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Effects of tertiary palliative care on the pattern of end-of-life care in patients with hematologic malignancies in Korea

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Abstract

Introduction: Patients with hematologic malignancies (HMs) often face challenges in accessing palliative care (PC) and receiving quality end-of-life (EOL) care. We examined factors associated with referrals to tertiary PC and the effects of tertiary PC on EOL care in patients with HMs.

Method: We included patients with HMs who were admitted to a university-affiliated hospital and died during hospitalization between January 2018 and December 2021. We investigated the receipt of PC consultations, patient characteristics, and EOL care indicators.

Results: Overall, 487 patients were included in the analysis, with 156 (32%) undergoing PC consultation. Sex, residence, disease status, and admission purpose were factors associated with the likelihood of PC consultation, and there has been an increasing trend in the frequency of consultations in recent cases. A higher proportion of patients who received PC completed advance statements and life-sustaining treatment documents. Patients who received PC had lower rates of aggressive EOL care, including chemotherapy and intensive care unit admission, than those who did not receive PC. Notably, PC reduced the number of blood transfusions.

Conclusion: Tertiary PC aims to reduce aggressive EOL care through patient-centered goal-of-care discussions. Therefore, there is an imperative need for concerted efforts toward seamless integration of PC.

KEYWORDS
end-of-life care, hematologic malignancy, palliative care

Novelty statements

What is the new aspect of your work?

In cases where patients with hematologic malignancies often receive aggressive end-of-life care owing to delays in palliative care referrals, our study focused on factors associated with consultation to tertiary palliative care; then, we conducted a comprehensive analysis of detailed end-of-life care indicators, including ICU admissions, chemotherapy, and transfusions based on the presence of tertiary palliative care.

What is the central finding of your work?

Patients who received palliative care had higher rates of completing advance statements, resulting in lower rates of aggressive end-of-life care and blood transfusions, and factors associated with consultation for tertiary palliative care included sex, residence, disease status, and admission purpose.

What is (or could be) the specific clinical relevance of your work?

Tertiary palliative care can greatly enhance end-of-life care for patients with hematologic malignancies through patient-centered, value-driven decision-making, emphasizing the need for concerted efforts toward appropriate integration of palliative care.

1 | INTRODUCTION

Treatment outcomes of hematologic malignancies (HMs) have been improving with advancements in anti-cancer therapies. However, a significant number of patients with HMs continue to face disease progression and poor outcomes.[1] Patients with HMs may receive aggressive care, including frequent hospitalization, emergency department (ED) visits, and intensive care unit (ICU) care at the EOL because of common complications such as cytopenia and infections. Moreover, patients with HMs may experience insufficient symptom control, including fewer opioid prescriptions,[2,3] despite a similar symptom burden as those with solid tumors.[4,5]

To maintain quality EOL care, early integration of tertiary palliative care (PC) into standard cancer care is beneficial for patients with advanced cancer, providing strong evidence for patients with incurable solid tumors.[6] Tertiary PC plays a role in managing goal-of-care discussions and difficult EOL symptoms. However, referral to tertiary PC for patients with HMs occurs less often and later in their disease course.[7] Several reasons explain the differences in tertiary PC referral between HMs and solid tumors. First, the heterogeneity of disease entities and their trajectories in HMs make prognostication difficult.[8] Second, attitudes toward the detail of PC referral and EOL care may differ between hemato-oncologists and oncologists.[9] Moreover, the need for disease-specific healthcare resources, such as transfusions or broad-spectrum antibiotics, often results in patients with HMs receiving PC only in an inpatient setting rather than an outpatient setting or at home.[10]

Despite recent reports of controlled trials demonstrating the efficacy of inpatient PC consultation in patients with HMs, when and how to provide tertiary PCs remains unknown.[11–13] Here, we aimed to identify factors associated with PC consultation and describe detailed EOL care among decedents with HMs who were or were not referred to a tertiary PC.

2 | MATERIALS AND METHODS

2.1 | Study design, setting, and participants

In this single-center, retrospective cohort study, we included patients aged ≥19 years with HMs who died during hospitalization at Seoul National University Hospital between January 2018 and December 2021. Hospitalizations with HM diagnosis were identified using the International Classification of Diseases, 10th revision codes C81–C88, C90–C96, and D45–D47. Seoul National University Hospital has a large cancer center that focuses on disease-directed treatment. This hospital offered the following tertiary PC services: outpatient PC clinics and inpatient PC consultations. Approximately 90% of inpatients referred to the PC consultation team are diagnosed with cancer, including HMs. The PC consultation team comprised two PC physicians (a professor specializing in hemato-oncology and a clinical fellow), a PC nurse, and medical social workers with sufficient expertise in PC. The two physicians and a nurse work full-time in the PC team. The detailed process of PC consultation has been described elsewhere.[14] After a referral from a primary care physician, the team offers a holistic distress assessment to the patients and families and identifies their values and preferences. The team also facilitates advance care planning (ACP) and shared decision-making among stakeholders by discussing the goals of EOL care with patients and delivering interview content with PC recommendations to primary care physicians.

To investigate the factors influencing the occurrence of PC consultations among inpatients with HM, we excluded patients who died in the ED or had received PC consultations prior to admission. The patients were divided into two groups based on the presence or absence of PC consultation: PC and non-PC groups. The PC group had their first encounter with a PC during hospitalizations, with at least one PC encounter. The cohort assembly is shown in Figure S1.

