

# Frailty Prevalence and Characteristics in Older Adults with Hematologic Cancer: a Descriptive Study

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## ABSTRACT

**Objective:** This study investigated the prevalence of frailty in older patients with hematologic cancer and assessed the association between older patients' characteristics and frailty. **Methods:** This descriptive study enrolled 90 older patients undergoing treatment for hematological malignancies at an oncology hospital. Frailty was assessed with the Edmonton Frailty Scale as not frail (0–4), apparently vulnerable (5–6), mildly frail (7–8), moderately frail (9–10), and severely frail (11–17). The association of frailty and older patient characteristics and diagnosis was assessed by logistic regression. **Results:** The prevalence of frailty (mild, moderately, and severely) was 42.2%, and “apparently vulnerable” frailty was 60%. The mean scale score was  $5.59 \pm 3.13$ . Frailty was more prevalent in patients who were  $\geq 75$  years of age, had  $\geq 4$  children, were diagnosed with leukemia, and were diagnosed

for  $\geq 2$  years. Gender, diagnosis, and employment were factors associated with the presence of frailty. Female gender and lack of employment were factors associated with a high risk of frailty. A diagnosis of multiple myeloma was associated with a low risk of frailty. **Conclusions:** The prevalence of frailty was high in older patients. Female and unemployed patients were at high risk for frailty. Frailty characteristics of older patients with hematologic cancer highlighted the need for comprehensive geriatric assessment and frailty screening, provided prevalence and characteristics of frailty in this group of patients during treatment, and highlighted the need for holistic care approach.

**Key words:** Frailty, geriatric oncology, hematology, older patients, oncology

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## Introduction

Global aging, increase in life expectancy and cancer incidence highlight the urgent need to develop healthcare policies for older patients.<sup>[1]</sup> Cancer incidence and cancer mortality in patients  $\geq 65$  years of age are 11 times higher and 15 times higher, respectively, compared to younger patients.<sup>[1,2]</sup> Leukemia, lymphoma, and myeloma together account for about 7% of newly diagnosed cancers. The incidence of Hodgkin lymphoma is 19 times higher at 60–64 years of age and 50 times higher at 80–84 years of age than at 20–24 years of age.<sup>[3]</sup> From these statistical changes emerges the need for a better understanding of how health status affects cancer treatment, survival, morbidity, functionality, and quality of life of elderly.<sup>[4–6]</sup>

Frailty is one of the functionality and quality of life issues among older patients. It has been defined as a syndrome associated with an onset of functional decline in older people.<sup>[7,8]</sup> Frailty, conceptually defined as a clinically recognizable state of older adults with increased vulnerability, results from an age-associated decline in physiologic reserve and function across multiple organ systems such that the ability to cope with every day or acute stressors is compromised.<sup>[9–11]</sup> Frailty with aging presents as the loss of muscle mass and bone density, diminished ability for self-care, poor nutritional status and food intake, sensory and cognitive deterioration, and fatigue.<sup>[3,12]</sup> Frailty increases with age, and older patients with cancer are more likely to become frail compared with those without cancer.<sup>[13]</sup> According to Handford *et al.* (2015), more than half of the older patients with cancer have prefrailty or frailty and these patients are at increased risk for poor chemotherapy tolerance, postoperative complications, and mortality.<sup>[14]</sup> Studies revealed that there was a statistically significant association between frailty and mortality at 5, 7, and 10 years' follow-up.<sup>[15,16]</sup> The health consequences of frailty require modification of cancer management that can worsen the prognosis. By itself, cancer treatment adds to frailty.<sup>[17,18]</sup> The weighted mean prevalence of frailty was reported as 9.9% (range 4%–59%) for older patients without cancer whereas the median estimates of frailty and prefrailty in older cancer patients were reported as 42% and 43%, respectively.<sup>[14]</sup>

Many of the previous studies regarding frailty focused on assessment, diagnostic accuracy, and outcomes in patients without cancer.<sup>[14,19]</sup> Cancer frailty studies that sampled older patients focused on breast, colorectal, and lung malignancies.<sup>[20]</sup> Among these clinical studies of hematological malignancies, only 5% included older and frail patients and 69% excluded older patients.<sup>[21]</sup> The limited representation of older adults in research, the scarcity of studies that examine the effect of frailty on hematologic

malignancies, and the need for the development of a care model for geriatric hematology patients require more studies to define frailty.<sup>[12,14,22]</sup>

This study believe to enrich geriatric oncology literature about routine frailty screening, outcome prediction, and functional status of older adults with hematologic cancer. In addition, data will support the need to develop new strategies and treatment modalities for older adults due to the sparse number of studies regarding this topic.<sup>[23,24]</sup>

This study aimed to determine the prevalence of frailty and level of frailty in older patients with hematological cancer and to examine the association between frailty and patient characteristics.

