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Trends and outcomes of chemotherapy timing in critically ill patients with hematologic malignancies using a Japanese national database

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Hematologic malignancies are a global public health concern, with high mortality rates in patients requiring critical care. The role of chemotherapy during intensive care unit (ICU) admission in this context remains unclear. This study aimed to analyze trends in survival rates based on chemotherapy timing and examine patient characteristics, ICU treatments, and clinical outcomes in each group. Using the Japanese Diagnosis Procedure Combination inpatient database, data from 21,837 patients aged ≥ 18 years who were hospitalized for hematologic malignancies and admitted to ICUs between April 1, 2012, and March 31, 2022, were analyzed. Patients were categorized based on chemotherapy timing as follows: no chemotherapy (NC), chemotherapy before ICU admission (CB), chemotherapy during ICU admission (CD), and chemotherapy after ICU discharge (CA). Mortality trends were assessed, with in-hospital mortality as the primary outcome variable. The CB group had the highest mortality rate, which decreased over time (61.2% in 2012 to 46.2% in 2021). The CD group had stable mortality rates (24.2% in 2012 and 22.6% in 2021), with a notable proportion of patients (55.4%) discharged home. These findings highlight the need for further investigation into the factors influencing ICU outcomes in patients receiving chemotherapy.

Keywords Chemotherapy, Hematologic malignancy, Intensive care unit, Mortality

Hematologic malignancies are a major global public health concern[1]. Therapeutic approaches for patients are evolving substantially owing to a deeper understanding of the complexities and variations inherent to hematologic malignancies. Owing to advancements in diverse chemotherapy regimens, immunotherapy, and hematopoietic stem cell transplantation (HSCT) techniques[2–4], patient prognosis has gradually improved[5]. However, mortality rates remain high among patients who require critical care interventions. A cohort study[6] indicated that approximately 14% of patients diagnosed with hematologic malignancies required intensive care. Although in-hospital mortality rates for this subgroup fluctuate, they consistently range from 30 to 60%[7–9].

In cases with poor prognoses, we observed a growing trend toward administering chemotherapy in an intensive care unit (ICU) setting with advanced organ support, which has been explored in various settings[10,11], although its impact on outcomes remains unclear. While some studies[12,13] suggest that chemotherapy in the ICU is feasible in selected cases, the heterogeneity of patient conditions and treatment responses necessitates further research on this topic.

Nevertheless, because of the diversity in chemotherapy effectiveness and disease severity, only a few studies[10,11] with small sample sizes have provided insights into chemotherapy administration in ICU settings

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and its correlation with patient mortality. Although several database studies[6,9] have been conducted on patients with hematologic malignancies, they did not focus on chemotherapy or HSCT. Occasionally, hematologists and intensivists face challenges in managing patients with hematologic malignancies in ICUs[14]. Therefore, accurate prognostic information regarding therapeutic options and disease categories is crucial for guiding treatment strategies.

This study aimed to investigate the characteristics of patients with hematologic malignancies requiring ICU admission, focusing on the correlation between chemotherapy timing and ICU admissions and patient characteristics. By dividing this analysis into two parts, we sought to provide clear insights into how the timing of chemotherapy, when coordinated with ICU admission, affects patient outcomes.

Results

Patient flowchart and annual proportion of admissions

Overall, 1,192,630 patients were admitted with hematologic malignancies, which were registered as the most resource-intensive medical condition, of whom 1,137,137 were aged ≥18 years. The number of patients who required intensive care was 22,576, with 739 excluded owing to missing admission cost data. A total of 21,837 patients were included in the analysis (Fig. 1).

Approximately 2% of adult patients with hematologic malignancies required intensive care. The proportions of patients in each disease category are shown in Supplementary Figure S1. The study cohort predominantly comprised patients with the following five hematologic malignancies: Non-follicular lymphoma (C83); Other and unspecified types of non-Hodgkin lymphoma (C85); Multiple myeloma and malignant plasma cell neoplasms (C90); Lymphoid leukemia (C91); Myeloid leukemia (C92). Figure 2 shows the annual proportion of admissions by fiscal year for each category. Throughout the study period, the no chemotherapy (NC) and chemotherapy before ICU admission (CB) groups consistently showed high proportions of admissions, whereas the chemotherapy during ICU admission (CD) and chemotherapy after ICU discharge (CA) groups showed lower proportions of admissions. However, the CD group demonstrated a gradual but steady increase in admissions, from 11.4% in 2012 to 15.5% in 2021.

Characteristics of patients in each group

Table 1 presents the background patient characteristics for each group, revealing significant differences among the groups. Emergency admissions were less frequent in the CB group than in the CD and CA groups. Analysis of disease categories revealed that the CB group was characterized by a predominance of two specific hematologic malignancies: Myeloid leukemia (C92) and non-follicular lymphoma (C83), accounting for 26.8% (1963 patients) and 24.8% (1812 patients) of the hematologic malignancies in the CB group, respectively. The other groups had a high proportion of non-follicular lymphoma (C83) and other and unspecified types of non-Hodgkin lymphoma (C85). Almost all patients who required HSCT belonged to the CB group. Catecholamine use before ICU admission was the highest in the CB group (13.7% [1001 patients]).

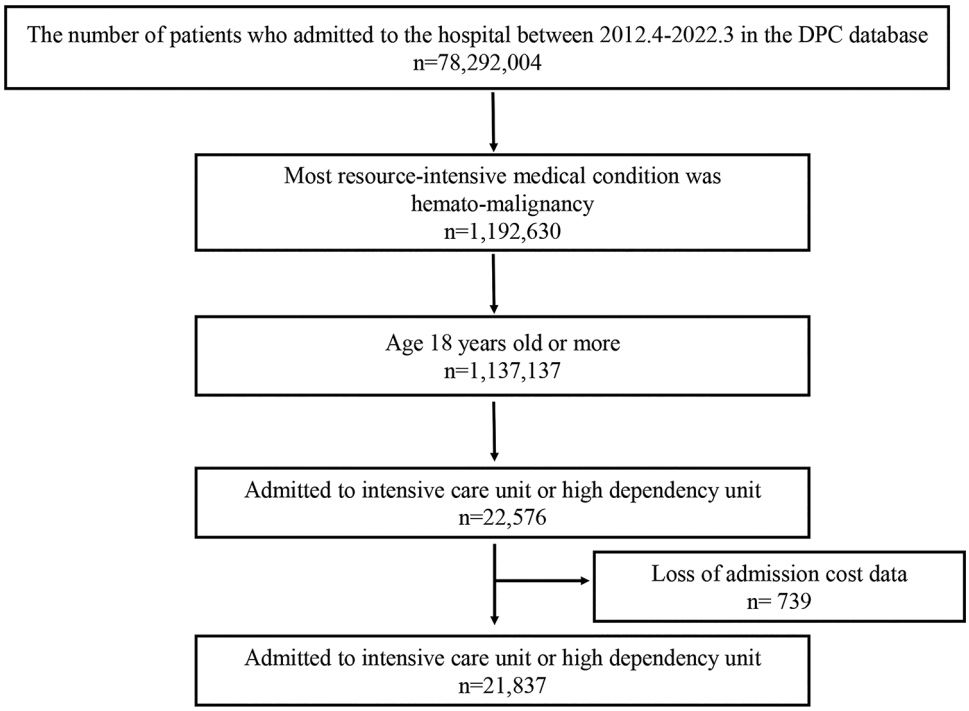

Fig. 1. Flowchart of patient selection. DPC, Diagnosis procedure combination.