2.2 | Data collection

Demographic and clinical data were retrospectively obtained from electronic medical records. Residences of each patient were categorized as "metropolitan" if they legally and administratively belonged to a designated metropolitan city, or else they were classified as rural. Comorbidity score was calculated using the Charlson Comorbidity Index, excluding age and diagnosis of HM and solid tumor.[15] Symptoms and laboratory findings on admission were also recorded. HM diagnosis was categorized into acute leukemia,[16] myelodysplastic syndrome (MDS), lymphoma,[17] multiple myeloma (MM), and others

(including myeloproliferative neoplasm).[18] The initial disease risk was defined according to disease subtype and cytogenetic findings.[19] Disease status at admission was defined as follows: unevaluable, indicating that the response could not be assessed owing to incomplete or ongoing first-line therapy or ongoing diagnostic procedures; controlled, denoting complete remission in cases of leukemia and MDS or complete remission and partial remission in cases of lymphoma and MM; and uncontrolled, encompassing other cases, including progression to acute leukemia.

For the quality of the EOL care indicators, we investigated the status of documentation on ACP, life-sustaining treatment (LST) decisions, and EOL healthcare utilization. After the new legislation on hospice PC and EOL decision-making was implemented in Korea in 2018,[20] patients can make advance statements in person through Advance Directives or Physicians' Order for LST when they do not want LST at EOL. The patient was considered to have made an "advance statement" if one of the two documents was present. Furthermore, at an imminently dying state, specific preferences should also be decided and documented (hereafter, "LST documentation") for the following treatments: cardiopulmonary resuscitation (CPR), mechanical ventilation, hemodialysis, anticancer treatment, transfusion, inotropic agents, and extracorporeal membrane oxygenation. Additionally, if a patient has no advance statements or cannot express the intent of the LST, first-degree family members should decide on behalf of the patient. Here, we reviewed the presence of advance statements, LST documentation, and documentation dates.

For EOL healthcare resource utilization, we investigated the use of aggressive treatments within the last month of life, including ED visit, ICU admission, CPR, mechanical ventilation, and hemodialysis.[21] Chemotherapy administration was investigated for the last month, 2 weeks, 1 week, and 3 days of life. We investigated active procedures including blood tests, imaging studies, Levin tube insertion, use and withdrawal of inotropics, intravenous antibiotics, and high-flow nasal cannula, in an imminently dying state within 3 days of death. The use of opioids and antipsychotics as comfort care was investigated. The place of death was classified into two types: ICU and general ward. Moreover, daily blood transfusion requirements within 7 days prior to death were investigated.

2.3 | Statistical analyses

Descriptive statistics are presented as median values with interquartile ranges (IQRs) or numbers with percentiles. Baseline characteristics and the quality of EOL indicators were compared between the PC and non-PC groups using Student's *t*-test or Wilcoxon rank-sum test for continuous variables and Fisher's exact test or Pearson's chi-squared test for categorical variables, as indicated. We performed a stepwise backward-selection multivariate logistic regression analysis to identify the relevant factors for PC referral. The stepwise variable selection method initially selected variables with p values of <.1 in univariate analyses and excluded variables with p values of ≥.05 by performing multivariate analysis. Moreover, multivariate logistic regression models were created to identify independent associations with the quality of EOL indicators. All models were adjusted for the same set of variables described above, regardless of statistical significance, and estimates were provided with odds ratios (ORs) and 95% confidence intervals (CIs). All tests were two-sided, and p values <.05 were considered statistically significant. For statistical analyses, the statistical software "R" version 4.1.3 (www.r-project.org) was used.

2.4 | Ethics Statement

This study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The study protocol was approved by the Institutional Review Board of Seoul National University Hospital (IRB no. H-2208-196-1355). The requirement for informed consent was waived by the institutional review board due to the retrospective nature of the study.

3 | RESULTS

Table 1 shows the demographics and clinical characteristics of 487 inpatient decedents with HM. The patients' median age was 63 (IQR, 55–72) years, and 282 (57.9%) patients were male. Among the 487 patients, 182 (37.4%), 53 (10.9%), 168 (34.5%), and 62 (12.7%) had acute leukemia, MDS, lymphoma, and MM, respectively. At admission, 48.5% of the patients had an uncontrolled disease status, and disease control was the most common purpose of admission (31%).

3.1 | Factors associated with palliative care consultation

Overall, 156 (32%) patients were referred for PC consultation after admission, and this percentage increased yearly. PC group comprised more women (53.8% vs. 36.6%), more metropolitan residents (67.9% vs. 55.9%), patients with more lines of therapy, and those with uncontrolled disease status at admission (60.9% vs. 42.6%) than the non-PC group. In the PC group, more patients were admitted to a hematology-oncology unit (72.4% vs. 61.6%) and for supportive care (31.4% vs. 19.3%) compared to the non-PC group.

Table 2 shows the differences in symptoms and laboratory findings at admission between the PC and non-PC groups. The PC group presented with more pain (48.7% vs. 28.1%), gastrointestinal symptoms (49.4% vs. 38.7%), and bleeding (13.5% vs. 6.3%) than the non-PC group. None of the blood test findings were associated with PC consultation, except for higher lactate dehydrogenase levels in the PC group than in the non-PC group.

Table 3 presents the factors associated with PC consultation using univariate and multivariate logistic regression analyses. In multivariate analysis, female sex (OR, 2.34; 95% CI, 1.48–3.69; $p < .001$), living in the metropolitan (OR, 1.74; 95% CI, 1.08–2.79; $p = .022$), uncontrolled disease status (OR, 2.36; 95% CI, 1.22–4.57; $p = .011$), admission to

TABLE 1 Baseline characteristics by PC consultation.

