Association Between Chronologic Age and Geriatric Assessment–Identified Impairments: Findings From the CARE Registry

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ABSTRACT

Background: The NCCN Guidelines for Older Adult Oncology recommend that, when possible, older adults with cancer undergo a geriatric assessment (GA) to provide a comprehensive health appraisal to guide interventions and appropriate treatment selection. However, the association of age with GA-identified impairments (GA impairments) remains understudied and the appropriate age cutoff for using the GA remains unknown. **Patients and Methods:** We designed a cross-sectional study using the Cancer and Aging Resilience Evaluation (CARE) registry of older adults with cancer. We included adults aged ≥ 60 years diagnosed with gastrointestinal malignancy who underwent a patient-reported GA prior to their initial consultation at the gastrointestinal oncology clinic. We noted the presence of GA impairments and frailty using Rockwood's deficit accumulation approach. We studied the relation between chronologic age and GA impairments/frailty using Spearman rank correlation and chi-square tests of trend. **Results:** We identified 455 eligible older adults aged ≥ 60 years with gastrointestinal malignancies; the median age was 68 years (range, 64–74 years) and colorectal (33%) and pancreatic (24%) cancers were the most common cancer type. The correlation between chronologic age and number of geriatric impairments was weak and did not reach statistical significance (Spearman ρ , 0.07; $P = .16$). Furthermore, the prevalence of domain-specific impairments or frailty was comparable across the 3 age groups (60–64 years, 65–74 years, ≥ 75 years) with the exception of comorbidity burden. Notably, 61% of patients aged 60 to 64 years had ≥ 2 GA impairments and 35% had evidence of frailty, which was comparable to patients aged 65 to 74 years (66% and 36%, respectively) and ≥ 75 years (70% and 40%, respectively). **Conclusions:** Using chronologic age alone to identify which patients may benefit from GA is problematic. Future studies should identify screening tools that may identify patients at high risk of frailty and GA impairments.

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Background

Up to 60% of all new cancer diagnoses and 70% of all cancer-related deaths occur among adults aged ≥ 65 years.¹ Older adults with cancer are at high risk of treatment-related toxicity and inferior survival, yet neither chronologic age nor clinician-assessed performance status (PS) adequately captures this vulnerability.² A geriatric assessment (GA) is a multidimensional tool to uncover this vulnerability or frailty and predicts the risk of morbidity and mortality among older adults with cancer.^{3–5} A growing body of literature shows that GA can predict chemotherapy-related toxicity,^{5,6} as well as mortality,⁴ guide clinical decision-making,⁷ and improve patient satisfaction⁸ among older adults with cancer. Specifically among gastrointestinal cancers, a GA has been shown to predict postsurgical complications among older adults with colorectal cancer⁹ and gastroesophageal¹⁰ and hepatocellular carcinoma,¹¹ as well as chemotherapy-related toxicity¹² and short- and long-term mortality.^{13–15} Given these substantial benefits, ASCO¹⁶ and NCCN guidelines¹⁷ currently recommend that all older adults with cancer undergo a GA.

However, the association between chronologic age and GA impairments and frailty remains understudied. Furthermore, ASCO recommends a GA should be performed among all older adults with cancer aged > 65 years, yet the rationale for this age cutoff remains unclear. Because patients with cancer are known to undergo accelerated aging through multiple mechanisms,¹⁸ extrapolating from the age cutoff used in the general population may be inaccurate. In this study, we examined the association between chronologic age and GA-identified impairments and frailty among adults aged ≥ 60 years with gastrointestinal malignancies.

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Patients and Methods

Study Population

Using participants from the University of Alabama at Birmingham (UAB) Cancer and Aging Resilience Evaluation (CARE) Study, an ongoing prospective registry enrolling older adults (≥ 60 years old) undergoing cancer care at UAB Hospitals and Clinics,^{19,20} we identified patients diagnosed with a gastrointestinal malignancy presenting to our medical oncology clinic for an initial consultation. We chose 60 years of age as a criterion for enrollment in this registry given the uncertainty surrounding the “right” age cutoff and to allow for meaningful age-related subanalyses, such as the current study.²¹ The UAB Institutional Review Board (IRB-300000092) approved this study.

