Research Letter to Editor

The geriatric assessment and sarcopenia to assess frailty in older patients with cancer

Christiaan D.A. Meerkerk [a], Cheryl P. Bruijnen [b], Frederiek van den Bos [c], Marielle H. Emmelot-Vonk [d], Remco de Bree [a,*]

[a] Department of Head and Neck Surgical Oncology, University Medical Center Utrecht, Heidelberglaan 100, 3584 CX Utrecht, the Netherlands
[b] Department of Medical Oncology, University Medical Center Utrecht, Heidelberglaan 100, 3584 CX Utrecht, the Netherlands
[c] Department of Geriatrics, University Medical Center Utrecht, Heidelberglaan 100, 3584 CX Utrecht, the Netherlands
[d] Department of Geriatrics, Leiden University Medical Center, Albinusdreef 2, 2333 ZA Leiden, the Netherlands

1. Introduction

The global cancer burden is rising rapidly and has surpassed 18 million newly diagnosed cases. [1] Cancer frequently leads to weight and muscle loss, followed by loss of muscle strength and quality particularly among older patients, a condition termed sarcopenia. [2] Sarcopenia is prevalent in 12% to 75% of cancer cases among older adults and varies depending on the tumor's location. [3–5] Older adults with cancer confront a dual risk of sarcopenia arising from aging and the cancer itself. [3] Sarcopenia is associated with adverse outcomes, encompassing postoperative complications, chemo- or radiotherapy-related toxicity resulting in reduced tolerance to the planned treatments, diminished quality of life, and reduced survival rates. [6–8] Identifying older patients suitable for complex treatment or requiring treatment adaptation becomes paramount in managing this vulnerable population.

The geriatric assessment (GA) serves as a compass for guiding treatment decisions. It comprehensively evaluates a patient's vulnerabilities, including functional, nutritional, cognitive, mood, physical, and comorbidity assessments. The GA's purpose is to identify impairments that could complicate treatment, aiding in the selection of the most appropriate therapeutic approach. [9,10] Substantial evidence supports the association between impaired GA domains and chemotherapy toxicity, morbidity, and mortality in older patients with cancer. [11,12]

Recognizing that not all older patients require a full GA is imperative, given its time-intensive nature and the scarcity of geriatric specialists. Consequently, several screening tools have been developed to distinguish patients capable of tolerating standard cancer treatment from those requiring a comprehensive GA to determine optimal treatment. [13] Among these tools, the Geriatric 8 (G8) is recommended in the Netherlands as a screening tool in patients with cancer. It stands out as a highly sensitive instrument widely adopted in clinical practice, despite its limited specificity; the G8 does have some limitations. [14,15]

Sarcopenia and frailty, with a particular emphasis on impaired physical function and disability, often overlap. While sarcopenia can be regarded as a component of frailty, the concept of frailty encompasses a broader spectrum, including social support and cognitive function. [16] Both conditions are intertwined with adverse health outcomes, necessitating a thorough exploration of their interconnectedness. [7,8,11,12]

* Corresponding author at: Department of Head and Neck Surgical Oncology, University Medical Center Utrecht, House Postal Number Q.05.4.300, PO BOX 85500, 3508 GA Utrecht, the Netherlands.
E-mail addresses: c.d.a.meerkerk-3@umcutrecht.nl (C.D.A. Meerkerk), C.P.Bruijnen@umcutrecht.nl (C.P. Bruijnen), f.van_den_Bos@lumc.nl (F. van den Bos), M.H.EmmelotVonk@umcutrecht.nl (M.H. Emmelot-Vonk), r.debree@umcutrecht.nl (R. de Bree).

Although GA is commonly used to assess frailty, more specific tests for screening frailty have been suggested in the literature. [17]

Given the G8's inherent limitation regarding specificity, the main goal of this study is to determine whether the addition of sarcopenia to the G8 could enhance the detection of frailty based on GA in older patients with cancer. Furthermore, the study delved into the association between sarcopenia and the individual components of the GA, shedding light on the complex interplay between these factors in the context of

Table 1

Characteristics of patients.