	Non-PC group $N = 331$	PC group $N = 156$	All $N = 487$	p value
Year of death, *n* (%)				.001
2018	108 (32.6)	24 (15.4)	132 (27.1)	
2019	70 (21.1)	36 (23.1)	106 (21.8)	
2020	66 (19.9)	43 (27.6)	109 (22.4)	
2021	87 (26.3)	53 (34.0)	140 (28.7)	
Age at admission, year, median (IQR)	63 (54–71)	64 (56–72)	63 (55–72)	.338
Age ≥ 65, *n* (%)	152 (45.9)	76 (48.7)	228 (46.8)	.631
Sex, male, *n* (%)	210 (63.4)	72 (46.2)	282 (57.9)	<.001
Marital status, married, *n* (%)	286 (86.4)	144 (92.3)	430 (88.3)	.082
Residence, *n* (%)				.015
Metropolitan	185 (55.9)	106 (67.9)	291 (59.8)	
Rural	146 (44.1)	50 (32.1)	196 (40.2)	
Religion, *n* (%)				.229
Yes	183 (55.3)	96 (61.5)	279 (57.3)	
None	148 (44.7)	60 (38.5)	208 (42.7)	
Education				.223
≤High school	170 (51.4)	68 (43.6)	238 (48.9)	
College	109 (32.9)	56 (35.9)	165 (33.9)	
Unknown	52 (15.7)	32 (20.5)	84 (17.2)	
Health insurance, *n* (%)				.499
National health insurance	300 (90.6)	145 (92.9)	445 (91.4)	
Medicaid/None	31 (9.4)	11 (7.1)	42 (8.6)	
CCI score, median (IQR)	1 (0–2)	1 (0–2)	1 (0–2)	.841
Diagnosis, *n* (%)				.051
Acute leukemia	124 (37.5)	58 (37.2)	182 (37.4)	
Myelodysplastic syndrome	44 (13.3)	9 (5.8)	53 (10.9)	
Lymphoma	103 (31.1)	65 (41.7)	168 (34.5)	
Multiple myeloma	44 (13.3)	18 (11.5)	62 (12.7)	
Others[a]	16 (4.8)	6 (3.8)	22 (4.5)	
Initial disease risk				.102
Favorable	24 (7.3)	5 (3.2)	29 (6.0)	
Intermediate	267 (80.7)	125 (80.1)	392 (80.5)	
Adverse	40 (12.1)	26 (16.7)	66 (13.6)	
Lines of therapy, median (IQR)	1 (1–3)	2 (1–3)	2 (1–3)	.007
History of HSCT, *n* (%)	103 (31.1)	38 (24.4)	141 (29.0)	.153
History of allogeneic HSCT, *n* (%)	75 (22.7)	23 (14.7)	98 (20.1)	.056
Disease status at admission, *n* (%)				<.001
Unevaluable	92 (27.8)	44 (28.2)	136 (27.9)	
Controlled	98 (29.6)	17 (10.9)	115 (23.6)	
Uncontrolled	141 (42.6)	95 (60.9)	236 (48.5)	
Route of admission, *n* (%)				.263
Via ED	193 (58.3)	100 (64.1)	293 (60.2)	
Regular hospitalization via OPD	138 (41.7)	56 (35.9)	194 (39.8)	
Admission department, *n* (%)				.026
Hemato-oncology	204 (61.6)	113 (72.4)	317 (65.1)	
Non-hemato-oncology	127 (38.4)	43 (27.6)	170 (34.9)	

TABLE 1 (Continued)

	Non-PC group $N = 331$	PC group $N = 156$	All $N = 487$	p value
Admission purpose, *n* (%)				.007
Disease evaluation	53 (16.0)	31 (19.9)	84 (17.2)	
Disease control (CTx, HSCT)	112 (33.8)	39 (25.0)	151 (31.0)	
Complication control	102 (30.8)	37 (23.7)	139 (28.5)	
Supportive care	64 (19.3)	49 (31.4)	113 (23.2)	
Time between first diagnosis and admission, month, median (IQR)	12 (4–29)	13 (5–35)	13 (4–31)	.335
Over 1 year, *n* (%)	169 (51.1%)	84 (53.8%)	253 (52.0%)	.633
Length of hospital stay, day, median (IQR)	24 (9–52)	25 (14–51)	24 (12–51)	.211

Abbreviations: CCI, Charlson comorbidity index; CTx, chemotherapy; ED; emergency department; HSCT, hematopoietic stem cell transplantation; IQR, interquartile range; OPD, outpatient department; PC, palliative care.
[a]The "Others" category consists of 22 patients, including 3 with chronic myeloid leukemia, 7 with myelofibrosis, 2 with polycythemia vera, 2 with essential thrombocythemia, 5 with chronic myelomonocytic leukemia, and 3 with histiocytic sarcoma.

TABLE 2 Symptoms and laboratory findings at admission by PC consultation.

	Non-PC group $N = 331$	PC group $N = 156$	All $N = 487$	p value
Symptoms, *n* (%)				
Pain	93 (28.1)	76 (48.7)	169 (34.7)	<.001
Fatigue	192 (58.0)	96 (61.5)	288 (59.1)	.521
Dyspnea	99 (29.9)	38 (24.4)	137 (28.1)	.245
Anorexia/nervosa/vomiting	128 (38.7)	77 (49.4)	205 (42.1)	.033
Drowsiness	62 (18.7)	20 (12.8)	82 (16.8)	.134
Sleep disturbance	35 (10.6)	21 (13.5)	56 (11.5)	.435
Depression	9 (2.7)	9 (5.8)	18 (3.7)	.159
Anxiety	30 (9.1)	14 (9.0)	44 (9.0)	1.000
Fever	135 (40.8)	52 (33.3)	187 (38.4)	.139
Bleeding	21 (6.3)	21 (13.5)	42 (8.6)	.015
CBC				
Hb <8, *n* (%)	100 (30.2)	49 (31.4%)	149 (30.6%)	.871
ANC <1000, *n* (%)	87 (26.3)	55 (35.3%)	142 (29.2%)	.054
PLT <20 K, *n* (%)	73 (22.1)	26 (16.7%)	99 (20.3%)	.208
Albumin <3.0 g/dL, *n* (%)	124 (37.5)	65 (41.7)	189 (38.8)	.430
LDH > ULN, *n* (%)	236 (71.3)	129 (82.7)	365 (74.9)	.009
Total bilirubin >2.0 mg/dL, *n* (%)	55 (16.6)	28 (17.9)	83 (17.0)	.814
AST >3 × ULN, *n* (%)	43 (13.0)	24 (15.4)	67 (13.8)	.566
ALT >3 × ULN, *n* (%)	41 (12.4)	13 (8.3)	54 (11.1)	.240
eGFR <60 mL/min/1.73 m^2, *n* (%)	137 (41.4)	59 (37.8)	196 (40.2)	.515
CRP >10, *n* (%)	132 (39.9)	62 (39.7)	194 (39.8)	1.000
PT INR >1.5, *n* (%)	52 (15.7)	20 (12.8)	72 (14.8)	.483