Geriatric Assessment

We conducted patient-reported GAs as previously described (supplemental eTable 1; available with this article at JNCCN.org).^{19,20} Our GA comprised the following domains: functional status, comorbidity, cognition, mental health status, nutrition, social support, and health-related quality of life, consistent with recommendations from the International Society of Geriatric Oncology (SIOG).³ We assessed functional status using the Older Americans Resources and Services (OARS) instrumental activities of daily living (IADLs),²² OARS activities of daily living (ADLs),²² patient-reported ECOG PS,²³ and number of falls within the last 6 months.²⁴ Nutritional status was evaluated using an abridged version of patient-generated subjective global assessment (PG-SGA).²⁵ Comorbidity assessment was performed using number of medications²⁶ and OARS comorbidity assessment.^{22,27} We assessed social support using Medical Outcomes Study-Social Support Survey,²⁸ mental health status using the Patient-Reported Outcomes Measurement Information System (PROMIS) Anxiety and Depression measures,^{29,30} and cognition using the PROMIS Cognitive Function measure.³¹ Lastly, health-related quality of life was examined using the PROMIS 10-item Global Health tool.³² The GA was completed by the patient. However, if the patient had any vision issues, a member of the study personnel or a primary caregiver could ask the patient the GA questions.

GA Impairments

Based on the GA evaluation, patients were classified as having GA impairment if they met ≥ 2 of the following criteria³³: ≥ 1 falls in the last 6 months, significant limitation in walking 1 block, impairment in ≥ 2 IADLs, any ADL impairment, significant weight loss (3% in 3 months or 6% within 6 months), presence of ≥ 4 comorbidities, poor social support for physical activity, significant interference in social activity, presence of anxiety (T-score ≥ 60) or

depression (T-score ≥ 60), cognitive impairment (T-score ≤ 60), or polypharmacy (≥ 9 medications).

Frailty Index

We constructed a frailty index (the CARE Frailty Index) using the principle of deficit accumulation approach originally described by Rockwood and Mitnitski³⁴ and following the standard procedures outlined by Searle et al.³⁵ Similar methods have been used by Guerard et al⁴ and Cohen et al³⁶ to construct frailty indices that have been shown to be predictive of chemotherapy toxicity³⁶ and all-cause mortality⁴ among older adults with cancer. We selected 44 GA variables from the CARE questionnaire, each of which captured a health deficit, and recoded responses using the convention that 0 indicated the absence of the deficit and 1 indicated the presence of deficit; for variables that included a single intermediate response (eg, “sometimes” or “maybe”), we used an additional value of 0.5. We then combined these individual scores into an aggregate frailty score reflecting the overall proportion of deficits (range, 0–1), where 0 = no deficit present and 1 = all 44 deficits present. We then categorized patients as robust (< 0.2), prefrail (0.2–0.35), and frail (> 0.35), as previously described.³⁵ In case of missing response data, we required that responses to at least 30 items be present to construct a valid frailty index. An index constructed with at least 30 variables has been previously shown to be sufficiently accurate for predicting adverse outcomes among older adults.³⁷ Additional details regarding our definition for GA impairment and construction of the CARE Frailty Index are provided in supplemental eAppendices 1 and 2.

