developed system using an independent database of the development cohort from the KNHIS data.

MATERIALS AND METHODS

Data source of the development cohort

Data for the development cohort were extracted from the KNHIS database. We first included adult patients (≥ 18 yr) who underwent alloSCT between January 2002 and December 2018 in the KNHIS database using the procedure codes V073, X5061, and/or X5063. These claims codes represent the performance of alloSCT, the collection of bone marrow stem cells, and the collection of mobilized peripheral blood stem cells. Thereafter, we confirmed that the final cohort comprised cases of acute leukemia classified based on the International Classification of Diseases, Tenth Revision (ICD-10) codes C92, C93, and/or C94 for acute

myeloid leukemia, C91 for acute lymphoblastic leukemia, and/or C95 for unclassified acute leukemia. The requirement for individual patient consent was waived because of the anonymous nature and public availability of the data.

Data source of the validation cohort

Data from consecutive adult patients with acute leukemia who underwent alloSCT between January 2019 and April 2020 at the Catholic Hematologic Hospital were used to construct the validation cohort. Data were collected until April 2021 to have at least a 1-year follow-up period. This study was approved by the Institutional Review Board of Seoul St. Mary's Hospital, Seoul, Korea (KC19ZNSI0396) and was conducted in accordance with the Declaration of Helsinki.

Definition of the development cohort

For individuals treated with multiple alloSCTs, the baseline date for calculating OS was defined as the date of the first alloSCT. We used the ICD-10 codes to define whether the patient presented with comorbidities, including previous non-hematologic malignancy (ICD-10 code: Cxx, except for C83, C86, C90, C91, C92, C93, C94, and/or C95 indicating hematologic malignancies), hypertension (ICD-10 code: I10, I11, I12, I13, I14, and/or I15), diabetes (ICD-10 code: E10, E11, E12, E13, and/or E14), dyslipidemia (ICD-10 code: E78), chronic obstructive pulmonary disease (COPD; ICD-10 code: J44), anxiety disorder (ICD-10: F30), and depression (ICD-10: F32 and/or F33). CVA was indicated when the patient was administered antiplatelet agents (drug codes: 117101ATB, 136901ATB, 157702ACR, 162403ATR, 165001ACH, 194930ATB, 492501ATB, 495201ATB, 498801ATB, 498900ATB, 501501ATB, 517900ACE, 517900ATE, 597301ATB, 597302ATB, 615901ATB, 615902ATB, 659501BIJ, and/or 667500ACE) and/or anti-coagulants (drug codes: 511401ATB, 511403ATB, 511402ATB, 511404ATB, 249103ATB, 249105ATB, 613701ACH, 613702ACH, 617001ATB, 617002ATB, 643602ATB, 643601ATB, and/or 643603ATB).

Construction and validation of the scoring system

In the development cohort, all risk factors potentially related to OS with a P -value of < 0.05 in the univariable analysis were entered into the multivariable model to confirm the factors associated with OS. Multivariable analysis was performed using the Cox proportional hazards regression model. The final parameters used in the scoring system were defined by a P -value of < 0.05 in the final multivariable model. The risk score for each significant parameter was assigned by adjusting the hazard ratio (HR) values to a log scale.

Using the scoring system created using the development cohort, we performed an analysis to validate whether the scoring system performed well as a reliable prognostic tool in the validation cohort. OS and the incidence of non-relapse mortality (NRM) and relapse were compared between the risk groups. Finally, discriminatory performance was assessed by receiver operating characteristic (ROC) curve analysis.

Statistical analysis

Numerical variables not exhibiting a normal distribution are presented as medians (range, minimum–maximum). Categorical variables are presented as numbers (%). OS was defined as the time from the date of alloSCT to death (from any cause) or the date of the last follow-up. OS rates at 1 year were calculated using the Kaplan-Meier method and compared using the log-rank test. We calculated the NRM probability and relapse rates using cumulative incidence estimation based on the competing risks of relapse and NRM. The area under the curve (AUC) of the ROC curve was calculated to predict the accuracy of the validation cohort analysis. An AUC value >0.7 was considered reliable [16]. DeLong’s test was used to compare the statistical differences between the AUCs. All statistical analyses were conducted using R statistical software (ver. 3.6.1, R Foundation for Statistical Computing, Vienna, Austria, 2019). Statistical significance was set at $P < 0.05$.

RESULTS

Patient characteristics

Development cohort: In total, 8,230 patients who underwent alloSCT between January 2002 and December 2018 were identified. Patients aged <18 years (N=1,060) and those having other hematologic diseases (N=3,361) were excluded from the analysis. Accordingly, 3,809 patients with acute leukemia were included in the development cohort (Fig. 1A). The baseline demographics are summarized in Table 1. Overall, the median age of the patients was 47 years (range, 18–74 yr), and 54.0% of the patients were males (N=2,055). Regarding the underlying comorbidities at baseline, previous non-hematologic malignancy, hypertension, diabetes, dyslipidemia, COPD, CVA, anxiety disorder, and depression were present in 387 (10.2%), 1,224 (32.1%), 1,125 (29.5%), 2,135 (56.1%), 191 (5.0%), 166 (4.4%), 900 (23.6%), and 613 (16.1%) patients, respectively. With a median follow-up of 50.2 months [95% confidence interval (CI), 47.7–