Abbreviations: ALT, alanine aminotransferase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; CBC, complete blood count; CRP, c-reactive protein; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; LDH, lactic acid dehydrogenase; PLT, platelet; PT, prothrombin time; ULN, upper limit of normal.

the department of hematology-oncology (OR, 1.94; 95% CI, 1.13–3.31; $p = .016$), admission for supportive care (OR, 2.46; 95% CI, 1.26–4.80; $p = .008$), pain at admission (OR, 1.98; 95% CI, 1.22–3.20; $p = .005$), bleeding at admission (OR, 2.19; 95% CI, 1.02–4.73; $p = .045$), and absolute neutrophil count <1000/μL (OR, 2.42; 95% CI, 1.44–4.08; $p = .001$) were associated with PC consultation. Compared with patients with MDS, patients with acute leukemia (OR, 2.63; 95% CI, 1.06–6.55; $p = .038$) and lymphoma (OR, 3.25; 95% CI, 1.22–8.62; $p = .018$) were more likely to consult to the inpatient PC team. Moreover, year of death remained an independent factor associated with PC

TABLE 3 Univariate and multivariate analysis of predictive factors associated with PC consultation.

	Univariable		Multivariable	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Year of death				
2018	1.00		1.000	
2019	2.31 (1.27–4.21)	.006	3.06 (1.53–6.10)	.002
2020	2.93 (1.63–5.27)	<.001	3.41 (1.73–6.74)	<.001
2021	2.74 (1.57–4.79)	<.001	3.52 (1.83–6.76)	<.001
Age at admission ≥65	1.12 (0.76–1.64)	.564		
Sex				
Male	1.00		1.00	
Female	2.02 (1.38–2.98)	<.001	2.34 (1.48–3.69)	<.001
Marital status				
Single	1.00			
Married	1.89 (0.97–3.68)	.062		
Residence				
Rural	1.00		1.00	
Metropolitan	1.67 (1.12–2.50)	.012	1.74 (1.08–2.79)	.022
Religion				
No	1.00			
Yes	1.29 (0.88–1.91)	.194		
Education				
High school	1.00			
College	1.28 (0.84–1.97)	.251		
Unknown	1.54 (0.91–2.59)	.106		
Health insurance				
Medicaid/none	1.00			
National health insurance	1.36 (0.67–2.79)	.398		
CCI score	1.01 (0.90–1.13)	.9		
Diagnosis				
Acute leukemia	2.29 (1.05–5.00)	.038	2.63 (1.06–6.55)	.038
Myelodysplastic syndrome	1.00		1.00	
Lymphoma	3.09 (1.41–6.74)	.005	3.25 (1.22–8.62)	.018
Multiple myeloma	2.00 (0.81–4.93)	.132	1.66 (0.53–5.20)	.387
Other	1.83 (0.56–5.97)	.314	1.87 (0.49–7.19)	.361
Initial disease risk				
Favorable	1.00			
Intermediate	2.25 (0.84–6.03)	.108		
Adverse	3.12 (1.06–9.21)	.039		
Lines of therapy	1.16 (1.05–1.29)	.004		
Previous SCT	0.71 (0.46–1.10)	.126		
Previous allogeneic SCT	0.59 (0.35–0.98)	.044		
Disease status at admission				
Controlled	1.00		1.00	
Uncontrolled	3.44 (1.97–6.00)	<.001	2.36 (1.22–4.57)	.011
Route of admission				
Regular hospitalization via OPD	1.00			
Via ER	1.28 (0.86–1.89)	.223		

TABLE 3 (Continued)

	Univariable		Multivariable	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Admission department				
Non-hemato-oncology	1.00		1.00	
Hemato-oncology	1.64 (1.08–2.48)	.020	1.94 (1.13–3.31)	.016
Admission purpose				
Disease evaluation	1.68 (0.95–2.98)	.077	1.61 (0.81–3.20)	.178
Disease control	1.00		1.00	
Complication control	1.04 (0.62–1.76)	.878	1.46 (0.74–2.90)	.280
Supportive care	2.20 (1.31–3.70)	.003	2.46 (1.26–4.80)	.008
Time between first diagnosis and admission >1 year	1.12 (0.76–1.64)	.566		
Symptoms				
Pain	2.43 (1.64–3.61)	<.001	1.98 (1.22–3.20)	.005
Fatigue	1.16 (0.78–1.71)	.460		
Dyspnea	0.75 (0.49–1.17)	.204		
Anorexia/nausea/vomiting	1.55 (1.05–2.27)	.026		
Drowsiness	0.64 (0.37–1.10)	.106		
Sleep disturbance	1.32 (0.74–2.35)	.352		
Depression	2.19 (0.85–5.63)	.104		
Anxiety	0.99 (0.51–1.92)	.975		
Fever	0.73 (0.49–1.08)	.115		
Bleeding	2.30 (1.21–4.35)	.011	2.19 (1.02–4.73)	.045
CBC				
Hb <8	1.06 (0.70–1.60)	.789		
ANC <1000	1.53 (1.01–2.30)	.043	2.42 (1.44–4.08)	.001
PLT <20 K	0.71 (0.43–1.16)	.169		
Albumin <3.0 g/dL	1.20 (0.80–1.81)	.380		
LDH > ULN	2.18 (1.39–3.41)	.001		
Total bilirubin >2.0 mg/dL	1.10 (0.67–1.81)	.715		
AST >3 × ULN	1.22 (0.71–2.09)	.475		
ALT >3 × ULN	0.64 (0.33–1.24)	.187		
eGFR <60 mL/min/1.73 m^2	0.86 (0.58–1.27)	.454		
CRP >10	0.99 (0.67–1.47)	.977		
PT INR >1.5	0.79 (0.45–1.37)	.403		