## Methods

### Setting and participants

The study aimed to determine the prevalence of frailty, level of frailty in older patients with hematological cancer, and the association between frailty and patient sociodemographic and clinical characteristics. The study included both in- and out-patients who were treated at a state-owned oncology hospital. Eligible patients were 65 years of age and older, diagnosed with hematological cancer and able to communicate (e.g., did not have a cognitive disease such as advanced Alzheimer's disease).

A sample size of 90 patients was determined to have a 90% power, 0.6 effect size, and 0.05 alpha. Of 126 patients screened for eligibility between May 2016 and February 2017, 120 were eligible, 6 were diagnosed with dementia, 16 refused to participate because of self-reported tiredness, and 14 were not able to meet with the investigator. Approximately 66.7% of patients were from the outpatient unit, and 33.3% of patients were from the inpatient unit.

### Ethical approval

The University Ethics Committee approved the study (#GO 15/488-27). Each participant signed a written informed consent form before participating.

### Data collection procedure and tools

Before data collection, patients were informed of the study and were asked to provide consent. After providing consent to participate, they were asked about the best time to answer questions, which was either immediately or at a scheduled time. Outpatients were interviewed after the treating physician's visit; inpatients were interviewed during the morning.

Data were collected using the patient data sheet and Frailty Scale. The data sheet collected information on age, education, employment/occupation, economic status, marital status, number of household members,

diagnosis, duration of diagnosis, treatment plan, and comorbidities. Frailty prevalence and frailty levels were scored on the Edmonton Frailty Scale that was developed by Rolfson *et al.* (2006).<sup>[25]</sup> A Turkish version of the scale that was published by Aygor and Fadiloglu in 2013 has a Cronbach alpha coefficient of 0.75.<sup>[26]</sup> The scale consists of 11 questions under 9 items: cognitive status, general health status, functional independence, social support, drug use, nutrition, mood, continence, and functional performance. General health status and extent of drug use were assessed by two questions; the other variables were assessed by one question. A clock-drawing test was used to assess cognitive status, and Timed Up and Go test were used for functional performance. Each question was scored from 0 to 2, and the resulting scores were summed and classified as not frail (0–4), apparently vulnerable (5–6), mildly frail (7–8), moderately frail (9–10), and severely frail (11–17).<sup>[25,26]</sup>

### Statistical analysis

Data analysis was performed with the Statistical Package for Social Sciences (SPSS Version 23, IBM Corp., Armonk, NY, USA). Descriptive statistics were reported for categorical and continuous variables. The assumption of normality was not verified by the Kolmogorov–Smirnov test (0.128,  $P = 0.001$ ). The Mann–Whitney-U test, Kruskal–Wallis test, and Chi-square test were used for data analysis. The level of significance was taken as  $P < 0.05$ .

## Results

The majority of patients were men (58.9%), 65–74 years of age (71.1%), married (78.9%), living with a caregiver (88.9%: 73.3% spouse, 15.6% children/friends), had >4 children (54.5%), currently not employed (96.7%: 56.7% retired, 40.0% homemaker), and had expenses equal to income (68%). About 85.0% of the patients had been diagnosed >2 years, 25.5% ( $n = 23$ ) of the patients were diagnosed with lymphoma (non-Hodgkin [ $n = 20$ ], diffuse B cell [ $n = 3$ ]), 23.3% of the patients were diagnosed with multiple myeloma, and 18.9% ( $n = 17$ ) of the patients were diagnosed with leukemia (acute myeloid [ $n = 13$ ], chronic lymphocytic [ $n = 3$ ], acute lymphoblastic [ $n = 1$ ]). During the study, 62.9% of the patients received chemotherapy, 35.5% of the patients received supportive follow-up care, and 20.2% of the patients received blood substitute transfusions.

The frailty levels were distributed as 40.0% not frail, 17.8% apparently vulnerable, 20.0% mildly frail, 16.7% moderately frail, and 5.5% severely frail. The overall prevalence of frailty was 60.0% of which 33.3% of patients were mildly frail, 29.6% of patients were apparently vulnerable, 27.8% of patients were moderately frail, and 9.3% of patients were severely frail [Table 1]. Frailty was more prevalent

in patients who were women  $\geq 75$  years of age and older, illiterate, single, had less income than expenses, had been diagnosed  $\geq 2$  years, and had one comorbid disease. The prevalence was significantly higher in patients with four or more children, those living with children/friends, and those diagnosed with leukemia [ $P < 0.005$ , Table 2].