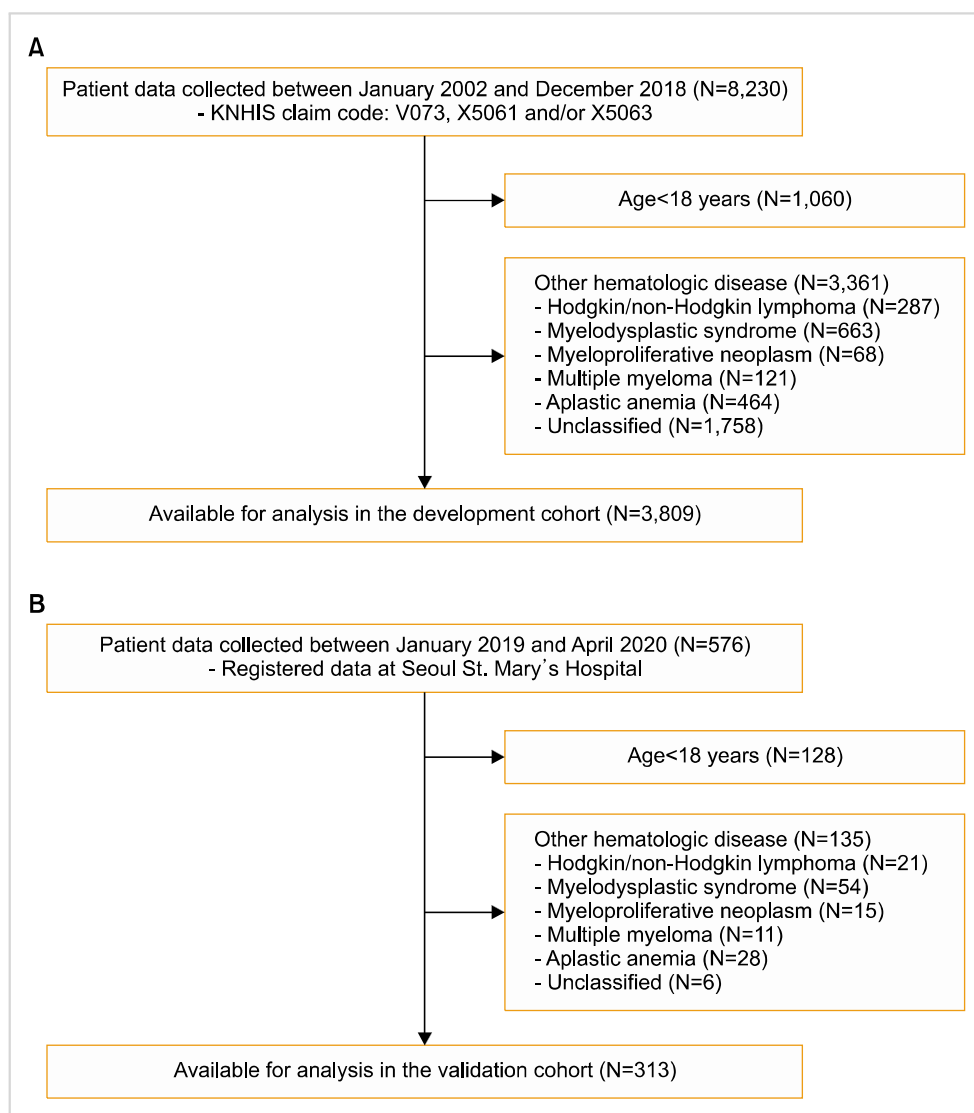


Fig. 1. Flow diagram of the construction of the development and validation cohorts. Abbreviation: KNHIS, Korean National Health Insurance Service.

Table 1. Demographics of the cohorts.

Variables	Development cohort (N=3,809)	Validation cohort (N=313)
Age at alloSCT, median, years (range)	47 (18–74)	48 (18–74)
< 30 years, no (%)	608 (16.0)	57 (18.2)
30–39 years, no (%)	614 (16.1)	60 (19.2)
40–49 years, no (%)	1,023 (26.9)	61 (19.5)
50–59 years, no (%)	1,072 (28.1)	78 (24.9)
60–69 years, no (%)	475 (12.5)	51 (16.3)
≥ 70 years, no (%)	17 (0.4)	6 (19.2)
Male, N (%)	2,055 (54.0)	152 (48.6)
Stem cell source		
Bone marrow stem cell, N (%)	469 (12.3)	3 (1.0)
Mobilized peripheral blood stem cell, N (%)	3,246 (85.2)	310 (99.0)
Cord blood, N (%)	94 (2.5)	12 (3.8)
HCT-CI, median, points (range)	NA	2 (0–8)
0 (low-risk)	NA	89 (28.4)
1–2 (intermediate-risk)	NA	126 (40.3)
≥ 3 (high-risk)	NA	98 (31.3)
Previous non-hematologic malignancy (%)		
Yes	387 (10.2)	20 (6.3)
No	3,422 (89.8)	293 (93.6)
Hypertension (%)		
Yes	1,224 (32.1)	74 (23.6)
No	2,585 (67.9)	239 (76.4)
Diabetes (%)		
Yes	1,125 (29.5)	43 (13.7)
No	2,684 (70.5)	270 (86.3)
Dyslipidemia (%)		
Yes	2,135 (56.1)	43 (13.7)
No	1,674 (43.9)	270 (86.3)
Chronic obstructive pulmonary disease (%)		
Yes	191 (5.0)	7 (2.2)
No	3,618 (95.0)	306 (97.8)
Cerebrovascular or cardiovascular disease (%)		
Yes	166 (4.4)	25 (8.0)
No	3,643 (95.6)	288 (92.0)
Anxiety disorder (%)		
Yes	900 (23.6)	46 (14.7)
No	2,909 (76.4)	267 (85.3)
Depression (%)		
Yes	613 (16.1)	35 (11.2)
No	3,196 (83.9)	278 (88.8)

Abbreviations: alloSCT, allogeneic stem cell transplantation; HCT-CI, hematopoietic cell transplantation-specific comorbidity index; NA, not available.