Abbreviations: ALT, alanine aminotransferase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; CBC, complete blood count; CCI, Charlson comorbidity index; CRP, c-reactive protein; eGFR, estimated glomerular filtration rate; ER, emergency room; Hb, hemoglobin; HSCT, hematopoietic stem cell transplantation; LDH, lactic acid dehydrogenase; OPD, outpatient department; OR, odds ratio; PLT, platelet; PT, prothrombin time; ULN, upper limit of normal.

consultation in the multivariate model (2019 [OR, 3.06; 95% CI, 1.53–6.10; $p = .002$], 2020 [OR, 3.41; 95% CI, 1.73–6.74; $p < .001$], 2021 [OR, 3.52; 95% CI, 1.83–6.76; $p < .001$]).

3.2 | Differences in quality of end-of-life care indicators between the PC and non-PC groups

The differences in the quality of EOL care indicators between the PC and non-PC groups are presented in Table 4. The proportion of patients with advance statement (34% vs. 18.4%, $p < .001$) and LST documentation (96.8% vs. 86.7%, $p = .001$) was higher in the PC group than in the non-PC group. Notably, the proportion of LST documentation by patients was higher in the PC group than in the non-PC group (34.4% vs. 19.9%, $p = .001$), with a longer time from LST documentation to death in the PC group than in the non-PC group (median [IQR], 4 [2–9] vs. 1 [0–3] day, $p < .001$).

The PC group was significantly less frequently admitted to the ICU (25% vs. 56.8%, $p < .001$) and received less CPR (3.8% vs. 22.4%, $p < .001$), mechanical ventilation (18.6% vs. 53.2%, $p < .001$), and

TABLE 4 Quality of End-of-life care indicators by PC consultation.

	Non-PC group $N = 331$	PC group $N = 156$	All $N = 487$	p value
Advance statement, *n* (%)	61 (18.4)	53 (34.0)	114 (23.4)	<.001
Time between advance statement and death, median, days (IQR)	10 (1–37)	9 (3–23)	9 (2–30)	.798
LST implementation documentation, n (%)	287 (86.7)	151 (96.8)	438 (89.9)	.001
Patient-determined	57 (19.9)	52 (34.4)	109 (24.9)	.001
Family-determined	230 (80.1)	99 (65.6)	329 (75.1)	
Time between LST implementation documentation and death, median, days (IQR)	1 (0–3)	4 (2–9)	1 (0–5)	<.001
Aggressive care within last 30 days, *n* (%)				
ED visit	145 (43.8)	64 (41.0)	209 (42.9)	.631
ICU care	188 (56.8)	39 (25.0)	227 (46.6)	<.001
CPR	74 (22.4)	6 (3.8)	80 (16.4)	<.001
Mechanical ventilator	176 (53.2)	29 (18.6)	205 (42.1)	<.001
Hemodialysis	131 (39.6)	23 (14.7)	154 (31.6)	<.001
Chemotherapy, *n* (%)				
Within last 30 days	179 (54.1)	85 (54.5)	264 (54.2)	1.000
Within last 14 days	117 (35.3)	49 (31.4)	166 (34.1)	.452
Within last 7 days	73 (22.1)	22 (14.1)	95 (19.5)	.052
Within last 3 days	42 (12.7)	10 (6.4)	52 (10.7)	.053
Active procedures at imminently dying state (within 3 days before death), *n* (%)				
Blood test	327 (98.8)	127 (81.4)	454 (93.2)	<.001
Imaging study	306 (92.4)	98 (62.8)	404 (83.0)	<.001
Levin tube insertion	230 (69.5)	53 (34.0)	283 (58.1)	<.001
Inotropics use	265 (80.1)	91 (58.3)	356 (73.1)	<.001
Inotropics withdrawal	23 (8.7)	20 (22.0)	43 (12.1)	.002
Intravenous antibiotics	311 (94.0)	139 (89.1)	450 (92.4)	.088
High-flow nasal cannula	103 (31.1)	40 (25.6)	143 (29.4)	.258
Blood transfusion				
Within last 7 days, *n* (%)				
RBC	265 (80.1)	114 (73.1)	379 (77.8)	.107
PLT	273 (82.5)	124 (79.5)	397 (81.5)	.504
FFP	119 (36.0)	30 (19.2)	149 (30.6)	<.001
Within last 3 days, *n* (%)				
RBC	186 (56.2)	48 (30.8)	234 (48.0)	<.001
PLT	228 (68.9)	80 (51.3)	308 (63.2)	<.001
FFP	95 (28.7)	14 (9.0)	109 (22.4)	<.001
Comfort care within last 3 days of life, *n* (%)				
Opioid administration	221 (66.8)	130 (83.3)	351 (72.1)	<.001
Antipsychotics administration	96 (29.0)	41 (26.3)	137 (28.1)	.606
Place of death, *n* (%)				<.001
ICU	168 (50.8)	17 (10.9)	185 (38.0)	
General ward	163 (49.2)	139 (89.1)	302 (62.0)	

Abbreviations: CPR, cardiopulmonary resuscitation; ED, emergency department; FFP, fresh frozen plasma; ICU, intensive care unit; IQR, interquartile range; LST, life-sustaining treatment; PC, palliative care; PLT, platelet; RBC, red blood cell.

renal replacement therapy (14.7% vs. 39.6%, $p < .001$) than the non-PC group (Figure 1). Moreover, 10.9% of the PC group died in the ICU compared with 50.8% of the non-PC group ($p < .001$). The rates of death in the ICU and ICU admission within 30 days of death were lower in the PC group among patients with acute leukemia and lymphoma (Figure S2).