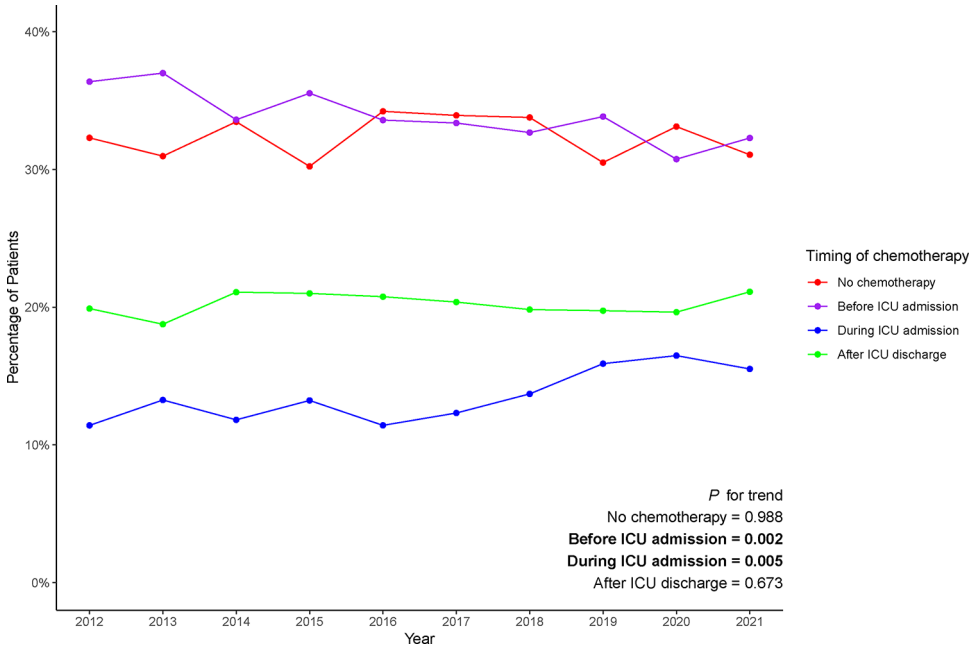

Fig. 2. Annual proportion of admissions per fiscal year within each category. ICU, intensive care unit.

Supplementary Tables S1 and S2 summarize the characteristics of the subgroups within the HSCT and non-HSCT groups, respectively. The HSCT patient data differed significantly in terms of the proportion of patients in each group. Almost all patients belonged to the CB group (NC group, 0.2%; CB group, 97.3%; CD group, 1.0%; and CA group, 1.5%). Cord blood transplantation was the most common type of HSCT. In contrast, the non-HSCT group showed nearly the same trends as those of the original cohort, including demographic data, therapeutic interventions in the ICU, and clinical outcomes.

Therapeutic interventions in the ICU, clinical outcomes, and trends

Table 2 presents the therapeutic interventions in the ICU and the clinical outcomes of all groups. The CB group showed the highest proportions of mechanical ventilation (MV), renal replacement therapy (RRT), extracorporeal membrane oxygenation (ECMO), and catecholamine use among the groups. The CB and CD groups required a longer duration of mechanical device use than the other groups. Supplementary Figure S2 illustrates the proportion of patients receiving MV, RRT, and ECMO during the study period, categorized according to the timing of chemotherapy. The highest proportion of MV use was observed in the CB group, which decreased over time. A similar trend was observed in the RRT trend graph. Considerable annual variation of 1–3% was observed in the use of ECMO across all the groups.

The overall in-hospital mortality rate in the study cohort was 31.8%, with significant differences among the groups. The CB group had the highest mortality rate (52.4%), while the NC, CD, and CA groups had rates of 23.9%, 24.8%, and 15.2%, respectively ($P < 0.01$). The proportion of patients discharged home was lowest in the CB group (NC group, 59.2%; CB group, 36.3%; CD group, 55.4%; and CA group, 63.9%; $P < 0.01$).

The mortality rate among HSCT patients was high at 69.9% (1422 patients), and all groups required long-term hospital admission. Figure 3 illustrates the mortality trends for each category. The mortality rate in the CB group showed a decreasing trend over time, aligning with improvements in overall treatment strategies and critical care interventions (61.2% in 2012 to 46.2% in 2021 [P_{trend}<0.001]). The NC and CD groups had stable mortality rates with a consistent proportion of patients being discharged home (NC group: 24.0% in 2012 and 24.9% in 2021 [P_{trend}=0.60]; CD group: 24.2% in 2012 and 22.6% in 2021 [P_{trend}=0.09]). In contrast, the mortality rate in the CA group decreased significantly from 20.1% in 2012 to 10.6% in 2021 (P_{trend}<0.001). Differences in patient characteristics, including disease severity at ICU admission, likely influenced these trends.

Supplementary Tables S3 and S4 detail the therapeutic interventions in the ICU and the clinical outcomes of the HSCT and non-HSCT subgroup cohorts, respectively. Within the HSCT category, the CB subgroup had the highest mortality rate (70.9%). Furthermore, the HSCT cohort incurred significantly higher admission costs than the non-HSCT cohort. The findings of the non-HSCT cohort were similar to those of the initial study population.

Subgroup analyses

Table 3 illustrates the CB subgroup analyses based on the time interval between chemotherapy administration and ICU admission. The proportion of patients who underwent HSCT was highest in the delayed group. This group also had the highest mortality rate and the greatest proportion of patients receiving invasive therapies during ICU admission.