A regression model was developed to assess the association between frailty and diagnosis and confounding demographic and clinical variables. After adjusting for all confounding variables, an association was found between frailty and diagnosis (odds ratio [OR] = 0.016), frailty and gender (OR = 162.11), and frailty and employment (OR = 895.61). Female patients were 162 times more likely to be frail, and those not employed were 895 times more likely to be frail. Patients with multiple myeloma were 0.016 times less likely to be frail than those with lymphoma and leukemia [Table 3].

## Discussion

Frailty is common among older patients with an estimated prevalence of 4%–59.1% in community-dwelling adults without cancer.<sup>[23]</sup> In this study, the overall prevalence of frailty in this sample of hematological oncology patients  $\geq 65$  years of age was 60.0% (included with “apparently vulnerable” cases). Frailty prevalence seems to be higher in older cancer patients. In a systematic review, Handforth *et al.*<sup>[14]</sup> found that the prevalence of frailty among older patients with cancer was between 6% and 86%. The lack of a gold standard for assessing frailty in research is challenging. The definition for frailty and the assessment of frailty varies across studies.<sup>[27]</sup> Differences in frailty prevalence can be explained by differences in assessment methods.<sup>[28]</sup> The most widely used assessments include Vulnerable Elders Survey (VES-13), Edmonton Frailty scale, the Geriatric 8, Groningen Frailty Index, and phenotype models such as the Fried or Balducci frailty criteria.<sup>[29]</sup> Prevalence estimates reported using the Edmonton Frailty Scale have similar ranges and are comparable to the results in this study.<sup>[19,23]</sup>

The study population was mostly mildly frail, and a very small percentage of the population was severely frail. An increased prevalence of frailty has been linked with cancer history.<sup>[21,24]</sup> Mohile *et al.*<sup>[30]</sup> reported an association of cancer diagnosis with vulnerability and frailty in older Medicare beneficiaries, and nearly half of the study population was vulnerable according to the VES-13. Gheihman *et al.*<sup>[31]</sup> indicated that old age with cancer is associated with higher levels of hopelessness and depression, which also linked with a higher burden of physical symptoms that cause frailty. In our study, patients who had one comorbid disease and who had been diagnosed with cancer for >2 years had

Table 1: Frailty levels distributed for patients' sociodemographic and disease characteristics (n=90)

Variable	n (%)	Frailty level				
		Not frail, n (%)	Apparently vulnerable, n (%)	Mild frail, n (%)	Moderate frail, n (%)	Severe frail, n (%)
Total sample	90 (100.0)	36 (40.0)	16 (17.8)	18 (20.0)	15 (16.7)	5 (5.5)
Age (years, mean: 71.2±5.5)						
65-74	64 (71.1)	28 (43.7)	11 (17.2)	11 (17.2)	13 (20.3)	1 (1.6)
≥75	26 (28.9)	8 (30.8)	5 (19.2)	7 (27.0)	2 (7.7)	4 (15.3)
Gender						
Male	53 (58.9)	23 (43.4)	12 (22.7)	7 (13.2)	9 (17.0)	2 (3.7)
Female	37 (41.1)	13 (35.1)	4 (10.9)	11 (29.7)	6 (16.2)	3 (8.1)
Education						
Illiterate	25 (27.9)	8 (32.0)	4 (16.0)	8 (20.0)	4 (16.0)	1 (4.0)
Elementary	40 (44.4)	17 (42.5)	7 (17.5)	8 (32.0)	5 (12.5)	3 (7.5)
Secondary and higher	25 (27.7)	11 (44.0)	5 (20.0)	2 (8.0)	6 (24.0)	1 (4.0)
Marital status						
Married	71 (78.9)	32 (45.1)	11 (15.5)	11 (15.5)	15 (21.1)	2 (2.8)
Single	19 (21.1)	4 (21.0)	5 (26.3)	7 (36.9)	0	3 (15.8)
Number of children (n=88)						
1-3	40 (45.5)	22 (55.0)	6 (15.0)	7 (17.5)	5 (12.5)	0
4 or more	48 (54.5)	14 (29.1)	10 (20.9)	10 (20.9)	10 (20.9)	4 (8.2)
Caregiver						
Spouse	66 (73.3)	32 (48.8)	11 (16.7)	9 (13.6)	13 (19.7)	1 (1.5)
Children/friends	14 (15.6)	2 (14.2)	3 (21.5)	4 (28.6)	2 (14.2)	3 (21.5)
None	10 (11.1)	2 (20.0)	2 (20.0)	5 (50.0)	0	1 (10.0)
Economic status						
Income equals expenses	63 (70.0)	27 (42.9)	13 (20.7)	13 (20.7)	8 (12.6)	2 (3.1)
Less income than expenses	27 (30.0)	9 (33.3)	3 (11.1)	5 (18.5)	7 (26.0)	3 (11.1)
Diagnosis						
Lymphoma*	23 (25.5)	7 (30.4)	7 (30.4)	4 (17.4)	5 (21.8)	0
Multiple myeloma	21 (23.3)	11 (52.4)	2 (9.5)	3 (14.3)	4 (19.1)	1 (4.8)
Leukemia**	17 (18.9)	3 (17.6)	1 (5.9)	8 (47.1)	4 (23.5)	1 (5.9)
Myelodysplastic syndrome	12 (13.3)	5 (41.7)	2 (16.7)	2 (16.7)	1 (8.3)	2 (16.7)
Leukocyte deficiencies	10 (11.1)	5 (50.0)	3 (30.0)	0	1 (10.0)	1 (10.0)
Aplastic anemia	7 (7.9)	5 (13.9)	1 (6.3)	1 (5.6)	0	0
Duration of diagnosis (years)						
<2	76 (84.4)	32 (42.1)	14 (18.4)	16 (21.0)	10 (13.2)	4 (5.3)
2 and more	14 (15.6)	4 (28.6)	2 (14.3)	2 (14.3)	5 (35.7)	1 (7.1)
Comorbidities (n=59)***						
1	32 (54.2)	10 (3.1)	6 (18.8)	8 (25.0)	7 (21.9)	1 (3.1)
2 and more	27 (45.8)	9 (33.3)	6 (22.2)	8 (29.6)	2 (7.4)	2 (7.4)