The PC group received significantly fewer blood tests (81.4% vs. 98.8%, $p < .001$), imaging studies (62.8% vs. 92.4%, $p < .001$),

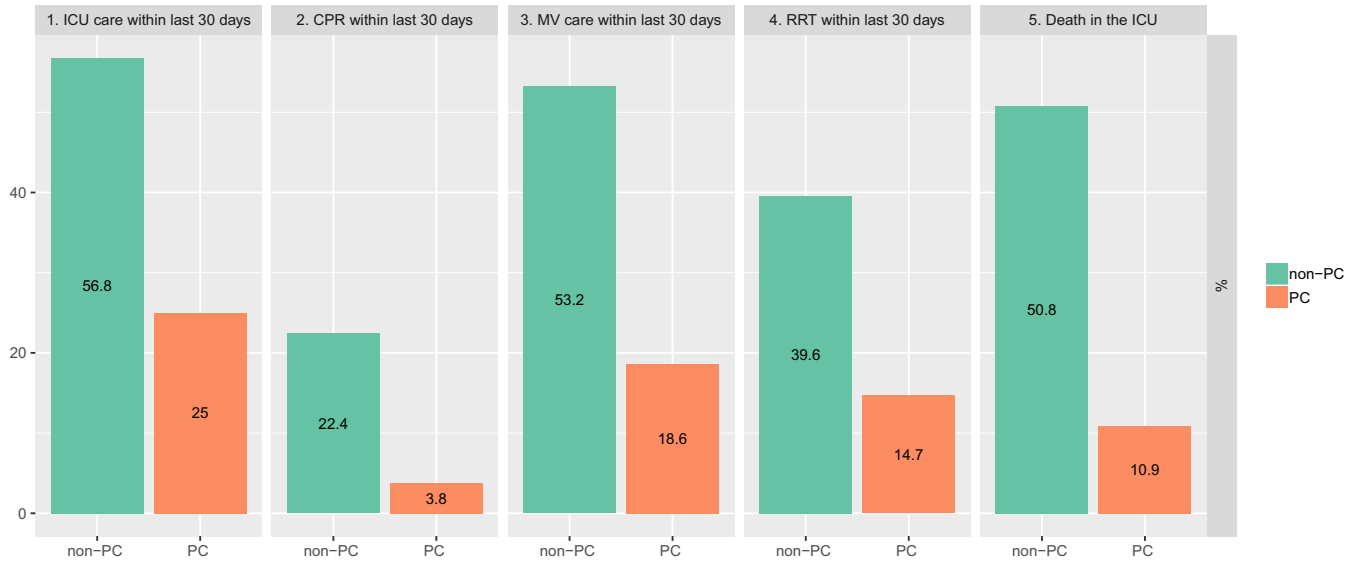

FIGURE 1 Major Differences in End-of-Life care Indicators by PC consultation. The proportion of patients receiving the following end-of-life care indicators based on PC referrals: ICU care, CPR, MV care, and RRT within the last 30 days of life, and death in the ICU.

Levin tube insertion (34% vs. 69.5%, $p < .001$), and inotropic use (58.3% vs. 80.1%, $p < .001$) than the non-PC group. However, inotropic withdrawal was more frequent in the PC group than in the non-PC group (22% vs. 8.7%, $p < .001$). Moreover, the PC group received more opioids within the last 3 days of life (83.3% vs. 66.8%, $p < .001$) than the non-PC group.

The PC group had lower transfusion rates of red blood cell (RBC) (30.8% vs. 56.2%, $p < .001$), platelet (PLT) (51.3% vs. 68.9%, $p < .001$), and fresh frozen plasma (FFP) (9% vs. 28.7%, $p < .001$) during the last 3 days of life than the non-PC group. Moreover, during the last 3 days of life, the PC group had lower daily transfusion amounts of RBC, PLT, and FFP than the non-PC group (Figure S3). This difference was also consistent with the total transfusion volume during the last 7 days of life.

Table 5 presents the factors associated with EOL care indicators through multivariate logistic regression analysis. PC consultation was associated with 46% decrease in the use of chemotherapy in the last 14 days of life (adjusted OR, 0.54; 95% CI, 0.34–0.86; $p = .009$), 73% decrease in the probability of ICU admission in the last 30 days of life (adjusted OR, 0.27; 95% CI, 0.17–0.42; $p < .001$), and 89% decrease in the probability of death in the ICU (adjusted OR, 0.11; 95% CI, 0.06–0.20; $p < .001$). Patients with acute leukemia, lymphoma, and MM received more chemotherapy in the last 2 weeks of life than those with MDS. Older age of ≥65 years was associated with lower odds of ICU admission or death in the ICU. Moreover, low initial disease risk was associated with higher odds of ICU admission or death in the ICU.