Statistical Analysis

We compared baseline characteristics between the 3 age groups (60–64, 65–74, and ≥ 75 years) using appropriate bivariate statistical tests, namely, analysis of variance/Kruskal Wallis for continuous variables and chi-square test/Fisher exact test for categorical variables depending on their underlying distribution. To measure the correlation between the number of geriatric impairments (a ranked variable) and chronologic age (continuous variable), we used Spearman rank correlation coefficient and tested the alternative hypothesis that the Spearman ρ was significantly different from 0. We compared the difference in proportion of various GA impairments and frailty categories among increasing age groups (60–64, 65–74, and ≥ 75 years) using chi-square tests of trend. To evaluate the difference between number of GA impairments across the 3 age groups, we used a nonparametric extension of Wilcoxon rank-sum test.³⁸ All statistical tests were 2-sided and the level of significance was 0.05. We used STATA, version 13 (StataCorp LLC) for all statistical analysis.

Results

Of the 523 consecutive adults aged ≥ 60 years with gastrointestinal malignancy seen for initial consultation at the UAB medical oncology clinic between September 2017 and October 2019, 455 (87%) enrolled in the CARE registry and underwent GA (supplemental eFigure 1). Of these, 367 (81%) had not started any systemic therapy, whereas the remaining (19%) had previously received treatment elsewhere. The median age of the entire cohort at the time of GA was 68 years (interquartile range [IQR], 64–74 years); 55% were male and 72% were non-Hispanic White. Overall, 28% of the 455 patients were aged 60–64 years, 47% were aged 65–74 years, and 25% were aged ≥ 75 years. Common cancer types included colorectal (33%) and pancreatic (24%); 46% had stage IV disease. The demographic and clinical characteristics were similar across the 3 age groups, with the exception of marital status and cancer stage, as summarized in Table 1. Compared with nonparticipants, patients enrolled in the CARE registry had similar age, sex, and cancer stage, with the exception of a higher proportion of nonresponders among patients with hepatobiliary and pancreatic cancer (supplemental eTable 2).

Relationship Between Chronologic Age and Geriatric Impairments

There was no significant correlation between chronologic age and number of geriatric impairments (Spearman ρ , 0.07; $P=.16$). Notably, even in the age group of 60–64 years, 61.4% of patients had GA impairments. This was not significantly different compared with patients aged 65–74 years (66.2%) and ≥ 75 years (70.5%; $P=.11$). We found similar rates of impairments in IADLs, ADLs, nutritional status, falls, cognitive, anxiety, depression, polypharmacy, and patient-reported ECOG PS across the age groups. However, there was a higher comorbidity burden (≥ 3) in the older group (39%, 56%, and 56% among ages 60–64 years, 65–74 years, and ≥ 75 years, respectively; $P<.01$) (Table 2). The increased comorbidity burden in the older age groups was mainly driven by a higher proportion of patients reporting arthritis, hypertension, and glaucoma (supplemental eTable 3).

Relationship Between Chronologic Age and Frailty

Overall, 37% ($n=108$) of the cohort were frail, whereas 30% ($n=128$) were prefrail and 33% ($n=143$) had robust frailty status. Compared with those who were prefrail or robust, patients who were frail were more likely to have an ECOG PS ≥ 2 (68% vs 26% vs 4%, respectively; $P<.001$) and a higher cancer stage (52% vs 42% vs 42%, respectively; $P=.03$), but did not differ significantly by treatment status (22% vs 20% vs 16%, respectively, were already on treatment; $P=.44$).

We then compared the rates of frailty categories across the different age groups. Notably, 26% and 35% of patients aged 60–64 years had evidence of prefrail and frail status. This was not significantly different compared with the proportion of patients with prefrail and frail status in the 65–74 age group (30% and 36%, respectively) and ≥ 75 age group (33% and 40%, respectively) ($P=.45$).

Discussion

In this study comprising an unselected cohort of older adults aged ≥ 60 years with gastrointestinal malignancies, we found no significant relationship between chronologic age and the presence of geriatric impairments or frailty. Furthermore, we found comparable prevalence of GA impairments and frailty in the 60–64 age group compared with those aged ≥ 65 years, suggesting that the traditional cutoff of 65 years for conducting comprehensive GA may not be accurate, and even patients aged <65 years could benefit from GA evaluation.