53.2], the 1-year, 3-year, and 5-year OS rates were estimated as 68.2% (95% CI, 66.7–69.7), 51.5% (95% CI, 49.8–53.2), and 46.8% (95% CI, 45.0–48.6) in the total cohort, respectively (Fig. 2).

Validation cohort: Data on 576 consecutive patients treated with alloSCT were collected. Following the exclusion of patients aged < 18 years (N=128) and those having other hematologic diseases (N=135), a validation cohort of 313 patients was eligible for analysis (Fig. 1B). The baseline characteristics of the validation cohort are shown in Table 1.

Analysis of factors associated with OS in the development cohort

The univariable analysis identified the following potential factors related to poor OS: age (≥ 65 years or 50–64 years compared with < 50 years); male sex; comorbidities such as previous non-hematologic malignancy, hypertension, diabetes, dyslipidemia, CVA, and anxiety disorder/depression. In the multivariable analysis, we confirmed that 5 variables, including advanced age (50–64 years or ≥ 65 years), male sex, non-hematologic malignancy, hypertension, and CVA, were significantly associated with poor OS, as shown in Table 2.

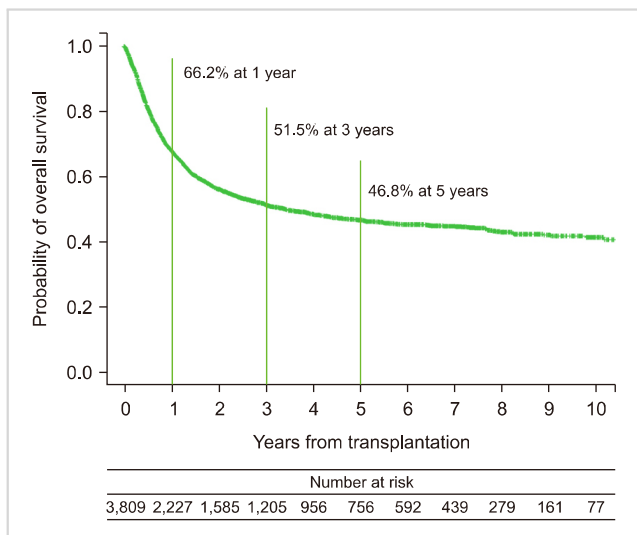


Fig. 2. Kaplan-Meier analysis to calculate the overall survival rate in the development cohort.

Comorbidity index score for survival outcome in the development cohort

Based on the multivariable analysis, an assigned risk score of each variable, obtained by the log-scale of the HR (Table 3) are as follows: age (50–64 years, 0.21 points; ≥65 years, 0.55 points), male sex (0.13 points), previous non-hematologic malignancy (0.17 points), hypertension (0.13 points), and CVA (0.4 points). The risk score was computed as the sum of each variable score, resulting in a median risk score of 0.2 and a range of 0–1.38. We then classified the patients into 10 subgroups, whose ranks were determined by the order of the decile risk scores. Based on the OS rates according to these 10 subgroups (Fig. 3A), the risk score was finally stratified into 4 risk groups (Fig. 3B): the 1-year OS/5-year OS rates were 73.5% [(95% CI, 71.4–75.6)/52.9% (95% CI, 50.4–55.6)], 66.2% [(95% CI, 63.6–68.9)/44.0% (95% CI, 41.0–47.2)], 61.9% [(95% CI, 57.2–67.0)/37.3% (95% CI, 31.9–43.6)], and 50.9% [(95% CI, 44.8–57.7)/29.6% (95% CI, 23.4–37.5)] in the low-risk (score ≤0.17), intermediate-risk (0.17 < score ≤0.4), high-risk (0.4 < score ≤0.55), and very high-risk (score >0.55) groups, respectively. The developed scoring system calculator is presented in the Supplementary calculator.

Table 2. Univariable and multivariable analysis for comorbidities associated with overall survival in the development cohort.

Variables	N	Univariable analysis		Multivariable analysis	
		1-year OS rate (95% CI)	P	Hazard ratio (95% CI)	P
Age			<0.001		
< 50 years	2,245	71.8 (69.9–73.8)		1	
50–64 years	1,438	64.1 (61.5–66.7)		1.228 (1.107–1.362)	<0.001
≥65 years	126	48.1 (39.6–58.4)		1.733 (1.340–2.232)	<0.001
Sex			<0.001		
Female	1,754	69.1 (66.9–71.3)		1	
Male	2,055	67.4 (65.3–69.6)		1.142 (1.038–1.255)	<0.001
Previous non-hematologic malignancy			0.002		
No	3,422	69.1 (67.5–70.7)		1	
Yes	387	60.3 (55.4–65.6)		1.182 (1.015–1.376)	0.031
Hypertension			<0.001		
No	2,585	70.8 (69.0–72.6)		1	
Yes	1,224	62.6 (59.8–65.5)		1.141 (1.026–1.268)	0.015
Diabetes			0.005		
No	2,684	69.2 (67.4–71.0)		1	
Yes	1,125	65.7 (62.9–68.7)		1.002 (0.899–1.117)	0.965
Dyslipidemia			0.007		
No	1,674	70.1 (67.9–72.4)		1	
Yes	2,135	66.6 (64.5–68.7)		1.036 (0.937–1.144)	0.486
Chronic obstructive pulmonary disease			0.21		
No	3,618	68.4 (66.8–70.0)		NA	
Yes	191	64.3 (57.4–71.9)		NA	
Cerebrovascular or cardiovascular disease			<0.001		
No	3,643	68.8 (67.2–70.4)		1	
Yes	166	54.1 (46.6–62.9)		1.498 (1.212–1.848)	<0.001
Anxiety disorder and/or depression			0.006		
No	3,501	68.8 (67.2–70.4)		1	
Yes	308	60.8 (55.4–66.8)		1.176 (0.996–1.386)	0.055

Abbreviations: CI, confidence interval; NA, not available; OS, overall survival.