	Total (n = 117)		Non sarcopenic (n = 100)		Sarcopenic (n = 17)		χ^2	*P-value*
Age (years) (M, SD)	76.00	5.84	75.66	6.21	78.00	7.11	N.A	0.22
BMI (kg/m2) (M, SD)	25.80	4.83	25.93	4.97	25.00	5.27	N.A	0.31
Sex (n, %)								
Male	64	55	56	56	8	47	0.469	0.49
Female	53	45	44	44	9	53		
Surgery specialty (n, %)								
Head and neck	22	18	14	14	8	47	–	**0.03****
Gastrointestinal	68	58	60	60	8	47		
Urologic	7	6	7	7	0	0		
Gynecological	17	15	16	16	1	6		
Other	3	3	3	3	0	0		
ASA Classification (n, %)								
I	5	4	5	5	0	0	–	**0.04****
II	59	50	55	55	4	24		
III	48	41	36	36	12	71		
IV	2	2	2	2	0	0		
Marital status (n, %)								
Living together	70	60	61	61	9	53	–	**0.049****
Living alone	46	39	39	39	7	41		
Other	1	1	0	0	1	6		
Polypharmacy (n, %)								
< 5	56	48	51	51	5	29	2.155	0.14
≥ 5	61	51	49	49	12	65		
Charlson comorbidity score (n, %)								
< 2	101	86	91	91	10	59	12.740	**<0.001***
≥ 2	16	14	9	9	7	41		
Weight loss 6 months prior to diagnosis (n, %)								
Non	86	73	77	77	9	53	4.206	**0.04****
>5%	31	27	23	23	8	47		
MMSE (n, %)								
> 24	107	92	91	91	16	94	N.A	N.A
≤ 24	1	1	1	1	0	0		
GDS impaired (n, %)								
No	94	80	82	82	12	65	1.523	0.22
Yes	23	20	18	18	5	29		
ADL impaired (n, %)								
No	95	81	86	86	9	53	8.234	**0.004***
Yes	21	18	14	14	7	41		
IADL impaired (n, %)								
No	74	63	70	70	4	24	12.093	**0.001***
Yes	42	36	30	30	12	71		
Nutrition impaired (n, %)								
No	78	67	69	69	9	53	1.849	0.17
Yes	38	33	30	30	8	47		
Cognition impaired (n, %)								
No	115	97	99	99	16	94	N.A	N.A
Yes	1	1	1	1	0	0		
Low walking speed (n, %)								
No	87	74	78	78	9	53	4.943	**0.03****
Yes	25	21	18	18	7	41		
Frailty (defined by GA) (n, %)								
Normal (GA < 2)	58	50	57	57	1	6	15.188	**<0.001***
Frail group (GA ≥ 2)	59	50	43	43	16	94		
Frailty Screening G8 (n, %)								
No	53	45	51	51	2	12	9.027	**0.003***
Yes	64	55	49	49	15	88		
Hospital duration (days, median)	8	8	7	7	11	13	N.A	0.51
Low HGS (n, %)								
No	94	80	94	94				
Yes	23	20	6	6				
Low SMI (n, %)								
No	92	79	92	92				
Yes	25	21	8	8				

Median(M), Standard deviation (SD); American Society of Anesthesiologists (ASA); Mini-Mental State Examination (MMSE); Geriatric Depression Scale (GDS); Activities of Daily Living (ADL); Instrumental Activities of Daily Living (IADL) Geriatric assessment (GA); Geriatric 8 (G8); handgrip strength (HGS); skeletal muscle index (SMI).

* . Association is significant at the 0.01 level (2-tailed).
** . Association is significant at the 0.05 level (2-tailed).

cancer care.

2. Materials and Methods

2.1. Study Population

This retrospective study was conducted at the Geriatric Department of the University Medical Center Utrecht, focusing on patients aged 70 years or older who attended the pre-operative screening clinic to undergo a GA for (suspected) solid malignancies from September 2016 to December 2017. This study was reviewed and approved by the local ethics committee (17–365/C). The requirement for informed consent from patients was waived because of its retrospective design. Sarcopenia was defined as the combination of low muscle strength and low skeletal muscle index (SMI) on cross-sectional imaging (computed tomography [CT] or magnetic resonance imaging [MRI]).