There is no universal agreement on the age at which a person becomes old. In the United States, age ≥ 65 years is generally considered the chronologic definition of an older adult, similar to what is used for Medicare eligibility. Accordingly, consensus recommendations for GA from ASCO and SIOG use 65 years as the age cutoff.^{3,16,17} However, emerging evidence suggests that cancer diagnosis and/or treatment can accelerate the human aging process through multiple mechanisms, including DNA damage and induction of aging-related biologic pathways, such as telomerase activity, DNA hypermethylation, and stem cell exhaustion.¹⁸ Hence, the age cutoffs assumed for the general population may not apply to patients with cancer. We postulate that this phenomenon may account for the high prevalence of GA impairments in our cohort aged <65 years.

In a prior study, Aleixo et al²¹ reported the prevalence of GA impairments among patients aged <65 years with early-stage breast cancer. Patients aged 50 to 64 years had a high prevalence of falls in the past 6 months (15%), abnormal timed up-and-go test >14 seconds (12%), and impaired IADLs (17%). However, patients aged 50 to 64 years comprised $<10\%$ of the study population and were derived from exercise intervention trials and compared with patients aged ≥ 65 years derived from a prospective registry, thus raising a possibility of selection bias. In comparison, our entire cohort includes unselected patients from a cancer registry who underwent initial consultation at the gastrointestinal oncology clinic. However, we report similar findings, with comparable rates of GA impairments and frailty among patients in the 60–65 age group.

Limitations of our study include being a single-institution analysis limited to gastrointestinal malignancies, and therefore our findings may not be generalizable to other

Table 1. Distribution of Baseline Demographic and Clinical Characteristics

Variable	60–64 Years n (%)	65–74 Years n (%)	≥75 Years n (%)	P Value
Total, N	128	215	112	
Age, median (IQR)	62 (61–63)	69 (66–71)	79 (77–81)	<.001
Sex				.16
Male	77 (60.2)	122 (56.7)	54 (48.2)	
Female	51 (39.8)	93 (43.3)	58 (51.2)	
Race				.25
White/Caucasian	91 (71.1)	147 (68.4)	90 (80.4)	
Black/African American	35 (27.3)	63 (29.3)	21 (18.8)	
Other	2 (1.6)	4 (1.9)	0 (0.0)	
Unknown	0 (0.0)	1 (0.5)	1 (0.9)	
Education				.90
Less than high school	24 (18.8)	34 (15.8)	14 (12.5)	
High school graduate	29 (22.7)	59 (27.4)	29 (25.9)	
Associate/Bachelor's degree	58 (45.3)	91 (42.3)	53 (47.3)	
Advanced degree	12 (9.4)	19 (8.8)	13 (11.6)	
Unknown	5 (3.9)	12 (5.6)	3 (2.7)	
Marital status				.01
Single	14 (10.9)	15 (7.0)	2 (1.8)	
Widowed/Divorced/Separated	23 (18.0)	52 (24.2)	44 (39.3)	
Married	86 (67.2)	138 (64.2)	62 (55.4)	
Unknown	5 (3.9)	10 (4.7)	4 (3.6)	
Cancer type				.91
Colorectal	41 (32.0)	65 (30.2)	43 (38.4)	
Pancreatic	28 (21.9)	56 (26.0)	24 (21.4)	
Hepatobiliary	23 (18.0)	40 (18.6)	17 (15.2)	
Gastroesophageal	14 (10.9)	22 (10.2)	11 (9.8)	
Other ^a	22 (17.2)	32 (14.9)	17 (15.2)	
Cancer stage				.05
I	9 (7.0)	15 (7.0)	10 (8.9)	
II	17 (13.3)	36 (16.7)	33 (29.5)	
III	39 (30.5)	58 (27.0)	25 (22.3)	
IV	63 (49.2)	102 (47.4)	42 (37.5)	
Unknown	0 (0.0)	4 (1.9)	2 (1.8)	
Treatment status				.27
Pretreatment	101 (78.3)	170 (79.1)	96 (85.7)	
During treatment	27 (21.7)	45 (20.9)	16 (14.3)	

Abbreviation: IQR, interquartile range.