Table 3. The final scoring model in the development cohort.

	Hazard ratio (95% CI)	Log _e value of hazard ratio
Age		
< 50 years	1 (reference)	0
50–64 years	1.228 (1.107–1.362)	0.21
≥ 65 years	1.733 (1.340–2.232)	0.55
Sex		
Female	1 (reference)	0
Male	1.142 (1.038–1.255)	0.13
Previous non-hematologic malignancy		
No	1 (reference)	0
Yes	1.182 (1.015–1.376)	0.17
Hypertension		
No	1 (reference)	0
Yes	1.141 (1.026–1.268)	0.13
Cerebrovascular or cardiovascular disease		-
No	1 (reference)	0
Yes	1.498 (1.212–1.848)	0.4

Abbreviation: CI, confidence interval.

Validation cohort analysis: validation of the scoring system

With a median follow-up of 18.8 months (95% CI, 18.1–20.0) in the validation cohort, the 1-year OS rate and 1-year cumulative incidence of NRM and relapse were 74.4% (95% CI, 69.2–78.9), 11.5% (8.3–15.3), and 23.0% (18.5–27.8), respectively (Supplementary Fig. 1). When the developed scoring system was applied to the validation cohort, the 1-year OS rates were measured differently according to the risk group ($P=0.085$), which were 79.4% (95% CI, 72.2–84.9) in the low-risk group, 74.2% (95% CI, 64.3–81.8) in the intermediate-risk group, 60.0% (95% CI, 35.7–77.6) in the high-risk group, and 61.1% (95% CI, 35.7–77.6) in the very high-risk group. There were significant differences in both the 1-year OS rate between a combined group of the low-risk and intermediate groups and another combined group of the high-risk and very high-risk groups at 77.4% (95% CI, 71.8–82.1) and 60.7% (95% CI, 46.7–72.1), respectively ($P=0.018$) (Fig. 4A).

The 1-year cumulative incidence of NRM was significantly different according to the risk groups ($P=0.035$), which was 7.5% (95% CI, 4.1–12.3) in the low-risk group, 11.3% (95% CI, 6.0–18.6) in the intermediate-risk group, 20.0% (95% CI, 5.9–40.0) in the high-risk group, and 25.0% (95% CI, 12.2–40.0) in the very high-risk group (Fig. 4B). However, we observed no significant difference in the 1-year cumulative incidence of relapse according to the risk group ($P=0.349$, Fig. 4C). In the ROC curve analysis, the developed scoring system achieved an AUC of 0.715 (95% CI, 0.658–0.772), indicating reliable discrimination of NRM events at 1 year in the validation cohort (Fig. 4D).

DISCUSSION

This study developed a new scoring system to predict patient prognosis after alloSCT in 3,809 patients with acute leukemia using a development cohort derived from a nationwide database. With a 5-year OS probability of 46.8% in the development cohort, we created a comorbidity index scoring system comprising age, sex, previous non-hematologic malignancy, hypertension, and CVA. The risk score was significantly stratified into 4 risk groups: low-risk, intermediate-risk, high-risk, and very high-risk groups associated with 1-year/5-year OS rate probabilities of 73.5%/52.9%, 66.2%/44%, 61.9%/37.3%, and 50.9%/29.6%, respectively. The validation cohort analysis indicated that the developed comorbidity index scoring system was statistically feasible for predicting OS and NRM. AlloSCT is generally planned as a consolidative procedure following intensive chemotherapy in patients who achieve complete remission after intensive chemotherapy. In the validation cohort analysis, we observed interesting findings that there were significant increasing trends in the proportion of patients presenting with comorbidities at pre-alloSCT compared with the diagnosis of their disease (Supplementary Fig. 2). Therefore, our results suggest that updated comorbidity profiles at the time of alloSCT, as well as the diagnosis of acute leukemia, should be monitored rigorously because complications following intensive chemotherapy could indicate a new comorbidity, although it was absent at the time of diagnosis.

In the validation cohort of the current study, we evaluated the feasibility of the developed scoring system, which provided discriminative predictability for OS and NRM. In addition to our system, HCT-CI, which comprises 17 different categories of organ dysfunction [8], has not only been used as the most reliable tool for the comorbidity-based risk assessment of survival and NRM after alloSCT but has also been successfully validated in transplant institutions worldwide [17–19]. However, the cohort size of the original study ($N=1,055$) for the establishment of HCT-CI, as well as studies of validation (the largest among all studies to the best of our knowledge, $N=324$), was relatively small compared with our study. Moreover, multi-institutional validation of the predictive power of HCT-CI has not yet been documented. Interestingly, a multicenter prospective study by a Japanese group found that HCT-CI failed to predict NRM [20]. Therefore, there is an unmet need for better tools to optimize comorbidities based on risk stratification for alloSCT. Although our developed comorbidity index model should be further validated in a future study, the supplemental analysis showed that our new index demonstrated better 1-year NRM prediction than the HCT-CI system in the validation cohort, with an AUC of 0.688 vs. 0.509, $P<0.001$ (Supplementary Fig. 3). This result also illustrated an AUC of 0.509 for HCT-CI in predicting 1-year NRM, which is not discriminated, as in the abovementioned results from the multicenter Japanese prospective study.