2.2. Geriatric Assessment

The GA included instruments to measure functional status, nutritional status, cognition, mood, physical function, and comorbidity. A patient was defined as frail if the GA had an abnormal outcome on at least two of the seven instruments used. [12,18]

2.3. Geriatric 8

The G8 is an eight-item questionnaire especially for patients with cancer. A score of ≤14 was considered to be positive indicating a high risk of frailty. [14]

2.4. Sarcopenia

As recommend by the European Working Group on Sarcopenia in Older People (EWGSOP) we used the combination of low muscle function and low muscle quantity for the diagnosis of sarcopenia. [3]

Further description of the methods is available in **Supplement 1.**

3. Results

Initially, 143 patients were selected for inclusion from a previously published study. [19] We excluded those patients with insufficient quality of diagnostic imaging (incomplete imaging at time of diagnoses [*n* = 17], presence of artefacts [*n* = 7]), and those for whom diagnostic imaging showed no reliable differentiation between muscle and surrounding tissue (*n* = 2) which impaired measurements of SMM. Finally, 117 patients were included for analyses.

Overall, the median age was 76 years (5.84 standard deviation [SD]). The majority of the patients were male (55%) and underwent gastrointestinal surgery (58%). All patients appeared to have cancer.

Of the included 117 patients, 23 (20%) patients had low muscle strength, 25 (21%) had low SMI. A total of 17 (15%) patients were defined as sarcopenic. Based on the GA, 59 (50%) patients were determined as frail. Based on the G8, 64 (55%) patients were defined as possibly frail. Of the 17 patients that were defined as sarcopenic, 16 (94%) patients were determined as frail on the GA and 15 (88%) were defined as possibly frail on the G8. An overview of the characteristics of patients are listed in Table 1.

Table 1 shows statistically significant differences for patients diagnosed with and without sarcopenia. Patients with sarcopenia were more likely to have an impaired physical function (41% versus 21%; *p* < 0.05), more likely to be impaired in activities of daily living (ADL) (41% versus 18%; *p* < 0.01), more likely to be impaired in instrumental ADL (IADL) (71% versus 36%; *p* < 0.01), more likely to have ≥2 comorbidities (41% versus 14%; p < 0.01) and to be frail (according GA) (94% versus 50%; p < 0.01).

3.1. Performance of the Screening Tool

Table 2 shows the diagnostic values of the G8 were a sensitivity of 76.6 (95% confidence interval [CI] 61.6–87.2), a specificity of 60.0 (95% CI 47.6–71.3), a positive predictive value (PPV) of 56.3 (95% CI 43.3–68.4), and a negative predictive value (NPV) of 79.2 (95% CI 65.5–88.7). The sensitivity and specificity of sarcopenia to predict frailty were 29.8 (95% CI 17.7–45.1) and 95.7 (95% CI 87.1–98.9), respectively, with a PPV and NPV of 82.4 (95% CI 55.8–95.3) and 67.0 (95% CI 56.8–75.9). When a positive screening for frailty was defined when a patient was sarcopenic and had an impaired G8, the sensitivity and specificity were 27.7% (95% CI 16.1–42.9) and 97.1% (95% CI 89.1–99.5), respectively, with a PPV and NPV of 86.7% (95% CI 58.4–97.7) and 66.7% (95% CI 56.6–75.5).

3.2. Association between Each GA Item and Sarcopenia

As shown in Table 3 **(Supplement 2),** multivariable analysis revealed only IADL (odds ratio [OR] 6.80, 95% CI 1.41–32.9, *P* = 0.017) as an independently associated GA item.

4. Discussion

In this study the G8, as a screening instrument for frailty based on GA, demonstrated a sensitivity of 76.6% and a specificity of 60.0%. A previous study involving 143 older patients (≥70 years) treated with surgery yielded comparable results: 82% sensitivity and 63% specificity. [18] Therefore, the G8 is effective at selecting patients for GA, but its limited specificity could imply that many older patients with cancer undergo extensive GAs unnecessarily. When combining the G8 with sarcopenia (low muscle function determined by handgrip strength and low muscle quantity determined by skeletal muscle mass) to screen for frailty, specificity increased to 97.1%, with a PPV of 86.7%. However, sensitivity dropped to 27.7%, and the NPV was 66.7%.

For a GA screening test, high sensitivity and NPV are essential, ensuring frail patients receive GA while minimizing evaluations for non-frail patients. Unfortunately, adding sarcopenia significantly reduced sensitivity and negative predictive value, possibly missing many frail patients in need of a GA. Conversely, specificity and PPV increased, reducing the need for GA to diagnose frailty. However, GA also guides treatment, and this study found sarcopenia associated only with IADL impairment. If GA guides tailored treatment for vulnerable older patients, a full GA may still be necessary to identify specific contributors to vulnerability.