^aOther includes anal cancer (n=10), gastrointestinal stromal tumor (n=14), appendicular cancer (n=3), neuroendocrine carcinoma (n=39), and gastrointestinal cancer not otherwise specified (n=5).

settings/populations. The reason for limiting our study to gastrointestinal malignancies was to eliminate the possibility of selection bias as mentioned earlier. Nevertheless, we recognize that our cohort is still quite diverse and there may be substantial variation in the proportion of

patients with GA impairment and frailty within individual cancer types and cancer stages. Almost half of our patients had stage IV disease, which may explain the high rate of GA impairments in our study. Notably, another study among patients with early-stage breast cancer reported similar

Table 2. Overall and Domain-Specific Geriatric Impairment and Frailty

Variable ^a	60–64 Years n (%)	65–74 Years n (%)	≥75 Years n (%)	P Value ^b
Total, N ^c	119	199	104	
GA impairment ≥2	78 (61.4)	141 (66.2)	79 (70.5)	.33
GA impairment count (0–13), median (IQR)	2 (1–4)	2 (1–5)	3 (1–6)	.11
Frailty score, median (IQR)	0.26 (0.13–0.41)	0.28 (0.15–0.40)	0.28 (0.17–0.48)	.29
Frailty category				.45
Robust	46 (38.2)	70 (34.0)	29 (26.6)	
Prefrail	33 (26.8)	62 (30.1)	36 (33.0)	
Frail	43 (35.0)	74 (35.9)	44 (40.4)	
IADL impairment ≥1	60 (47.2)	111 (52.1)	66 (58.9)	.20
ADL impairment ≥1	26 (20.5)	42 (19.7)	27 (24.1)	.64
ECOG PS ≥2	40 (33.6)	65 (25.3)	29 (27.1)	.61
≥1 fall in 6 mo	24 (18.9)	37 (17.6)	27 (24.1)	.34
Malnutrition	55 (43.3)	103 (48.4)	56 (50.0)	.54
Cognitive impairment	11 (8.7)	12 (5.6)	9 (8.0)	.54
Anxiety	23 (18.1)	44 (20.7)	17 (15.2)	.50
Depression	19 (15.0)	26 (12.2)	15 (13.4)	.75
≥3 comorbidities	48 (39.0)	112 (56.3)	59 (55.7)	.006
≥9 medications	23 (19.0)	50 (25.3)	29 (27.1)	.29

Abbreviations: ADL, activities of daily living; GA, geriatric assessment; IADL, instrumental activities of daily living; IQR, interquartile range; PS, performance status.

^aSeparate pairwise comparisons were conducted between age group 60–64 vs 65–74 years and between 60–64 vs ≥75 years with overall similar findings, with the exception of greater comorbidity burden in the higher age group (results not shown).

^bRepresents unadjusted P values. Additional sensitivity analyses were performed accounting for marital support and cancer stage (Mantel-Haenszel test using marital support and cancer stage as stratifying variables in case of categorical variables, Poisson and linear regression for GA impairment count and frailty score, respectively, controlling for marital support and cancer stage); however, the results remained unchanged (results not shown).

^cTotal number of patients with available data to calculate the number of GA impairments. Patients were required to have nonmissing information on at least 11 domains (85%) to have a valid result.

findings.²¹ All patients who underwent GA evaluation did so at the time of initial contact with the UAB health system. Consequently, not all patients who presented for an initial appointment were previously untreated, and approximately 20% had already undergone cancer therapy at another facility. Furthermore, by limiting our sample to patients completing GA at their initial visit, we may have excluded patients with severe illness requiring hospitalization for urgent treatment or hospice care, such as those with more aggressive malignancies, including hepatobiliary and pancreatic cancers. This may have potentially biased our findings. We did not have data on treatment-related toxicity, treatment discontinuation, or healthcare utilization, which need to be explored in future studies.