Compared with prior studies depicting risk stratification

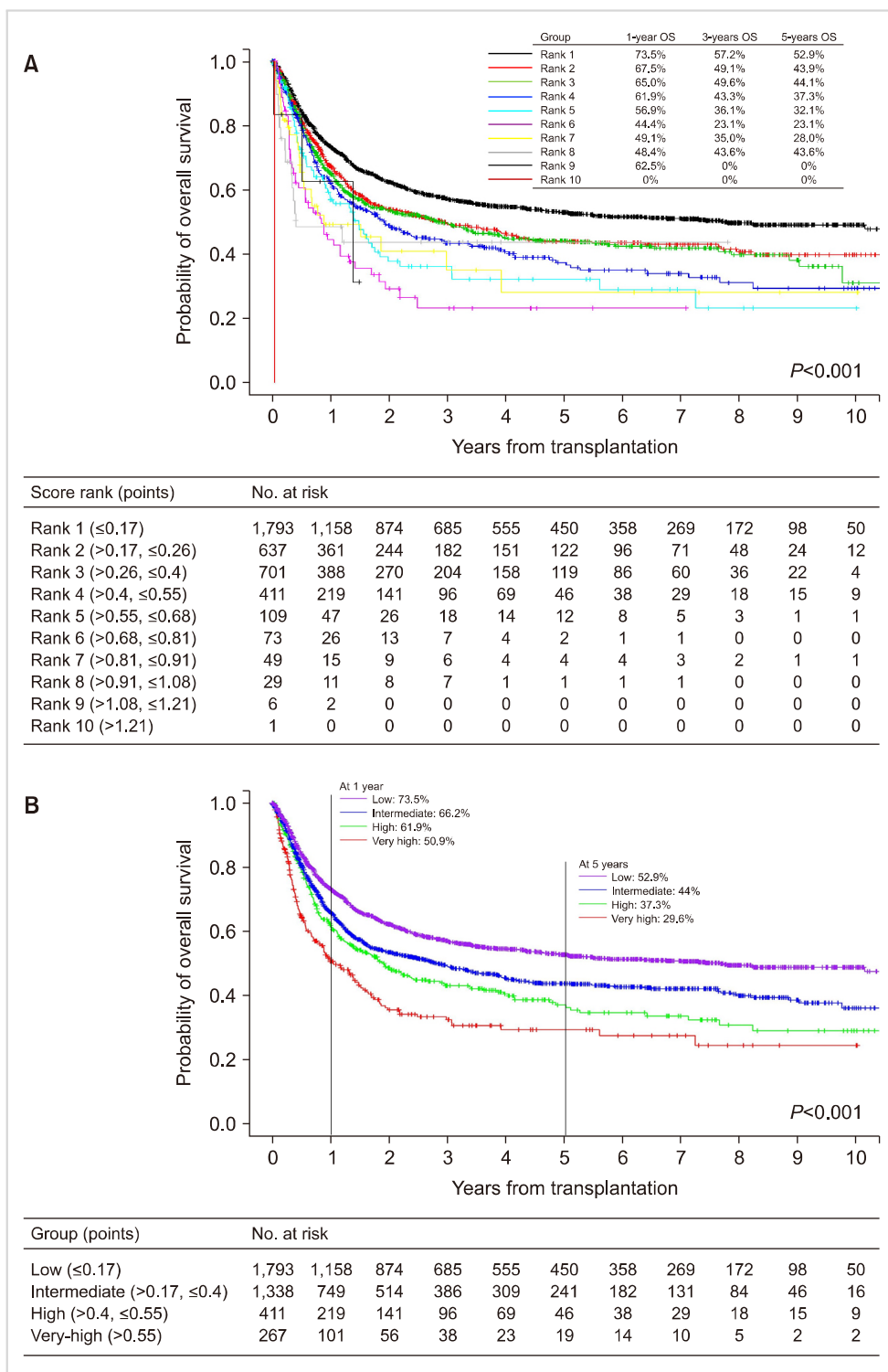


Fig. 3. Probability of overall survival (OS) according to (A) decile risk scores and (B) the final risk groups in the development cohort. Using decile risk scores, we classified the patients into 10 groups: rank 1 (score ≤ 0.17), rank 2 (score, >0.17 and ≤ 0.26), rank 3 (score, >0.26 and ≤ 0.4), rank 4 (score, >0.4 and ≤ 0.55), rank 5 (score, >0.55 and ≤ 0.68), rank 6 (score, >0.68 and ≤ 0.81), rank 7 (score, >0.81 and ≤ 0.91), rank 8 (score, >0.91 and ≤ 1.08), rank 9 (score, >1.08 and ≤ 1.21), and rank 10 (>1.21). Based on the 5-year OS rates in each rank group, we then stratified the patients into 4 risk groups. The low-risk group included patients with rank 1; the intermediate-risk group included patients with ranks 2 and 3; the high-risk group included patients with rank 4; and the very high-risk group included patients with ranks 5, 6, 7, 8, 9, and 10. The log-rank test showed significant differences in the OS among the risk groups ($P<0.001$).

according to comorbidities, our results had several strengths. First, to the best of our knowledge, the risk factors for survival were analyzed using a nationwide cohort comprising the largest number of patients from a Korean multicenter cohort. Second, unlike the aforementioned scoring systems that require endoscopy, echocardiography, pulmonary function tests, and various laboratory tests to generate the results, our scoring system was created using easily accessible data

such as age and underlying comorbidities. Third, despite the small number of variables comprising the scoring system, we believe that the discriminatory power, as well as the validity of our system for predicting survival in the validation cohort, which was distinctively independent of the development cohort, appeared to be reliable.