	NC	CB	CD	CA	
	n = 7080	*n* = 7320	*n* = 3008	*n* = 4429	*P* value
Age, years (median [IQR])	73.0 [64.0, 80.0]	64.0 [53.0, 72.0]	69.0 [61.0, 76.0]	71.0 [63.0, 78.0]	< 0.01
Sex, male, % (n)	58.8 (4163)	62.5 (4574)	58.1 (1748)	59.3 (2628)	< 0.01
BMI category, % (n)					< 0.01
Underweight (< 18.5 kg/m^2)	16.3 (1156)	17.3 (1264)	13.6 (409)	15.4 (680)	
Low–normal weight (18.5–22.5 kg/m^2)	37.6 (2659)	41.7 (3052)	39.1 (1175)	40.8 (1806)	
High–normal weight (22.5–25.0 kg/m^2)	22.0 (1557)	20.9 (1528)	22.5 (677)	22.2 (985)	
Overweight (25.0–30.0 kg/m^2)	3.1 (223)	2.9 (215)	4.9 (148)	3.1 (138)	
Obese (> 30.0 kg/m^2)	16.3 (1154)	15.6 (1142)	17.1 (515)	15.5 (686)	
Unknown	4.7 (331)	1.6 (119)	2.8 (84)	3.0 (134)	
Smoking history, % (n)					0.01
None	56.9 (4025)	54.9 (4021)	56.0 (1685)	56.4 (2498)	
Current smoker	31.5 (2230)	32.1 (2348)	30.2 (909)	30.4 (1346)	
Unknown	11.7 (825)	13.0 (951)	13.8 (414)	13.2 (585)	
Emergent admission, % (n)	53.2 (3764)	32.3 (2364)	63.1 (1898)	66.7 (2953)	< 0.01
Ambulance use, % (n)	24.1 (1703)	7.2 (527)	25.1 (756)	26.7 (1181)	< 0.01
Academic hospital, % (n)	21.3 (1508)	36.9 (2700)	36.7 (1105)	33.8 (1499)	< 0.01
Hospital volume, % (n)					< 0.01
High	17.9 (1270)	29.9 (2190)	27.8 (836)	28.1 (1243)	
High–normal	11.9 (844)	17.0 (1243)	13.6 (409)	12.9 (571)	
Normal	7.9 (561)	11.3 (827)	10.4 (312)	11.7 (516)	
Low–normal	24.4 (1727)	26.4 (1930)	26.2 (788)	25.5 (1130)	
Low	37.8 (2678)	15.4 (1130)	22.0 (663)	21.9 (969)	
ICU admission frequency, % (n)					< 0.01
Once	97.0 (6868)	94.6 (6928)	91.9 (2764)	94.5 (4185)	
Twice	2.8 (200)	4.8 (352)	7.1 (215)	4.9 (216)	
Three times	0.1 (9)	0.5 (37)	0.8 (23)	0.6 (26)	
Four times	0.0 (3)	0.0 (2)	0.2 (6)	0.0 (2)	
Five times	0.0 (0)	0.0 (1)	0.0 (0)	0.0 (0)	
Fiscal year, % (n)					< 0.01
2012	5.6 (396)	6.1 (446)	4.7 (140)	5.5 (244)	
2013	5.8 (411)	6.7 (491)	5.9 (176)	5.6 (249)	
2014	9.4 (668)	9.2 (671)	7.8 (236)	9.5 (421)	
2015	8.8 (626)	10.1 (736)	9.1 (274)	9.8 (435)	
2016	11.4 (806)	10.8 (791)	8.9 (269)	11.0 (489)	
2017	11.2 (796)	10.7 (783)	9.6 (289)	10.8 (478)	
2018	11.8 (833)	11.0 (806)	11.2 (338)	11.0 (489)	
2019	11.0 (777)	11.8 (862)	13.5 (405)	11.4 (503)	
2020	13.1 (924)	11.7 (858)	15.3 (460)	12.4 (548)	
2021	11.9 (843)	12.0 (876)	14.0 (421)	12.9 (573)	
Charlson comorbidity index (median [IQR])	1.0 [0.0, 2.0]	0.0 [0.0, 1.0]	1.0 [0.0, 2.0]	1.0 [0.0, 2.0]	< 0.01
Japan coma scale, % (n)					< 0.01
0	87.0 (6162)	96.4 (7057)	77.2 (2323)	76.2 (3373)	
1–3	10.0 (709)	2.8 (206)	17.9 (538)	20.1 (890)	
10–30	1.7 (122)	0.5 (40)	3.2 (95)	2.6 (113)	
100–300	1.2 (87)	0.2 (17)	1.7 (52)	1.2 (53)	
Disease category, % (n)					< 0.01
Hodgkin lymphoma (C81)	1.6 (115)	1.2 (91)	0.9 (26)	0.7 (32)	
Follicular lymphoma (C82)	3.7 (259)	2.5 (180)	2.4 (71)	2.1 (92)	
Non-follicular lymphoma (C83)	24.4 (1728)	24.8 (1812)	40.3 (1212)	49.3 (2184)	
Mature T/NK-cell lymphomas (C84)	2.0 (143)	4.4 (320)	2.9 (88)	2.5 (112)	
Other and unspecified types of non-Hodgkin lymphoma (C85)	40.9 (2895)	9.7 (713)	27.0 (813)	22.3 (986)	
Other specified types of T/NK-cell lymphoma (C86)	0.8 (56)	1.1 (80)	1.2 (37)	0.8 (36)	
Malignant immunoproliferative diseases and certain other B-cell lymphomas (C88)	2.8 (195)	0.3 (19)	1.3 (40)	0.5 (21)	
Multiple myeloma and malignant plasma cell neoplasms (C90)	7.4 (523)	13.5 (991)	8.6 (258)	10.5 (466)	
Lymphoid leukemia (C91)	4.0 (282)	13.2 (963)	4.3 (128)	4.3 (189)	

Continued

	NC	CB	CD	CA	
	n = 7080	*n* = 7320	*n* = 3008	*n* = 4429	*P* value
Myeloid leukemia (C92)	10.3 (731)	26.8 (1963)	9.8 (296)	6.1 (271)	
Monocytic leukemia (C93)	0.4 (27)	0.7 (48)	0.3 (10)	0.2 (10)	
Other leukemias of specified cell type (C94)	0.2 (13)	0.4 (27)	0.5 (14)	0.2 (9)	
Leukemia of unspecified cell type (C95)	1.3 (91)	1.4 (103)	0.3 (10)	0.4 (16)	
Other and unspecified malignant neoplasms of lymphoid, hematopoietic, and related tissue (C96)	0.3 (22)	0.1 (10)	0.2 (5)	0.1 (5)	
Catecholamine use before ICU admission, % (n)	2.2 (154)	13.7 (1001)	2.4 (71)	1.6 (71)	< 0.01
HSCT during admission, % (n)	0.1 (5)	27.0 (1979)	0.7 (20)	0.7 (30)	< 0.01

Table 1. Patient characteristics. BMI, body mass index; CA, chemotherapy after ICU discharge; CB, chemotherapy before ICU admission; CD, chemotherapy during ICU admission; HSCT, hematopoietic stem cell transplantation; ICU, intensive care unit; IQR, interquartile range.

	NC	CB	CD	CA	
	n = 7080	*n* = 7320	*n* = 3008	*n* = 4429	*P* value
Therapeutic intervention in the ICU					
Catecholamine use, % (n)	25.0 (1767)	57.8 (4229)	35.2 (1059)	21.4 (947)	< 0.01
MV, % (n)	18.3 (1293)	57.6 (4216)	34.9 (1051)	16.6 (735)	< 0.01
RRT, % (n)	5.2 (367)	29.9 (2191)	19.0 (572)	6.4 (284)	< 0.01
ECMO, % (n)	0.4 (31)	1.0 (76)	0.8 (24)	0.7 (30)	< 0.01
Duration of MV, days (median [IQR])	3.0 [1.0, 8.0]	6.0 [2.0, 14.0]	7.0 [3.0, 15.0]	3.0 [1.0, 7.0]	< 0.01
Duration of RRT, days (median [IQR])	4.0 [2.0, 8.0]	7.0 [3.0, 14.0]	7.0 [4.0, 12.0]	6.0 [3.0, 14.0]	< 0.01
Duration of ECMO, days (median [IQR])	1.0 [1.0, 2.5]	2.0 [1.0, 6.2]	2.5 [1.0, 8.0]	1.0 [1.0, 1.0]	< 0.01
Clinical outcomes					
ICU stay, days (median [IQR])	1.0 [1.0, 3.0]	4.0 [2.0, 11.0]	4.0 [1.0, 10.0]	1.0 [1.0, 3.0]	< 0.01
Tracheostomy, % (n)	2.1 (150)	7.3 (538)	6.4 (192)	3.0 (135)	< 0.01
Admission cost, US dollar (median [IQR])	9738.4 [6196.6, 15959.7]	42296.5 [22680.6, 84422.1]	24816.0 [14042.5, 40,171.0]	26446.7 [17292.4, 38940.5]	< 0.01
Hospital stay, days (median [IQR])	17.0 [10.0, 32.0]	66.0 [37.0, 112.0]	41.0 [21.0, 73.0]	57.0 [38.0, 87.0]	< 0.01
Mortality rate, % (n)	23.9 (1692)	52.4 (3839)	24.8 (746)	15.2 (675)	< 0.01
Proportion of home discharge cases, % (n)	59.2 (4192)	36.3 (2657)	55.4 (1665)	63.9 (2831)	< 0.01

Table 2. Therapeutic interventions employed in the ICU and clinical outcomes of all groups. CA, chemotherapy after ICU discharge; CB, chemotherapy before ICU admission; CD, chemotherapy during ICU admission; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IQR, interquartile range; MV, mechanical intervention; RRT, renal replacement therapy.