Conclusions

Our study adds to the growing body of evidence that chronologic age is an imperfect marker of presence of GA impairment and frailty. Furthermore, GA impairments are seen even among adults aged <65 years, and GA may

aid in the clinical management of even younger populations than previously considered.

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eFigure 1: Study Cohort Selection

eTable 1: Overview of GA Measures by Domain

eTable 2: Baseline Demographic and Clinical Characteristics

eTable 3: Patterns of Comorbidity Burden Among Older Adults

eAppendix 1: Definition of GA Impairment

eAppendix 2: Construction of CARE Frailty Index

eFigure 1. Study cohort selection.
Abbreviations: CARE, Cancer and Aging Resilience Evaluation; GA, geriatric assessment; UAB, University of Alabama.

eTable 1. Overview of GA Measures by Domain	
GA Domain	Patient-Reported Measures
Function	OARS IADLs OARS ADLs Patient-reported ECOG PS Number of falls in last 6 mo
Nutrition	Patient-generated subjective GA
Cognition	PROMIS Cognitive Function
Psychologic	PROMIS Short Form v1.0 – Anxiety 4a PROMIS Short Form v1.0 – Depression 4a
Social support	MOS-SSS (Emotional/Informational Support subscales)
Comorbidity	Number of medications OARS comorbidity assessment Self-reported vision and hearing loss
HRQoL	PROMIS Global-10

Abbreviations: ADL, activities of daily living; GA, geriatric assessment; HRQoL, health-related quality of life; IADL, instrumental activities of daily living; MOS-SSS, Medical Outcomes Study-Social Support Survey; OARS, Older Americans Resources and Services; PROMIS, Patient-Reported Outcomes Measurement Information System; PS, performance status.

eTable 2. Baseline Demographic and Clinical Characteristics

Variable	Participants n (%)	Nonparticipants n (%)	P Value
Total, N	455	68	
Age, median (IQR)	62 (61–63)	69 (66–71)	.75
Age category			.94
60–64 y	128 (28.1)	17 (29.3)	
65–75 y	215 (47.3)	26 (44.8)	
≥75 y	112 (24.6)	15 (25.9)	
Sex			.12
Male	253 (55.6)	31 (45.6)	
Female	202 (44.4)	37 (54.4)	
Race			<.01
White/Caucasian	328 (72.1%)	48 (70.6)	
Black/African American	119 (26.2)	13 (19.1)	
Other	6 (1.3)	6 (8.8)	
Unknown	2 (0.4)	1 (1.5)	
Cancer type			.02
Colorectal	149 (32.7)	17 (25.0)	
Pancreatic	108 (23.7)	23 (33.8)	
Hepatobiliary	80 (17.6)	19 (27.9)	
Gastroesophageal	47 (10.3)	5 (7.4)	
Other	71 (15.6)	4 (5.9)	
Cancer stage			.26
I	34 (7.5)	3 (4.4)	
II	86 (18.9)	10 (14.7)	
III	122 (26.8)	22 (32.4)	
IV	207 (45.5)	30 (44.1)	
Unknown	6 (1.3)	4 (2.5)	

Abbreviation: IQR, interquartile range.