There are several limitations to our study. In the development cohort analysis, we were unable to investigate all varia-

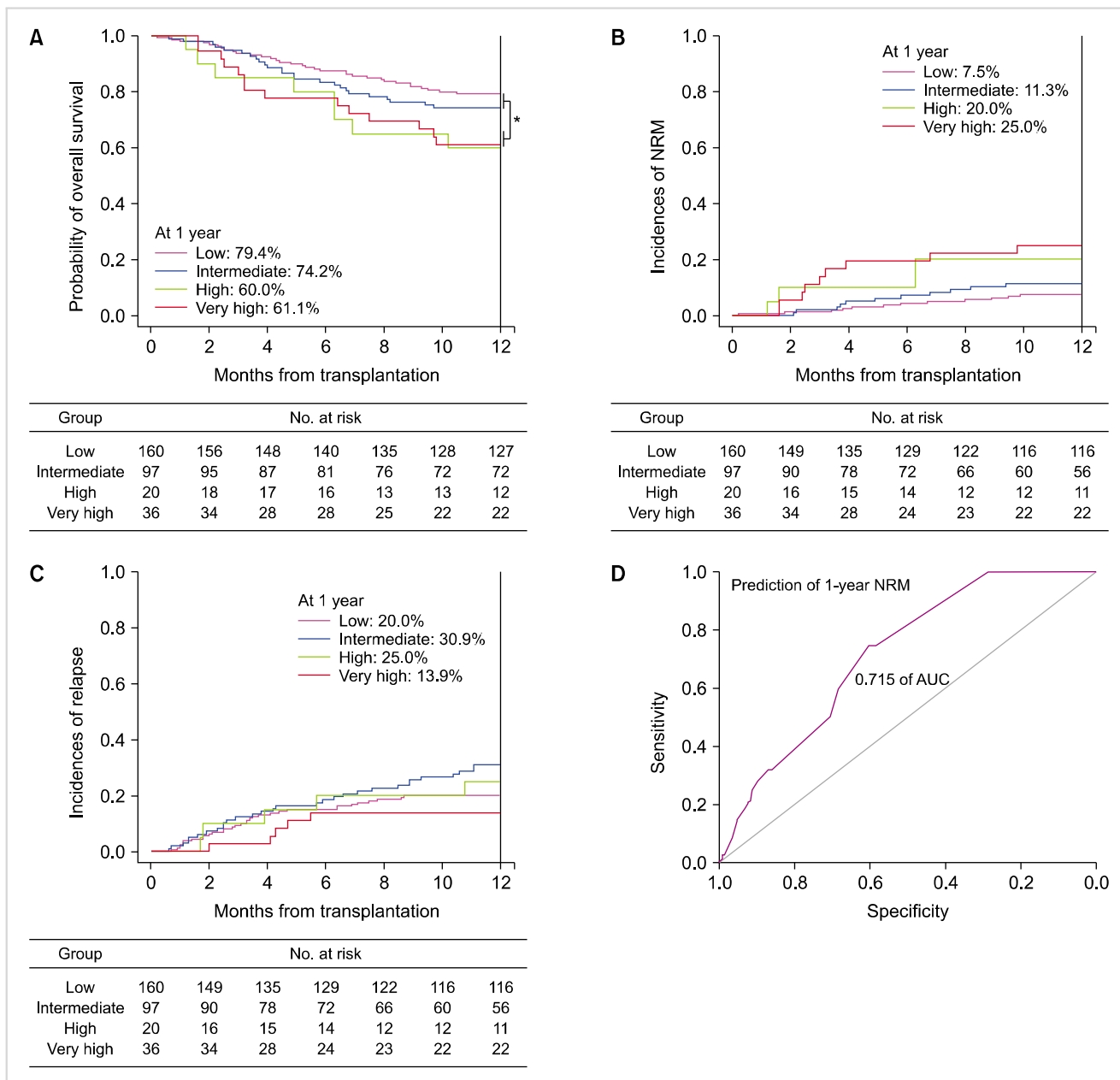


Fig. 4. Validation of the developed scoring system in the validation cohort. **(A)** The 1-year overall survival (OS) rate was divided according to the risk groups ($P=0.085$). The *post-hoc* analysis illustrated a better 1-year OS rate in the low- or intermediate-risk groups than that in the high- or very high-risk groups ($P=0.018$, * is indicated in the Fig. 1A for the *post-hoc* analysis). **(B)** The cumulative incidence of non-relapse mortality (NRM) was significantly divided according to the risk groups ($P=0.035$), **(C)** whereas the cumulative incidence of relapse was not significantly different between the 4 risk groups ($P=0.349$). **(D)** A receiver operating characteristic curve analysis achieved an area under the curve (AUC) of 0.715 (95% CI, 0.658–0.772) for predicting NRM events 1-year post-allogeneic hematopoietic stem cell transplantation.

bles comprising the HCT-CI because the KNHIS database has the inherent limitation that concrete results derived from laboratory tests, echocardiography, and pulmonary function tests were absent. In this regard, the severity of the comorbidity could not be assessed. Second, due to unreliable data related to the cause of death in the KNHIS data, the cumulative incidence of relapse-related death or NRM was not explored in the development cohort analysis. Third, this study could be limited by the relatively small size, short-term follow-up, and retrospective design of the

validation cohort. Fourth, we believe that the results of the current study cannot be generalized because other important factors, including characteristics of acute leukemia and treatment factors, were not entered as covariants to verify the prognostic impact of patient-related comorbidities.

Despite these limitations, our study provides a feasible scoring system based on comorbidity information that is easy to obtain for predicting survival prognosis among patients with acute leukemia who undergo alloSCT. Therefore, the current results could be attributed to better clinical deci-

sion-making based on patient-driven risk-adaptive strategies for alloSCT.