\*Non-Hodgkin lymphoma n=20, diffuse large B-cell lymphoma n=3, \*\*Acute myeloid leukemia n=3, Chronic lymphocytic leukemia n=3, acute lymphoblastic leukemia n=1, \*\*\*Comorbidities listed as hypertension n=32, diabetes mellitus n=24 heart failure n=8. Charlson Index Score: 0: n=57, 1-2, n=33 (1: n=28, 2: n=5)

a higher prevalence of frailty than patients who had been diagnosed with cancer for <2 years. Fried demonstrated a relationship between frailty and cardiovascular diseases, pulmonary diseases, diabetes, and two or more comorbid diseases.<sup>[9]</sup> In our study, one-third of the comorbidities included diabetes and hypertension, which explains the likelihood of frailty when accompanied with cancer. The result more years with cancer more frailty may be explained by the fact of disease progression, increasing number of complications, toxicities, physical and psychosocial fatigue throughout treatment, hospital procedures, longitudinal follow-up, and an isolated lifestyle following the diagnosis resulted in an increase in the frailty levels of the patients.<sup>[32]</sup>

Age, education, marital status, and economic status were not found to be associated with frailty. Older age, female sex, less education, single, and less income were factors related to a high prevalence of frailty in this study, which is consistent with other studies.<sup>[30,33-35]</sup> The increased prevalence of frailty and the increased likelihood of frailty in female patients is in line with the frailty criteria described by Rockwood.<sup>[36]</sup> Education and income associated with frailty impacted utilization of healthcare services, adherence to treatment regimen, and self-care abilities. Accordingly, less education and less income may lead to dependency on others, which, along with paternalist cultural care behavior, may trigger dependency in activities of daily living and boost frailty.<sup>[34,35]</sup>

Table 2: Frailty scale scores, frailty status, and sociodemographic and disease characteristics (n=90)