eTable 3. Patterns of Comorbidity Burden Among Older Adults				
Comorbidity	60–64 Years n (%)	65–74 Years n (%)	≥75 Years n (%)	P Value
Total, N	128	215	112	
Arthritis				<.001
Yes	27 (22.1)	81 (42.0)	55 (53.9)	
No	95 (77.9)	112 (58.0)	47 (46.1)	
Circulation trouble in arms or legs				.28
Yes	18 (14.9)	33 (17.3)	24 (22.9)	
No	103 (85.1)	158 (82.7)	81 (77.1)	
Depression				.43
Yes	28 (23.0)	37 (18.9)	17 (16.2)	
No	94 (77.0)	159 (81.1)	88 (83.8)	
Diabetes				.18
Yes	36 (29.3)	73 (37.2)	29 (28.2)	
No	87 (70.7)	123 (62.8)	74 (71.8)	
Emphysema				.30
Yes	7 (5.8)	21 (10.8)	8 (7.9)	
No	113 (94.2)	173 (89.2)	93 (92.1)	
Glaucoma				.04
Yes	3 (2.5)	12 (6.2)	11 (10.8)	
No	118 (97.5)	182 (93.8)	91 (89.2)	
Hypertension				.005
Yes	61 (49.6)	134 (67.7)	64 (61.5)	
No	62 (50.4)	64 (32.3)	40 (38.5)	
Heart disease				.05
Yes	16 (13.1)	47 (24.2)	23 (22.1)	
No	106 (86.9)	147 (75.8)	81 (77.9)	
Chronic liver or kidney disease				.84
Yes	26 (21.1)	37 (18.9)	19 (18.3)	
No	97 (78.9)	159 (81.1)	85 (81.7)	
Other cancers or leukemia				.31
Yes	26 (21.5)	39 (20.3)	29 (27.9)	
No	95 (78.5)	153 (79.7)	75 (72.1)	
Osteoporosis				.07
Yes	4 (3.4)	19 (9.9)	11 (10.9)	
No	115 (96.6)	172 (90.1)	90 (89.1)	
Stomach or intestinal disorders				.05
Yes	42 (34.7)	61 (31.8)	48 (45.7)	
No	79 (65.3)	131 (68.2)	57 (54.3)	
Stroke				.09
Yes	4 (3.3)	18 (9.1)	11 (10.4)	
No	117 (96.7)	180 (90.9)	95 (89.6)	

eAppendix 1. Definition of GA Impairment

GA impairment was defined as presence of ≥ 2 of the following 13 domain-specific impairments. Using a cutoff of ≥ 2 impairments was chosen to be consistent with prior publications. If a patient answered ≥ 11 questions (85%), we would calculate the number of GA impairments and categorize as presence/absence of GA impairment.

1. History of ≥ 1 falls in the past 6 months.
2. Significant limitations in walking one block. Patients responding “limited a lot” to the question “Does your health limit you in walking one block?”
3. Presence of ≥ 2 limitations in IADLs.
4. Presence of any impairment in ADLs.
5. Presence of significant weight loss. This is defined as 3% weight loss within 3 months or 6% weight loss within 6 months.
6. Patient-reported ECOG PS ≥ 3 (ie, able to do little activity/pretty much bedridden).
7. Interference in social activity. Patient responding “most of the time or all of the time” to the question “During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (eg, visiting friends, relatives)?”
8. Multimorbidity defined as presence of ≥ 4 comorbidities.
9. Significant impairment in any tangible support on the MOS-SSS. Patients responding as “none” or “a little” or “some of the time.”
10. Anxiety defined as PROMIS Anxiety T-score > 60 .
11. Depression defined as PROMIS Depression T-score > 60 .
12. Cognitive impairment defined as PROMIS Cognitive Function T-score < 40 .
13. Polypharmacy defined as taking ≥ 9 daily medications.

Abbreviations: ADL, activities of daily living; GA, geriatric assessment; IADL, instrumental activities of daily living; MOS-SSS, Medical Outcomes Study-Social Support Survey; PROMIS, Patient-Reported Outcomes Measurement Information System; PS, performance status.