Table 4 reveals the comparison of patient characteristics and outcomes by chemotherapy regimen. Among the high-intensity regimens, VPDL was associated with younger age, acute lymphoid leukemia, therapeutic interventions in the ICU, and mortality. Patients receiving MP had the highest rates of HSCT, MV, RRT, and mortality, as well as the highest admission costs. In contrast, the low-to-intermediate-intensity regimens, such as R-CVP and R-CHOP, were associated with lower mortality rates and less intensive care.

Table 5 demonstrates the comparison of patient characteristics and outcomes by hospital volume. The high volume category was associated with the highest rates of HSCT, MV, RRT, and catecholamine use. Mortality was high despite the frequent use of therapeutic interventions in the ICU.

Discussion

This study explored the characteristics and outcomes of patients with hematologic malignancies requiring intensive care, focusing on disease categories, invasive therapies during ICU admission, chemotherapy timing relative to ICU admission, and mortality. The CB group constituted the largest group. It included almost all patients who underwent HSCT and had the highest mortality rate. Subgroup analysis of the CB group showed that the delayed group, which had the highest mortality rate, mainly comprised patients who underwent HSCT. Additional subgroup analyses suggested that treatment intensity, underlying malignancy type, and frequency of HSCT are key factors affecting prognosis and healthcare resource utilization.

A general trend of high mortality rates was observed across all patient groups. However, a decline in mortality rate was observed over time in the CB group, even though it had the highest mortality rate among the groups. We also observed a reduction in MV use, particularly in the CB group. The CD group experienced a consistent increase in ICU admissions each year. No changes in the use of invasive therapies during ICU admission and mortality were reported in the CD group. In contrast, the CA group showed a decline in mortality. Subgroup

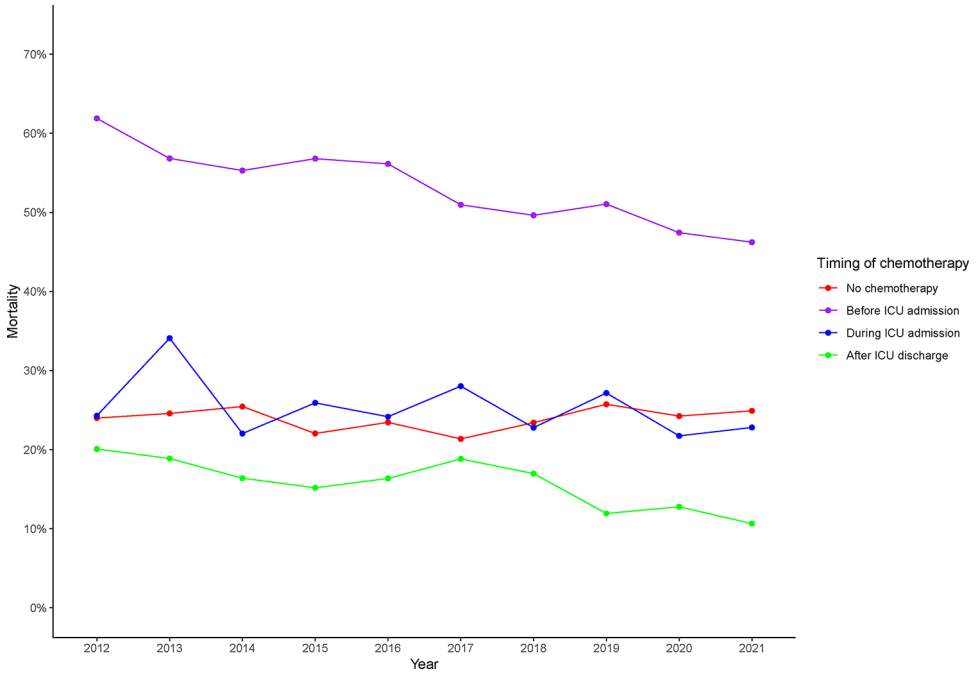

Fig. 3. Mortality trends for each category. ICU, intensive care unit.

analysis of the CB group showed that the delayed group primarily consisted of patients who underwent HSCT. This group also had the highest mortality rate.

This study represents one of the largest investigations of patients with hematologic malignancies requiring intensive care. To our knowledge, this is the first epidemiological study to examine baseline characteristics and outcomes by chemotherapy timing using a nationwide database.

In this study, mortality trends improved over time, consistent with a previous study[15]. Two possible explanations may account for these findings. One explanation is the advancement in the management of hematologic malignancies and severe illness. Over time, the prognosis of patients in the CB group suggests improved outcomes for those with hematologic malignancies[5], as well as the standardization of therapeutic approaches for severe illnesses such as acute respiratory distress syndrome[16] and sepsis[17]. Moreover, the proportion of patients receiving MV decreased, particularly in the CB group. Avoiding MV may reduce mortality in patients with hematologic malignancies[18]. Another explanation is the change in ICU admission criteria. Advanced care planning and palliative care interventions may reduce ICU admissions among patients with severe illness[19]. This trend suggests that optimizing the timing of ICU admission could facilitate earlier intervention when patients are still in a potentially treatable state. Previous studies have demonstrated an association between delayed ICU admission and increased mortality in patients requiring intensive care[20], including those with cancer[21,22]. However, the CB group also had the highest proportion of patients requiring catecholamine support before ICU admission. Although we were unable to collect data on catecholamine dose, this finding suggests that ICU admission was delayed in the CB group, potentially contributing to its higher mortality rate[23].

Approximately 55% of the patients in the CD group were discharged home, suggesting that their prognosis was not particularly poor, consistent with previous studies[10,11]. While previous studies were conducted at single institutions, limiting the generalizability of their findings, our use of a nationwide database elucidated similar trends on a national scale. Prompt initiation of organ support and careful administration of chemotherapy may be crucial for achieving a favorable prognosis[24]. However, the effectiveness of chemotherapy during ICU admission varied across disease categories, highlighting the need to consider its timing within a personalized medicine approach.

The CA group had the highest proportion of patients requiring an ambulance, yet exhibited the lowest mortality rate among the groups. This finding may suggest that patients in this group were admitted for close monitoring rather than due to acute deterioration, although further investigation is needed to clarify this pattern.