4 | DISCUSSION

We determined that 32% of decedents with HMs were referred for PC consultation, indicating that PC referrals remain rarer in HMs compared with solid cancers, with >40% of decedents with solid cancers being referred for PC consultation at the same institution, despite the growing number of PC referrals over time. These results are consistent with those of Western studies.[22] Patients referred to tertiary PC were more likely to complete advance statements and LST documentation and receive less aggressive care at EOL than those not referred. Patients with HM referred to tertiary PC received less chemotherapy within 14 days of death, less LST in the last month of life, and greater emphasis on comfort care as opposed to active care in an imminently dying state than those not referred. This indicates the necessity for further expansion of PCs in HM, along with the accompanying benefits. Notably, we examined detailed healthcare utilization at the individual level for a substantial number of patients.

To develop future strategies for PC integration, identifying factors related to PC consultation referral is necessary. Multivariate logistic analysis revealed that sex and residency influenced the decision to consult for PC. Compared to their counterparts, we found that female and metropolitan residents were more likely to consult the PC team, which is consistent with the results of previous studies.[23,24] Possible explanations include different medical conditions and preferences for treatment and care delivery based on sex.[25] Residents in metropolitan areas may also have greater access to PC than those in rural areas; therefore, they may be less resistant to PC. Notably, patients with MDS tended to be the least referred to the PC team. This trend has been reported in previous studies,[26] and possibly, the more unpredictable and heterogeneous nature of MDS among HMs is one of the reasons for the decrease in referrals to the PC team.[27] Furthermore, the tendency of patients with MDS to die from complications, rather than disease progression, may also contribute to the low inclination toward PC referrals. HM physicians can refer patients more often than non-HM physicians as they have sufficient comprehension of the complex prognosis of HM.[28] Given the effects of disease status at admission and the purpose of admission on PC referrals, patients with poor

TABLE 5 Multivariate analysis of predictive factors associated with end-of-life care indicators.

	CTx in the last 14 days of life		ICU care in the last 30 days of life		Death in ICU	
	aOR (95% CI)	*p* value	aOR (95% CI)	*p* value	aOR (95% CI)	*p* value
PC consultation, receipt	0.54 (0.34–0.86)	.009	0.27 (0.17–0.42)	<.001	0.11 (0.06–0.20)	<.001
Age ≥65	0.72 (0.47–1.10)	.127	0.63 (0.41–0.96)	.030	0.58 (0.37–0.91)	.017
Male sex	0.85 (0.56–1.30)	.453	0.77 (0.50–1.16)	.209	0.66 (0.42–1.03)	.067
Marital status, married	1.01 (0.52–1.96)	.972	1.10 (0.58–2.08)	.777	1.15 (0.59–2.24)	.679
Residence, metropolitan	1.14 (0.75–1.73)	.555	1.20 (0.80–1.80)	.387	1.48 (0.96–2.29)	.075
Religion, religious	0.55 (0.36–0.84)	.005	0.73 (0.48–1.09)	.119	0.78 (0.51–1.20)	.258
Health insurance, nation	2.11 (0.93–4.80)	.074	0.77 (0.38–1.58)	.477	0.57 (0.27–1.19)	.134
Diagnosis						
Myelodysplastic syndrome	Ref	Ref	Ref	Ref	Ref	Ref
Acute leukemia	8.98 (3.29–24.48)	<.001	1.06 (0.55–2.05)	.869	0.81 (0.41–1.61)	.555
Lymphoma	5.81 (2.13–15.90)	.001	1.15 (0.59–2.26)	.682	0.98 (0.49–1.98)	.961
Multiple myeloma	4.54 (1.50–13.78)	.008	1.25 (0.56–2.77)	.592	0.82 (0.36–1.89)	.645
Other	3.80 (0.97–14.94)	.056	1.23 (0.40–3.75)	.721	0.85 (0.27–2.73)	.791
Initial disease risk, low	0.70 (0.28–1.72)	.435	3.80 (1.45–9.91)	.006	4.89 (1.84–12.98)	.001
Disease status at admission, uncontrolled	3.63 (2.05–6.43)	<.001	0.75 (0.46–1.22)	.242	0.78 (0.47–1.27)	.314
Department, hemato-oncology	1.50 (0.96–2.34)	.075	0.35 (0.23–0.54)	<.001	0.48 (0.31–0.75)	.001
Intercept	−3.2856		0.5368		0.7689	
Hosme-Lemeshow test	0.3808		0.8691		0.3068	

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; CTx, chemotherapy; ICU, intensive care unit; PC, palliative care.

health receive more referrals. Notably, uncontrolled disease status showed a strong positive correlation with PC referral. It is common in real-world practice for PC referral to be led by the attending physician based on the disease status, which could be a contributing factor for delayed PC referral in patients with HMs. For timely PC integration, PC referral should be conducted according to the patient's needs, and there is a need to improve this aspect through routine screening for patients' PC needs. Consistent with previous findings, pain, hemorrhage, and neutropenia are the most common PC-related supportive care needs.[29,30] Among hospitalized patients who have died, inpatient PC consultations occurred in individuals with a greater likelihood of dying. This may be related to the fact that patients and HM physicians view PC and EOL care as equivalent.[28] Patients with HM who died in the hospital and who had potential EOL care needs were the primary participants of this study. Therefore, the fact that they were not referred for PC consultation demonstrates that it is necessary to promote and activate tertiary PC referral earlier.

Several barriers to PC referral need to be considered in the context of Korea, aside from the prognostic uncertainty in HMs. First, since laws regarding hospice PC and EOL decision-making have recently been enacted, awareness among patients and physicians is not widespread. Several studies conducted in Korea before 2018 found that some patients and physicians perceived PC referrals as unnecessary.[31,32] Our data, showing an increase in PC referrals from 2018 to 2021, suggest a growing awareness of PC. Another potential barrier is insufficient financial support. In Korea, a physician cares for a relatively large number of patients, and it is difficult to allocate sufficient time for ACP discussions.[33] Additional financial burden for patients hampers the PC referral.[32] Therefore, it is necessary to improve the awareness of both patients and physicians along with advancements in the system and financial support.