eAppendix 2. Construction of CARE Frailty Index

We constructed a frailty index (the CARE Frailty Index) using the principle of deficit accumulation approach originally described by Rockwood and Mitnitski¹ and following the standard procedures outlined by Searle et al.² Similar methods have been used by Guerard et al³ and Cohen et al⁴ to construct frailty indices that have been shown to be predictive of chemotherapy toxicity⁴ and all-cause mortality³ among older adults with cancer. We selected 44 GA variables from the CARE questionnaire, each of which captured a health deficit, and recoded responses using the convention that 0 indicated the absence of the deficit and 1 indicated the presence of deficit; for variables that included a single intermediate response (eg, “sometimes” or “maybe”), we used an additional value of 0.5. We then combined these individual scores into an aggregate frailty score reflecting the overall proportion of deficits (range, 0–1), where 0 = no deficit present and 1 = all 44 deficits present. We then categorized patients as robust (<0.2), prefrail (0.2–0.35), and frail (>0.35), as previously described.² In case of missing response data, we required that responses to at least 30 items be present to construct a valid frailty index. An index constructed with at least 30 variables has been previously shown to be sufficiently accurate for predicting adverse outcomes among older adults.⁵

The 44 variables used for construction of CARE Frailty Index are as follows:

1. Falls ≥ 1 : 1 point
2. Walk one block = limited a lot: 1 point
3. IADL mobility (unable to/with some help): 1 point
4. IADL shopping (unable to/with some help): 1 point
5. IADL meal prepare (unable to/with some help): 1 point
6. IADL housework (unable to/with some help): 1 point
7. IADL medication (unable to/with some help): 1 point
8. IADL money (unable to/with some help): 1 point
9. ADL get in and out of bed (unable to/with some help): 1 point
10. ADL dress (unable to/with some help): 1 point
11. ADL bath (unable to/with some help): 1 point
12. Global health: good = 0.5 point, fair/poor = 1 point
13. Global quality of life: good = 0.5 point, fair/poor = 1 point
14. Global physical health: good = 0.5 point, fair/poor = 1 point
15. Global mental health: good = 0.5 point, fair/poor = 1 point
16. Global satisfaction with social activities and relationship: good = 0.5 point, fair/poor = 1 point
17. Global everyday activities: moderately = 0.5 point, a little/not at all = 1 point
18. Global anxious/depression: sometimes = 0.5 point, often/always = 1 point
19. Global fatigue: moderate = 0.5 point, severe/very severe = 1 point
20. Global pain: pain level 4–6 = 0.5 point, pain level 7–10 = 1 point
21. Global social activities and roles: good = 0.5 point, fair/poor = 1 point
22. Weight loss: 3- or 6-month weight loss $\geq 5\%$: 1 point
23. Food intake less than usual: 1 point
24. Activities and function (self-rated activity) ≥ 2 (in bed or chair less than half the day/able to do little activity/pretty much bedridden): 1 point
25. Anxiety PROMIS T-score > 60 : 1 point
26. Depression PROMIS T-score > 60 : 1 point
27. Impaired Cognition: PROMIS T-score < 40 : 1 point
28. Number of daily medications ≥ 9 : 1 point
29. Social activity interference: some of the time = 0.5 point, most/all of the time = 1 point

Comorbidities

30. Eyesight fair/poor/totally blind: 1 point
31. Hearing fair/poor/totally deaf: 1 point
32. Other cancers or leukemia: 1 point
33. Arthritis or rheumatism: 1 point
34. Glaucoma: 1 point
35. Emphysema or chronic bronchitis: 1 point
36. High blood pressure: 1 point

(continued on next page)

eAppendix 2. Construction of CARE Frailty Index (cont.)

- 37. Heart disease: 1 point
- 38. Circulation trouble in arms or legs: 1 point
- 39. Diabetes: 1 point
- 40. Stomach or intestinal disorders: 1 point
- 41. Osteoporosis: 1 point
- 42. Chronic liver or kidney disease: 1 point
- 43. Stroke: 1 point
- 44. Depression: 1 point

Abbreviations: ADL, activities of daily living; CARE, Cancer and Aging Resilience Evaluation; GA, geriatric assessment; IADL, instrumental activities of daily living; PROMIS, Patient-Reported Outcomes Measurement Information System.

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