This study has several limitations. First, due to the nature of the Japanese Diagnosis Procedure Combination (DPC) inpatient database, we were unable to assess key clinical indicators, such as laboratory values or functional status, which limited our ability to comprehensively evaluate disease severity. Prognostic tools such as the International Prognostic Index or International Prognostic Scoring System were not available for analysis in this study. Moreover, the DPC database did not include complete information on chemotherapy dosing, making it difficult to fully assess chemotherapy regimens. Second, important severity markers, including the Sepsis-related Organ Failure Assessment score, Acute Physiology and Chronic Health Evaluation II score, and specific reasons for ICU admission (e.g., sepsis, tumor necrosis syndrome, acute respiratory distress syndrome, and acute kidney injury), were not recorded, which may have influenced the observed outcomes. This lack of information hindered the assessment of chemotherapy-related complications in patients who underwent chemotherapy prior to ICU

	Overall	Early	Intermediate	Delayed	*P* value
	n = 7320	*n* = 748	*n* = 3113	*n* = 3459	
Baseline					
Emergent admission, % (n)	32.3 (2364)	53.2 (398)	33.5 (1044)	26.7 (922)	< 0.01
Ambulance use, % (n)	7.2 (527)	16.6 (124)	7.2 (224)	5.2 (179)	< 0.01
Academic hospital, % (n)	63.1 (4620)	67.8 (507)	68.2 (2123)	57.5 (1990)	< 0.01
Disease category, % (n)					< 0.01
Hodgkin lymphoma (C81)	2.5 (180)	2.0 (15)	2.6 (82)	2.4 (83)	
Follicular lymphoma (C82)	1.2 (91)	0.8 (6)	1.3 (42)	1.2 (43)	
Non-follicular lymphoma (C83)	13.2 (963)	6.3 (47)	10.5 (328)	17.0 (588)	
Mature T/NK-cell lymphomas (C84)	0.3 (19)	0.3 (2)	0.3 (8)	0.3 (9)	
Other and unspecified types of non-Hodgkin lymphoma (C85)	0.7 (48)	1.1 (8)	0.6 (18)	0.6 (22)	
Other specified types of T/NK-cell lymphoma (C86)	13.5 (991)	14.8 (111)	16.6 (518)	10.5 (362)	
Malignant immunoproliferative diseases and certain other B-cell lymphomas (C88)	26.8 (1963)	25.3 (189)	22.1 (688)	31.4 (1086)	
Multiple myeloma and malignant plasma cell neoplasms (C90)	24.8 (1812)	31.3 (234)	28.5 (887)	20.0 (691)	
Lymphoid leukemia (C91)	9.7 (713)	12.0 (90)	10.5 (327)	8.6 (296)	
Myeloid leukemia (C92)	0.4 (27)	0.3 (2)	0.4 (11)	0.4 (14)	
Monocytic leukemia (C93)	0.1 (10)	0.0 (0)	0.1 (4)	0.2 (6)	
Other leukemias of specified cell type (C94)	1.1 (80)	1.2 (9)	1.3 (40)	0.9 (31)	
Leukemia of unspecified cell type (C95)	4.4 (320)	3.3 (25)	4.0 (126)	4.9 (169)	
Other and unspecified malignant neoplasms of lymphoid, hematopoietic, and related tissue (C96)	1.4 (103)	1.3 (10)	1.1 (34)	1.7 (59)	
Catecholamine use before ICU admission, % (n)	13.7 (1001)	6.1 (46)	11.4 (354)	17.4 (601)	< 0.01
HSCT during admission, % (n)	27.0 (1979)	1.7 (13)	13.2 (412)	44.9 (1554)	< 0.01
Chemotherapy regimen, % (n)					
Hyper-CVAD	8.2 (602)	8.3 (62)	7.3 (227)	9.0 (313)	0.03
R-DHAP	5.0 (364)	4.7 (35)	4.0 (126)	5.9 (203)	< 0.01
EPOCH	5.1 (373)	4.8 (36)	4.3 (133)	5.9 (204)	0.01
R-CHOP	10.2 (745)	10.2 (76)	11.3 (353)	9.1 (316)	0.01
BR	1.5 (110)	1.2 (9)	1.5 (47)	1.6 (54)	0.77
R-CVP	13.2 (963)	13.8 (103)	14.2 (443)	12.1 (417)	0.03
MP	11.3 (826)	1.9 (14)	5.4 (168)	18.6 (644)	< 0.01
VPDL	1.5 (109)	0.3 (2)	1.4 (44)	1.8 (63)	0.01
Therapeutic intervention in the ICU					
Catecholamine use, % (n)	64.0 (4688)	48.4 (362)	63.2 (1968)	68.2 (2358)	< 0.01
MV, % (n)	57.6 (4216)	49.5 (370)	54.7 (1704)	61.9 (2142)	< 0.01
RRT, % (n)	29.9 (2191)	27.0 (202)	27.0 (841)	33.2 (1148)	< 0.01
ECMO, % (n)	1.0 (76)	0.1 (1)	1.0 (30)	1.3 (45)	< 0.01
Duration of MV, days (median [IQR])	6.0 [2.0, 14.0]	4.0 [2.0, 10.0]	5.0 [2.0, 11.0]	7.0 [3.0, 17.0]	< 0.01
Duration of RRT, days (median [IQR])	7.0 [3.0, 14.0]	5.0 [3.0, 10.0]	6.0 [3.0, 12.0]	8.0 [4.0, 17.0]	< 0.01
Duration of ECMO, days (median [IQR])	2.0 [1.0, 6.2]	30.0 [30.0, 30.0]	2.0 [1.0, 5.0]	2.0 [1.0, 7.0]	0.18
Clinical outcomes					
ICU stay, days (median [IQR])	4.0 [2.0, 11.0]	3.0 [2.0, 7.0]	4.0 [2.0, 9.0]	5.0 [2.0, 13.0]	< 0.01
Tracheostomy, % (n)	7.3 (538)	5.2 (39)	5.7 (177)	9.3 (322)	< 0.01
Admission cost, US dollar (median [IQR])	42296.5 [22680.6, 84422.1]	22432.5 [12656.2, 41797.9]	28130.1 [17346.3, 48578.7]	72152.3 [40,517.6, 129625.1]	< 0.01
Hospital stay, days (median [IQR])	66.0 [37.0, 112.0]	33.0 [16.0, 61.0]	43.0 [27.0, 69.0]	100.0 [68.0, 147.0]	< 0.01
Mortality, % (n)	52.4 (3839)	39.3 (294)	47.3 (1472)	59.9 (2073)	< 0.01
Proportion of home discharge cases, % (n)	36.3 (2657)	48.5 (363)	41.1 (1280)	29.3 (1014)	< 0.01

Table 3. Subgroup analysis of admission timing in patients receiving chemotherapy before ICU admission. BR, bendamustine and rituximab; ECMO, extracorporeal membrane oxygenation; EPOCH, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin; HSCT, hematopoietic stem cell transplantation; Hyper-CVAD, hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone; ICU, intensive care unit; IQR, interquartile range; MP, melphalan and prednisone; MV, mechanical ventilation; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; R-CVP, rituximab, cyclophosphamide, vincristine, and prednisolone; R-DHAP, rituximab, dexamethasone, cytarabine, and cisplatin or carboplatin; RRT, renal replacement therapy; VPDL, vincristine, prednisolone, daunorubicin, and L-asparaginase.