We found that patients who received PC consultations had a positive relationship with the completion of the AD statement and LST documentation. ACP explores patients' personal values and supports them in understanding and sharing their values and preferences for situations they cannot decide by themselves. Completing the AD statement and LST documentation helps clinicians provide goal-aligned care for patients.[34] Patients with HM want an honest prognosis and communication from medical professionals,[35] but ACP in this population is difficult owing to challenges in determining the correct timing, barriers to clinician-patient communication, and challenges in the documentation.[36] PC consultation can facilitate relevant discussions about EOL care among patients, family members, and primary physicians who may feel uncomfortable initiating these discussions.[37] This is valuable because, regardless of what care the patient receives afterward, they likely receive the most appropriate EOL care aligned with their values and preferences.

Our study results showing that PC consultation reduces the receipt of CPR, mechanical ventilation, and hemodialysis are consistent with previous study results.[38] Moreover, concurrent with previous studies,[38,39] the rate of ICU admission in the last month and the mortality rate in the ICU among patients receiving tertiary PC decreased after adjusting for multiple factors. However, the ICU admission rate was 25% in our study, substantially higher than the rate of 11.3% in PC-referred patients with solid tumors.[40]

Cultural differences from Western countries and the relatively lower cost burden on individual patients for ICU care in Korea owing to wide insurance coverage may be the reasons for high ICU admission rates.[41] In addition to PC consultation, initial disease risk was also significantly associated with ICU care in the last 30 days of life and death in the ICU. Notably, having a low initial disease risk was linked to a higher odds ratio for both ICU care and death in the ICU. Patients with low initial disease risk may hold a strong belief in a favorable prognosis, leading them to hope for recovery through ICU care, even if they later receive PC consultations. The category of diagnosis or the status of disease control were not relevant factors. The lack of disease subtype-specific or disease control status-specific differences in ICU-related EOL outcomes suggests that a decision toward ICU use in patients with HM may partly be made based on incorrect expectations or information about the prognosis of HM, rather than appropriate knowledge about the inherent characteristics of each subtype of HM or responsiveness of the current treatment.[42] Our results indirectly suggest that in-depth discussion about prognostic expectations between patients and physicians and active collaboration of both specialist PC and disease-specific hemato-oncologists can improve the EOL care in patients with HMs.

In this study, PC reduced chemotherapy within 2 weeks of death. Overall, 34.1% of the patients received chemotherapy in the last 2 weeks of life, which is higher than the 17.4–28% reported in the United States and Europe.[2,26] Owing to the lack of distinct boundaries between curative care and PC, there is a debate over chemotherapy in patients with HM during the EOL period. Patients with refractory HM often have only a few weeks to live, suggesting that palliation is more crucial than chemotherapy.[43] However, some patients may benefit from chemotherapy.[44] Amidst the controversy surrounding the role of chemotherapy, a patient-centered, goal-aligned approach is essential, and PC integration appears to facilitate this.

For disease-specific reasons, patients with HM may need relatively aggressive treatment toward EOL; nonetheless, treatment during the impending death phase does not differ markedly among patients regardless of the disease characteristics. What matters is how the balance between comfort care and potentially aggressive active care influences the experience of dying. PC consultation also reduced several other types of active care in EOL. Given that imaging and blood tests are unlikely to benefit terminally ill patients in EOL care relative to their costs, these costs can be reduced through PC referrals.[45,46] There was a significant difference between the PC and non-PC groups in terms of both the frequency and amount of blood transfusions received. Transfusions are frequently performed in patients with HM[47]; however, transfusions at the EOL are an issue. Identifying transfusions as aggressive care is problematic because blood transfusions serve as a vital service for improving the quality of life at EOL for some patients with HMs. However, since transfusions are generally not administered concurrently in hospice settings, there are instances where unnecessary transfusions cause delays in referral to hospice care.[3] In our study, PC consultation reduced the number of RBC and PLT transfusions at EOL. Considering that the PC group had more bleeding symptoms at admission and no significant difference in anemia or thrombocytopenia, it is likely that it is common for patients with HM to receive transfusion based on symptoms and for more optimal chemotherapy or based on blood cutoff levels. There is also a misconception that stopping transfusion will hasten death.[48] As there is no recommended cutoff level for patients with HM, and symptom control is the most important indication for transfusion in patients in PC, the decision to transfuse should be based on patients' needs in terms of comfort.[49,50]

This study has some limitations. First, this was a single-center, retrospective study conducted in a tertiary hospital, which may be subject to bias and may not be generalizable to patients with HM in all settings. Furthermore, since the PC doctor in our study specializes in hemato-oncology, there might be an increased likelihood of increased PC referrals. Second, because this was an electronic medical record-based study, it was not possible to examine the reasons for consultation and patient- or caregiver-reported outcomes together.

Despite these limitations, our study is the first to address PC consultation and EOL care for patients with HMs in Korea, where aggressive EOL care is more common than in the West. Our study reveals the benefits of merging PC teams in EOL care. We analyzed the effect of prognostic disease factors, such as current disease status or initial disease risk, on PC referral and EOL care indicators. These findings provide valuable insights into the role of tertiary PC and suggest the way forward for EOL care for patients with HMs. In conclusion, EOL care for patients with HM requires patient-centered and value-driven decision-making through the integration of PC teams.

AUTHOR CONTRIBUTIONS

Dong Hyun Kim: collected data, organized data, analyzed data, wrote the original draft, reviewed, and edited the final draft. **Shin Hye Yoo** and **Dong-Yeop Shin**: concept and design, supervision, interpretation of data, reviewed and edited final draft. All authors reviewed and approved the final manuscript for submission.

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CONFLICT OF INTEREST STATEMENT

None of the authors have any conflicts of interest to disclose.

DATA AVAILABILITY STATEMENT

The datasets generated during the current study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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