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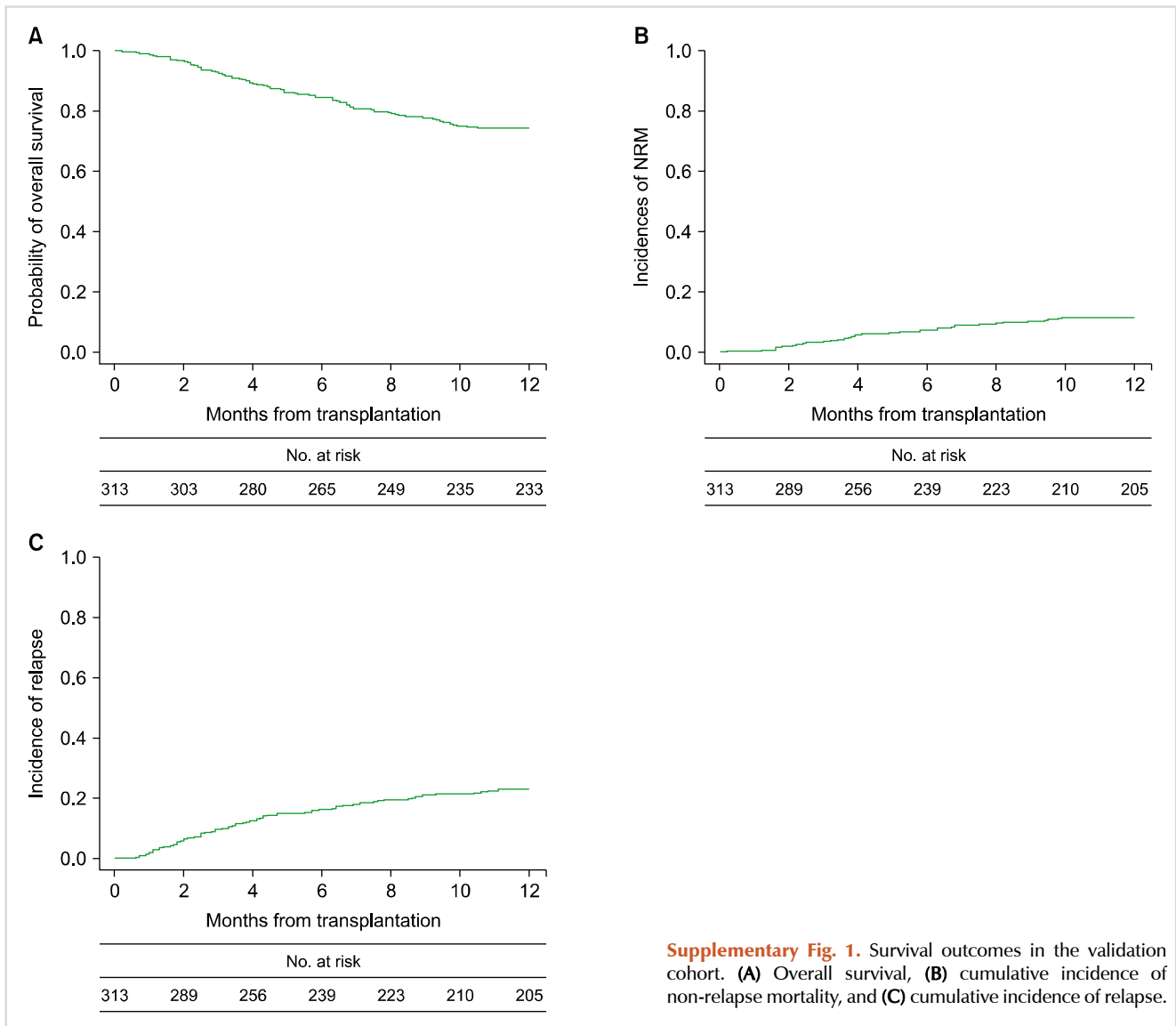
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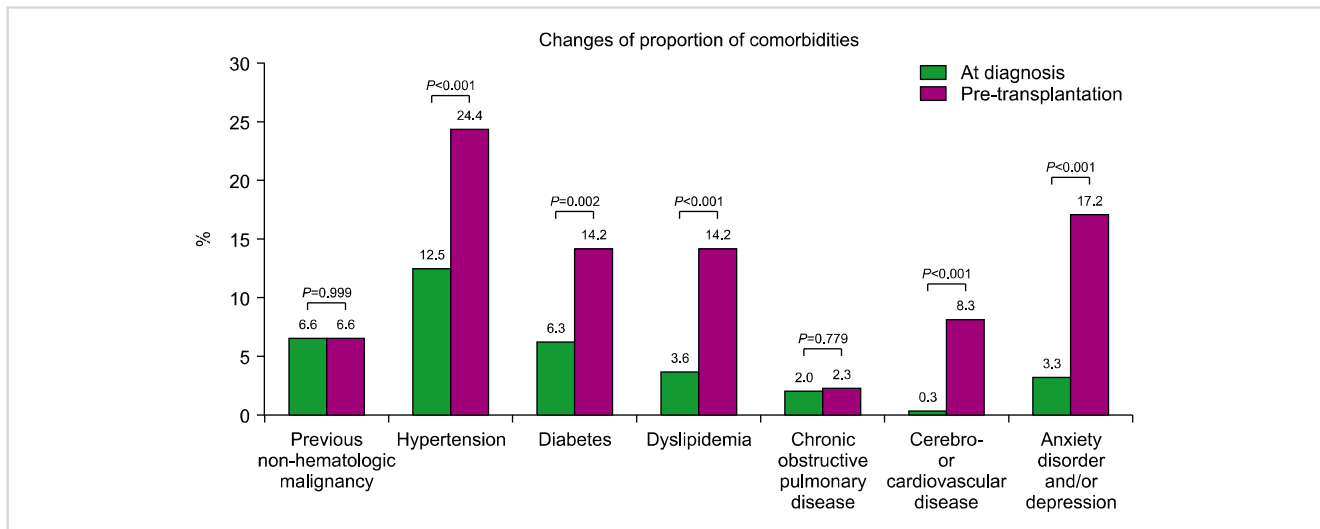
Authors' Disclosures of Potential Conflicts of Interest