	High				Intermediate–low			
	Hyper-CVAD	EPOCH	VPDL	R-DHAP	R-CHOP	R-CVP	BR	MP
	n = 1129	*n* = 648	*n* = 136	*n* = 806	*n* = 1976	*n* = 2554	*n* = 199	*n* = 900
Age, years (median [IQR])	65.0 [54.0, 72.0]	64.0 [55.0, 71.0]	50.0 [34.0, 60.2]	65.0 [57.0, 72.0]	69.0 [61.0, 76.0]	71.0 [63.0, 78.0]	70.0 [63.0, 76.0]	58.0 [47.0, 65.0]
Sex, male, % (n)	60.7 (685)	62.3 (404)	57.4 (78)	60.2 (485)	58.6 (1158)	59.2 (1511)	64.8 (129)	57.7 (519)
BMI category, % (n)								
Underweight (< 18.5 kg/m^2)	13.6 (153)	16.4 (106)	16.9 (23)	15.1 (122)	16.2 (321)	16.3 (416)	20.6 (41)	20.6 (185)
Low–normal (18.5–22.5 kg/m^2)	42.0 (474)	40.7 (264)	36.0 (49)	41.6 (335)	38.9 (769)	39.2 (1002)	35.7 (71)	45.6 (410)
High–normal (22.5–25.0 kg/m^2)	20.9 (236)	19.6 (127)	20.6 (28)	20.5 (165)	21.5 (425)	21.4 (546)	23.1 (46)	17.1 (154)
Overweight (25.0–30.0 kg/m^2)	16.7 (188)	18.2 (118)	17.6 (24)	16.9 (136)	16.9 (334)	16.5 (422)	16.6 (33)	12.3 (111)
Obesity (> 30.0 kg/m^2)	4.8 (54)	3.5 (23)	8.1 (11)	3.7 (30)	4.0 (80)	4.0 (103)	2.5 (5)	2.9 (26)
Unknown	2.1 (24)	1.5 (10)	0.7 (1)	2.2 (18)	2.4 (47)	2.5 (65)	1.5 (3)	1.6 (14)
Emergent admission, % (n)	54.0 (610)	54.9 (356)	52.2 (71)	52.9 (426)	56.1 (1109)	56.3 (1439)	45.2 (90)	18.3 (165)
Ambulance use, % (n)	14.8 (167)	17.6 (114)	10.3 (14)	16.4 (132)	18.4 (364)	19.3 (493)	16.1 (32)	4.2 (38)
Academic hospital, % (n)	38.7 (437)	35.3 (229)	37.5 (51)	42.6 (343)	35.6 (703)	33.2 (848)	30.2 (60)	48.7 (438)
Hospital volume, % (n)								
High	29.3 (331)	28.1 (182)	34.6 (47)	38.1 (307)	28.7 (568)	28.0 (716)	24.1 (48)	44.2 (398)
High–normal	16.3 (184)	14.2 (92)	18.4 (25)	12.8 (103)	15.0 (297)	14.3 (364)	15.6 (31)	14.4 (130)
Normal	11.1 (125)	13.4 (87)	11.0 (15)	11.3 (91)	10.4 (206)	10.5 (268)	9.0 (18)	13.9 (125)
Low–normal	26.7 (302)	28.2 (183)	23.5 (32)	24.4 (197)	25.9 (512)	26.2 (669)	26.6 (53)	18.7 (168)
Low	16.6 (187)	16.0 (104)	12.5 (17)	13.4 (108)	19.9 (393)	21.0 (537)	24.6 (49)	8.8 (79)
Charlson comorbidity index (median [IQR])	1.0 [0.0, 2.0]	1.0 [0.0, 2.0]	0.0 [0.0, 1.0]	1.0 [0.0, 2.0]	1.0 [0.0, 2.0]	1.0 [0.0, 2.0]	1.0 [0.0, 2.0]	0.0 [0.0, 1.0]
Japan Coma Scale, % (n)								
0	90.8 (1025)	91.7 (594)	98.5 (134)	82.3 (663)	90.0 (1778)	90.0 (2298)	95.5 (190)	98.8 (889)
1–3	6.9 (78)	5.9 (38)	0.0 (0)	14.9 (120)	7.6 (150)	7.3 (187)	4.0 (8)	0.6 (5)
10–30	1.2 (13)	0.9 (6)	0.7 (1)	2.1 (17)	1.3 (26)	1.7 (44)	0.5 (1)	0.6 (5)
100–300	1.2 (13)	1.5 (10)	0.7 (1)	0.7 (6)	1.1 (22)	1.0 (25)	0.0 (0)	0.1 (1)
Disease category, % (n)								
Hodgkin lymphoma (C81)	0.4 (5)	0.5 (3)	0.0 (0)	0.2 (2)	0.0 (0)	0.0 (0)	0.0 (0)	1.4 (13)
Follicular lymphoma (C82)	2.2 (25)	1.9 (12)	0.0 (0)	2.4 (19)	3.6 (72)	3.8 (96)	27.6 (55)	2.6 (23)
Non-follicular lymphoma (C83)	49.5 (559)	46.6 (302)	8.8 (12)	69.4 (559)	70.9 (1401)	70.3 (1796)	47.7 (95)	8.9 (80)
Mature T/NK-cell lymphomas (C84)	6.0 (68)	9.0 (58)	0.7 (1)	1.1 (9)	0.2 (3)	0.2 (4)	0.0 (0)	6.2 (56)
Other and unspecified types of non-Hodgkin lymphoma (C85)	18.8 (212)	21.6 (140)	1.5 (2)	20.6 (166)	24.3 (481)	24.5 (626)	18.6 (37)	4.3 (39)
Other specified types of T/NK-cell lymphoma (C86)	1.6 (18)	1.9 (12)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.6 (14)
Malignant immunoproliferative diseases and certain other B-cell lymphomas (C88)	0.2 (2)	0.0 (0)	0.0 (0)	0.2 (2)	0.2 (3)	0.3 (7)	4.0 (8)	0.1 (1)
Multiple myeloma and malignant plasma cell neoplasms (C90)	1.9 (22)	0.6 (4)	0.0 (0)	0.0 (0)	0.1 (1)	0.0 (1)	0.0 (0)	19.2 (173)
Lymphoid leukemia (C91)	17.2 (194)	16.8 (109)	77.2 (105)	3.1 (25)	0.7 (13)	0.8 (20)	2.0 (4)	22.6 (203)
Myeloid leukemia (C92)	1.0 (11)	0.3 (2)	3.7 (5)	2.7 (22)	0.1 (1)	0.1 (3)	0.0 (0)	30.7 (276)
Monocytic leukemia (C93)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.8 (7)
Other leukemias of specified cell type (C94)	0.1 (1)	0.2 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.6 (5)
Leukemia of unspecified cell type (C95)	0.9 (10)	0.5 (3)	6.6 (9)	0.1 (1)	0.1 (1)	0.0 (1)	0.0 (0)	1.1 (10)
Other and unspecified malignant neoplasms of lymphoid, hematopoietic, and related tissue (C96)	0.2 (2)	0.3 (2)	1.5 (2)	0.1 (1)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
HSCT during admission, % (n)	9.3 (105)	11.7 (76)	18.4 (25)	11.9 (96)	1.5 (29)	1.6 (41)	3.0 (6)	84.4 (760)
Therapeutic intervention in the ICU								
Catecholamine use, % (n)	51.6 (582)	55.2 (358)	61.0 (83)	43.7 (352)	40.8 (806)	41.4 (1057)	42.7 (85)	72.1 (649)
MV, % (n)	44.8 (506)	45.5 (295)	57.4 (78)	35.6 (287)	33.8 (668)	34.3 (877)	33.7 (67)	67.1 (604)
RRT, % (n)	20.5 (231)	26.7 (173)	21.3 (29)	18.7 (151)	15.7 (310)	15.2 (389)	19.6 (39)	46.7 (420)
ECMO, % (n)	0.8 (9)	1.5 (10)	1.5 (2)	0.2 (2)	1.4 (28)	1.4 (36)	0.5 (1)	1.1 (10)
Duration of MV, days (median [IQR])	6.0 [3.0, 15.0]	7.0 [3.0, 15.0]	4.0 [2.0, 13.0]	6.0 [2.0, 16.0]	5.0 [2.0, 12.2]	5.0 [2.0, 12.0]	5.0 [2.0, 11.5]	9.0 [4.0, 21.0]
Duration of RRT, days (median [IQR])	6.0 [3.0, 12.0]	6.0 [4.0, 11.0]	3.0 [2.0, 5.0]	5.0 [4.0, 11.0]	6.0 [3.0, 10.0]	6.0 [3.0, 10.0]	5.0 [4.0, 8.0]	10.0 [4.0, 19.0]
Duration of ECMO, days (median [IQR])	2.0 [1.0, 8.0]	1.5 [1.0, 7.2]	3.0 [2.0, 4.0]	1.0 [1.0, 1.0]	1.0 [1.0, 2.5]	1.0 [1.0, 2.0]	2.0 [2.0, 2.0]	3.5 [1.2, 11.8]
Continued								