Variable	Frailty scale score		P	Frailty status		P
	Median (minimum-maximum)	IQR (Q1-Q3)		Not frail (n)	Frail (n)	
Age (years)						
65-74	5 (0-11)	5 (8-4)	0.119	28	36	0.257
75 and older	7 (1-11)	4 (8-5)		8	18	
Gender						
Male	5 (0-11)	4 (8-4)	0.075	23	30	0.434
Female	7 (1-11)	5 (7-4)		13	24	
Education						
Illiterate	7 (1-11)	4 (8-5)	0.544	8	17	0.629
Elementary	5 (0-11)	5 (8-3)		17	23	
Secondary and higher	5 (0-11)	5 (8-4)		11	14	
Marital status						
Married	5 (0-11)	4 (8-4)	0.142	32	39	0.059
Single	7 (3-11)	3 (8-5)		4	15	
Number of children <sup>a</sup>						
1-3 <sup>b</sup>	4 (0-10)	5 (7-3)	<0.05	22	18	<0.05
4 or more <sup>a</sup>	6.5 (0-11)	5 (9-4.5)		14	34	
Caregiver <sup>a</sup>						
Spouse <sup>b</sup>	5 (0-11)	5 (8-4)	<0.05	32	34	<0.05
Children/friends <sup>a</sup>	8 (3-11)	5 (10-7)		2	8	
None	5 (3-11)	4 (8-4.5)		2	12	
Economic status						
Income equals expenses	5 (0-11)	4 (8-4)	0.090	27	36	0.401
Less income than expenses	7 (1-11)	5 (10-5)		9	18	
Diagnosis <sup>a</sup>						
Lymphoma	6 (0-10)	2 (7-5)	<0.05	7	16	0.110
Multiple myeloma	4 (1-11)	5 (7-2)		11	10	
Leukemia <sup>a</sup>	8 (3-11)	4 (10-7)		3	14	
Myelodysplastic syndrome	5 (1-11)	6 (9-3.5)		5	7	
Leukocyte deficiencies	4.5 (0-11)	6 (7-3)		5	5	
Aplastic anemia <sup>b</sup>	3 (1-8)	6 (7-2.5)		5	2	
Duration of diagnosis (years)						
<2	5 (0-11)	4 (8-4)	0.197	32	44	0.345
2 and more	7 (0-11)	6 (10-5)		4	10	
Comorbidities (n=9)						
1	7 (1-11)	5 (8.5-4)	0.059	10	22	0.866
2 and more	6 (1-11)	4 (8-4)		9	18	

<sup>a</sup>Group differences are between a and b. IQR: Interquartile range

Table 3: Adjusted regression analysis of the association of diagnosis, gender, and employment with frailty

Variable	OR (95% CI)	P
Gender	162.116 (2.26-11,621.41)	<0.05
Diagnosis		
Multiple myeloma	0.016 (0.00-0.42)	<0.05
Employment		
Not employed: Homemaker	895.61 (3.00-2,677,170.8)	<0.05

OR: Odds ratio, CI: Confidence interval

Patients with  $\geq 4$  children and who lived with children/friends were significantly frailer than other groups. The increased frailty of such patients is believed to be related to the physical stress of childbearing, the number of household members, and possible financial hardship. In

our culture, caring for older family members is common. A high frailty level thus becomes a care dependency issue for widows/singles, those who suffer from fatigue, or those who have other needs for support and care and need to live with caregivers (e.g., children or friends).<sup>[37,38]</sup>

Among the hematologic malignancies, leukemia, lymphoma, myelodysplasia, aplastic anemia, and leukocyte deficiencies have a higher likelihood of frailty than multiple myeloma. This association has been linked to differences in prognosis, treatment, and diagnostic procedures. Frail, older patients with myelodysplastic syndrome, acute myeloid leukemia, lymphoma, and multiple myeloma have been shown to have worse disease-related outcomes compared to same-aged older people without these conditions. Research efforts for myeloma have produced the myeloma-specific

comorbidity index, which enables researchers to score survival and toxicity risk prediction.<sup>[22]</sup> The previous studies allowed for the development of age-specific therapies or therapies well tolerated by older patients for multiple myeloma, a frequent hematologic malignancy in older patients.<sup>[3,39]</sup>

This study had some limitations that include a relatively small number of participants and lack of analysis for the association of disease severity and frailty. Although illness trajectory was not considered, patients were enrolled from both inpatient and outpatient units, and inpatient/outpatient status can be interpreted as a severity marker. The caring behavior and paternalist culture of Turkey may have some effect on frailty (protection vs. acceleration); thus, cultural impact should be considered when comparing and generalizing results. The relatively small number of participants as well as the cross-sectional design (no longitudinal follow-up) may have affected the power of association. Beyond these limitations, this is one of the first studies of frailty in hematology-oncology patients that includes regression analysis of confounding variables.

## Conclusion

Patients with higher prevalence of frailty included those  $\geq 75$  years of age, women, with  $>4$  children, with low income, diagnosed for  $>2$  years, living with children/friends, and followed-up for leukemia. The findings highlight the importance of considering these covariates when evaluating older patients with hematologic cancer. Frailty and vulnerability screening should be a concern in patient follow-up treatment and care. We believe that data from this study will contribute considerably in identifying risk groups and predispositions for frailty to understand the health status and needs of older adults diagnosed with hematologic cancer, and we believe that data from this study will contribute to creating an optimal care plan.

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## Conflicts of interest

There are no conflicts of interest.

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