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

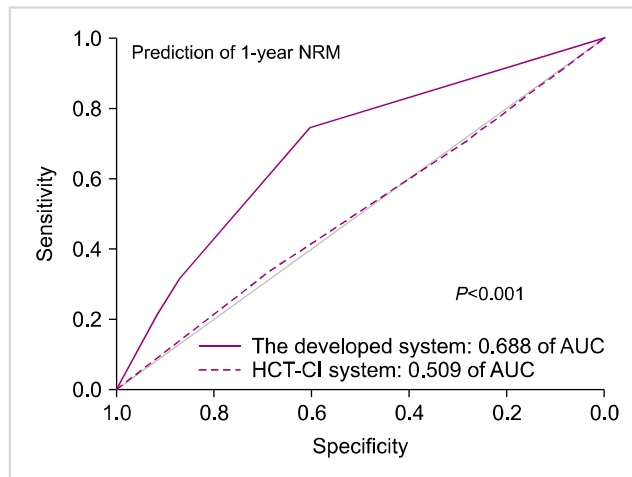
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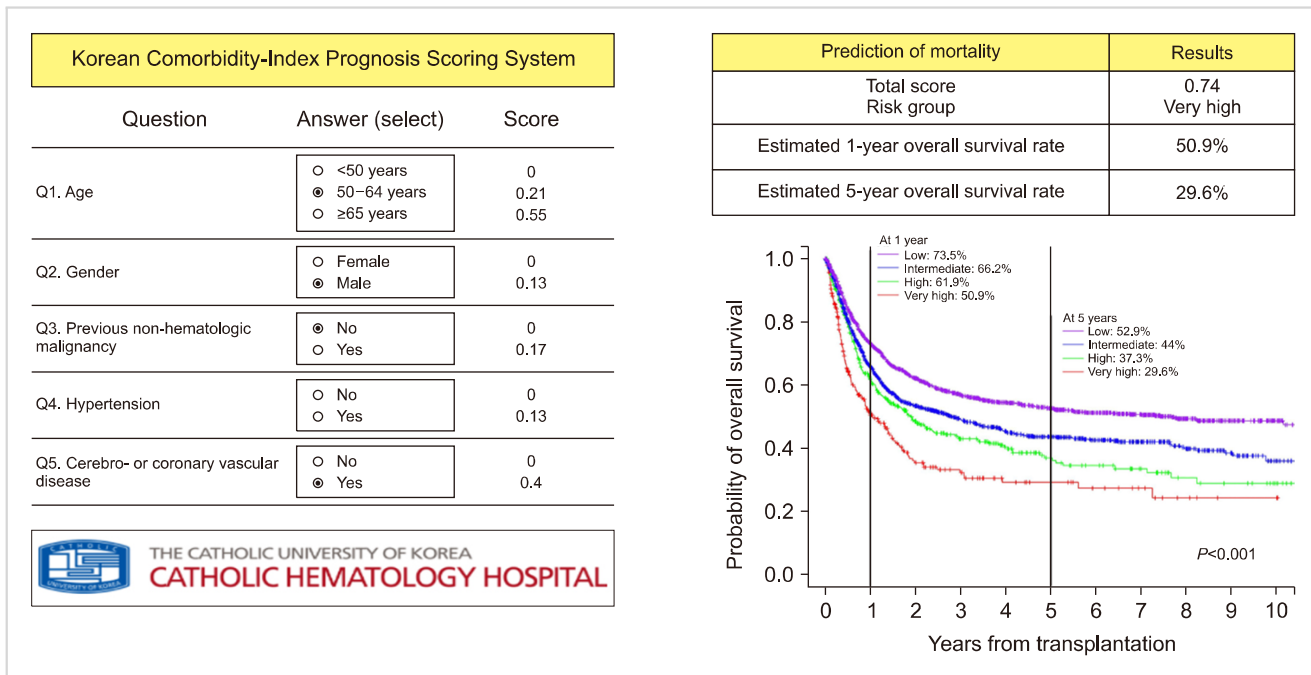




Supplementary Fig. 2. Comparisons of proportions of patients harboring comorbidities at between diagnosis and pre-transplantation. There were statistical significances in increasing hypertension [12.5% (N=39) vs. 24.4% (N=73), $P<0.001$], diabetes [6.3% (N=20) vs. 14.2% (N=44), $P=0.002$], dyslipidemia [3.6% (N=11) vs. 14.2% (N=44), $P<0.001$], Cerebro- or cardiovascular disease [0.3% (N=1) vs. 8.3% (N=26), $P<0.001$], and anxiety disorder and/or depression [3.3% (N=10) vs. 17.2% (N=54), $P<0.001$] whereas there were no significant differences of proportions of patients who presented a previous non-hematologic malignancy and chronic obstructive pulmonary disease. Each P -value was computed by chi-square test.



Supplementary Fig. 3. Comparison of area under the curve (AUC) of receiver operating characteristics to predict 1-year non-relapse mortality between the developed system and the prior HCT-CI system. Abbreviation: HCT-CI, hematopoietic cell transplantation-comorbidity index.



Supplementary calculator. We can provide the supplementary calculator based on Excel sheet as follows (an example).