	High				Intermediate–low			
	Hyper-CVAD	EPOCH	VPDL	R-DHAP	R-CHOP	R-CVP	BR	MP
	n = 1129	*n* = 648	*n* = 136	*n* = 806	*n* = 1976	*n* = 2554	*n* = 199	*n* = 900
Clinical outcomes								
ICU stay, days (median [IQR])	4.0 [1.0, 9.0]	5.0 [2.0, 10.0]	3.0 [2.0, 9.0]	3.0 [1.0, 7.0]	3.0 [1.0, 7.0]	3.0 [1.0, 7.0]	3.0 [1.0, 6.0]	8.0 [3.0, 14.0]
Tracheostomy, % (n)	6.9 (78)	7.1 (46)	6.6 (9)	7.4 (60)	7.0 (138)	6.7 (172)	5.0 (10)	11.1 (100)
Admission cost, US dollar (median [IQR])	39818.3 [23708.0, 68478.9]	45524.7 [26572.9, 76894.8]	50,870.1 [24860.7, 83773.6]	39881.8 [27376.0, 72030.6]	27271.1 [17928.8, 44021.1]	26895.3 [17719.0, 43281.9]	28672.6 [19451.7, 48501.5]	109383.7 [68622.0, 176669.4]
Hospital stay, days (median [IQR])	77.0 [47.0, 132.0]	85.0 [50.0, 148.0]	69.0 [39.0, 131.8]	80.0 [49.0, 130.8]	59.0 [39.0, 98.0]	59.0 [39.0, 97.0]	62.0 [35.0, 101.5]	115.0 [72.8, 175.0]
Mortality, % (n)	35.7 (403)	38.9 (252)	46.3 (63)	27.0 (218)	17.7 (349)	18.2 (465)	34.2 (68)	64.2 (578)
Proportion of home discharge cases, % (n)	52.2 (589)	49.4 (320)	49.3 (67)	55.0 (443)	65.8 (1301)	63.7 (1627)	52.8 (105)	24.1 (217)

Table 4. Comparison based on chemotherapy regimen. BMI, body mass index; BR, bendamustine and rituximab; ECMO, extracorporeal membrane oxygenation; EPOCH, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin; HSCT, hematopoietic stem cell transplantation; Hyper-CVAD, hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone; ICU, intensive care unit; IQR, interquartile range; MP, melphalan and prednisone; MV, mechanical ventilation; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; R-CVP, rituximab, cyclophosphamide, vincristine, and prednisolone; R-DHAP, rituximab, dexamethasone, cytarabine, and cisplatin or carboplatin; RRT, renal replacement therapy; VPDL, vincristine, prednisolone, daunorubicin, and L-asparaginase.

	High	High–normal	Normal	Low–normal	Low	*P* value
	n = 5539	*n* = 3067	*n* = 2216	*n* = 5575	*n* = 5440	
Baseline						
Chemotherapy timing, n (%)						
No chemotherapy	22.9 (1270)	27.5 (844)	25.3 (561)	31.0 (1727)	49.2 (2678)	< 0.01
Chemotherapy before ICU admission	39.5 (2190)	40.5 (1243)	37.3 (827)	34.6 (1930)	20.8 (1130)	
Chemotherapy during ICU admission	15.1 (836)	13.3 (409)	14.1 (312)	14.1 (788)	12.2 (663)	
Chemotherapy after ICU discharge	22.4 (1243)	18.6 (571)	23.3 (516)	20.3 (1130)	17.8 (969)	
Academic hospital, % (n)	61.2 (3388)	43.7 (1339)	45.5 (1009)	15.1 (843)	4.3 (233)	< 0.01
HSCT during admission, % (n)	16.2 (900)	12.6 (385)	11.6 (256)	7.1 (394)	1.8 (99)	< 0.01
Therapeutic intervention in the ICU						
Catecholamine use, % (n)	45.1 (2499)	45.2 (1385)	44.2 (980)	40.8 (2274)	33.1 (1803)	< 0.01
MV, % (n)	38.4 (2126)	37.7 (1157)	34.4 (763)	34.1 (1899)	24.8 (1350)	< 0.01
RRT, % (n)	20.5 (1136)	18.7 (575)	16.2 (360)	15.0 (837)	9.3 (506)	< 0.01
ECMO, % (n)	1.1 (60)	0.8 (25)	0.6 (14)	0.7 (39)	0.4 (23)	0.03
Duration of MV, days (median [IQR])	6.0 [2.0, 15.0]	6.0 [2.0, 13.0]	6.0 [2.0, 13.0]	5.0 [2.0, 11.0]	4.0 [2.0, 10.0]	< 0.01
Duration of RRT, days (median [IQR])	7.0 [3.0, 15.0]	7.0 [3.0, 13.0]	6.0 [3.0, 12.0]	6.0 [3.0, 13.0]	5.5 [2.0, 11.0]	< 0.01
Duration of ECMO, days (median [IQR])	1.0 [1.0, 3.2]	2.0 [1.0, 7.0]	1.0 [1.0, 2.0]	1.0 [1.0, 3.5]	1.0 [1.0, 5.0]	0.51
Clinical outcomes						
ICU stay, days (median [IQR])	3.0 [1.0, 8.0]	2.0 [1.0, 7.0]	2.0 [1.0, 6.0]	2.0 [1.0, 6.0]	2.0 [1.0, 4.0]	< 0.01
Tracheostomy, % (n)	6.0 (332)	5.2 (158)	5.2 (115)	4.6 (255)	2.8 (155)	< 0.01
Admission cost, US dollar (median [IQR])	29545.1 [15087.5, 57297.7]	26496.5 [12122.5, 49934.1]	24566.2 [12899.6, 47008.0]	21262.5 [10,981.8, 39380.3]	15306.6 [8525.1, 27788.8]	< 0.01
Hospital stay, days (median [IQR])	51.0 [26.0, 92.0]	47.0 [21.0, 84.5]	47.0 [24.0, 85.0]	39.0 [20.0, 73.0]	31.0 [15.0, 63.0]	< 0.01
Mortality, % (n)	32.9 (1823)	35.2 (1080)	32.3 (715)	33.0 (1842)	27.4 (1492)	< 0.01
Proportion of home discharge cases, % (n)	51.5 (2854)	50.1 (1537)	51.5 (1142)	53.3 (2972)	52.2 (2840)	< 0.01

Table 5. Comparison based on hospital volume. ECMO, extracorporeal membrane oxygenation; HSCT, hematopoietic stem cell transplantation; ICU, intensive care unit; IQR, interquartile range; MV, mechanical ventilation; RRT, renal replacement therapy.

admission. Third, the NC group may have included patients who received chemotherapy in outpatient settings or at different hospitals, which could have affected the comparisons. Finally, although chemotherapy during ICU admission was not associated with poor clinical outcomes, the variability in patient characteristics, disease severity, and treatment approaches complicate direct comparisons. The findings suggest that close monitoring

and individualized treatment decisions may play a critical role in patient management; however, further studies are necessary to determine optimal strategies for chemotherapy administration in ICU settings.

Despite these limitations, the study benefits from the use of an extensive dataset, providing valuable insights into trends in ICU care for patients with hematologic malignancies in Japan. These findings contribute to a broader understanding of critical care practices in this patient population and highlight the need for continued research to refine the treatment approaches.

This study highlights the trends in ICU admissions and treatment strategies for patients with hematologic malignancies. The CB group had the highest mortality rate, although outcomes improved over time. The CD group had a lower mortality rate; however, the differences in patient characteristics likely influenced this finding. Subgroup analyses showed that delayed ICU admission after chemotherapy, high-intensity regimens, and treatment in high-volume hospitals were associated with higher ICU burden and mortality, reflecting greater disease severity and treatment complexity. These results underscore the complexity of chemotherapy decision-making in ICU settings and the necessity for further research to inform individualized treatment strategies.

Methods

Study design and data source

This study adhered to the tenets of the Declaration of Helsinki and was performed in accordance with the REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement[25]. The study was approved by the Institutional Review Board of Tohoku University, Sendai, Japan (approval number: 2022-1-444; approval date: August,29 2022). Given the de-identified nature of the data, the requirement for written informed consent was waived by the Institutional Review Board of Tohoku University.

We sourced data from the DPC database. This comprehensive repository contains discharge summaries and administrative claims from > 1100 acute care hospitals. It collates information on approximately 7 million inpatients annually, representing approximately 50% of all acute care hospitalizations in Japan. The database contains comprehensive details, such as patient demographics, smoking history, anthropometric measurements, initial level of consciousness, functional status upon admission, admission status, ambulance utilization, surgical details, diagnoses coded according to the International Classification of Diseases (Tenth Revision) (ICD-10), and presented in the Japanese script, procedures based on Japanese medical and surgical nomenclature, medication prescriptions, drug administration protocols, and discharge outcomes[26,27].

Study population

We identified all patients aged ≥ 18 years who were hospitalized for hematologic malignancies classified as medical resource diseases and admitted to the ICU between April 1, 2012, and March 31, 2022. Supplementary Table S5 lists the hematologic malignancies according to the ICD-10 codes. Patients with missing inpatient care cost data were excluded.

Group assignments

The patients were categorized into four distinct groups based on the timing of initiation of their first chemotherapy relative to initial ICU admission: NC, CB, CD, and CA. Each patient's dates of chemotherapy initiation and ICU admission were identified using longitudinal claims data. Group assignment was based solely on the initial dates of chemotherapy and ICU admission, irrespective of whether chemotherapy was administered several times or patients had repeated ICU admissions. For example, patients in whom chemotherapy was initiated within 3 days of hospitalization, who were subsequently admitted to the ICU, and for whom additional chemotherapy was administered after ICU discharge, were included in the CB group. Approximately 40 chemotherapeutic agents, which have been approved for the treatment of hematologic malignancies in Japan, were included in this assessment. The DPC database contains details of the drugs prescribed during hospitalization. Supplementary Table S6 lists the agents used to treat hematologic malignancies.

Data collection and outcome information

We extracted patient demographic and clinical variables from the DPC database, including sex, age, body mass index (BMI), smoking status, emergency admissions, utilization of emergency medical services, admission to a teaching hospital, fiscal year, Charlson Comorbidity Index[28], Japan Coma Scale score on admission[29], primary diagnosis characterized by ICD-10 codes (Supplementary Table S5), receipt of HSCT during hospitalization, ICU admission frequency, and hospital caseload. HSCT involves hematopoietic progenitor cells derived from either the patient (autologous HSCT) or a donor (allogeneic HSCT). Hospital caseloads were stratified into quintiles (high, high–normal, normal, low–normal, and low) according to the annual number of admissions for hematologic malignancies requiring intensive care. We also collected data on the therapeutic interventions administered in the ICU, including catecholamine use, MV, RRT, and ECMO. The duration of each invasive procedure was recorded.

Additionally, we identified the following chemotherapy regimens (Supplementary Table S6), which were administered during hospitalization: BR (bendamustine and rituximab), EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin), hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone), MP (melphalan and prednisone), R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), R-CVP (rituximab, cyclophosphamide, vincristine, and prednisolone), R-DHAP (rituximab, dexamethasone, cytarabine, and cisplatin or carboplatin), and VPDL (vincristine, prednisolone, daunorubicin, and L-asparaginase)[30–33]. Supplementary Table S6 does not contain information on cisplatin due to its infrequent use as a standalone chemotherapeutic agent[34]. In this case, R-DHAP refers to rituximab, dexamethasone, and cytarabine. Chemotherapy regimens were categorized into high- and low-to-intermediate-intensity groups based on treatment intensity and clinical use. High-intensity regimens (EPOCH, hyper-CVAD,

R-DHAP, and VPDL) are typically more toxic and require intensive care, whereas low-to-intermediate-intensity regimens (BR, MP, R-CHOP, and R-CVP) are less intensive and used to treat older or frail patients[30–33].

The primary outcome was the in-hospital mortality rate. Secondary outcomes included length of ICU stay, duration of hospitalization, frequency of tracheostomy, home discharge rate, and associated admission costs.

Statistical analyses

Continuous variables are presented as mean ± standard deviation for normally distributed data or as median (interquartile range) for non-normally distributed data. Categorical variables are presented as a number (percentage). To evaluate mortality trends across fiscal years within each category, we conducted the Cochran–Armitage test and calculated the *P* value for trend.

Continuous variables among the four groups were compared using the Kruskal–Wallis test, and categorical variables among the four groups were compared using Pearson's chi-square test. As a subgroup analysis, we divided this cohort into two groups: patients who required HSCT (HSCT group) and those who did not (non-HSCT group). Subsequently, we compared the four groups. The specific counts for each HSCT type are presented in Supplementary Table 1.

Additional subgroup analyses were also performed: (1) CB subgroup analyses based on the time interval between chemotherapy administration and ICU admission (early [< 8 days], intermediate [8–29 days], and delayed [≥ 30 days]); (2) Comparison of patient characteristics and outcomes by chemotherapy regimen; and (3) Comparison of patient characteristics and outcomes by hospital volume.

Two-sided *P* values < 0.05 were considered statistically significant. All statistical analyses were conducted using R (version 4.3.1) (2023-06-16).

Data availability

The datasets analyzed during the current study are not publicly available due to agreements with the hospitals that supply data to the database but are partially available from the corresponding author on reasonable request.

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YI: Conceptualization, Methodology, Investigation, Writing - original draft.KT: Formal analysis, Data curation, Writing—review & editing. TK: Conceptualization, Writing—review & editing. YK: Conceptualization, Writing—review & editing. SI: Conceptualization, Writing—review & editing. SY: Conceptualization, Writing—review & editing. KFus: Data curation, Writing—review & editing. KFuj: Data curation, Writing—review & editing. MY: Writing—review & editing, Supervision, Project administration.

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Declarations

Competing interests
The authors declare no competing interests.

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