Several studies have explored sarcopenia's association with frailty and found a moderate association between muscle mass and frailty. [20] In patients with head and neck cancer, studies have shown associations between SMM and frailty measures, with the G8 score being an independent variable correlated with SMM. [21,22] In another study, low SMI predicted frailty diagnosed by GA in older patients with head and neck cancer, independently of comorbidities and muscle strength. [23]

Sarcopenia and frailty, both linked to age-related musculoskeletal

Table 2
Diagnostic value of sarcopenia for predicting frailty defined as ≥2 impaired geriatric assessment instruments.

	Sarcopenia	G8	Sarcopenia + G8
Sensitivity	29.8% (17.7–45.1%)	76.6% (61.6–87.2%)	27.7% (16.1–42.9%)
Specificity	95.7% (87.1–98.9%)	60.0% (47.6–71.3%)	97.1% (89.1–99.5%)
Positive predictive value	82.4% (55.8–95.3%)	56.3% (43.3–68.4%)	86.7% (58.4–97.7%)
Negative predictive value	67.0% (56.8–75.9%)	79.2% (65.5–88.7%)	66.7% (56.6–75.5%)

Geriatric 8 (G8); 95% Confidence interval (CI)

Table 3

Association between each geriatric assessment item and sarcopenia.

GA item	Univariate logistic regression			Multivariate logistic regression*		
	OR	95% CI	*P-value*	OR	95% CI	*P-value*
ADL	4.78	1.53–14.91	***0.007***	1.95	0.42–9.16	0.40
IADL	7.00	2.09–23.47	***0.002***	6.80	1.41–32.96	***0.02***
Nutritional status	2.50	1.87–7.15	**0.048**	3.11	0.84–11.50	0.09
Mood	2.07	0.64–6.70	0.22	–	–	–
Physical Function	3.37	1.11–10.26	***0.03***	1.57	0.37–6.72	0.54
Comorbidity	3.77	1.31–10.87	***0.01***	2.68	0.74–9.7	0.13

Geriatric Assessment (GA); Odds Ratio (OR); 95% Confidence Interval (CI); Activities of Daily Living (ADL); Instrumental Activities of Daily Living (IADL).

* Including age and sex, no regression analysis for cognitive status performed.

changes, share causes and consequences, such as alterations in body composition and impaired physical function. Both sarcopenia and frailty are highly prevalent age-related conditions that are associated with adverse outcomes. [7,24] Other studies propose that sarcopenia could be the biological substrate for the development of frailty. [5,25] Although sarcopenia and frailty have some commonalities and are often used interchangeably, they appear to represent separate entities with different constructs. Thereby in the G8 screening, malnutrition is a major part, and also a major problem in patients with head and neck cancer. However, frailty is more than malnutrition only and its consequence, sarcopenia. [26,27] In literature the definition of frailty is still developing. Two major frailty definitions are proposed: the physical phenotype of frailty (Fried) [28] and the multiple deficit model (Rockwood). [29] In this study we chose the multiple deficit model by using the GA as the gold standard for frailty, as recommend by the International Society of Geriatric Oncology (SIOG). [30]

There is growing consensus that although sarcopenia may be a component of frailty, frailty is more multifaceted than sarcopenia alone. Also, the "physical" definition of frailty is suggested to have a complex interrelationship with sarcopenia. [18,23] Our findings support this consensus.

Our study had limitations, including its retrospective nature and the use of two different imaging techniques (CT or MRI). But research has demonstrated excellent correlation between these two imaging modalities in assessing SMM at the C3 level. [31] Moreover, a relatively small percentage of patients had an impaired G8 (55%) and were sarcopenic (15%). However, this is the first study, to our knowledge, investigating the impact of adding sarcopenia to the G8 and its association with each GA item. Furthermore, all muscle tissue measurements were performed manually by a single researcher, who was blinded to outcomes regarding frailty and sarcopenia. In this study frailty was defined as an abnormal outcome on at least two of the seven instruments used in the GA [12], whereas other instruments may be more specific to assess frailty. [17]

5. Conclusion

In this study, the addition of sarcopenia to the G8 did improve the specificity and PPV. Unfortunately, the sensitivity and NPV decreased greatly. The high specificity and PPV of the combination of G8 and sarcopenia may suggest that a GA is unnecessary simply for the diagnosis of frailty if both the G8 score is ≤14 and sarcopenia is diagnosed. However, to guide treatment a full GA is still needed.

CRediT authorship contribution statement

Christiaan D.A. Meerkerk: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Visualization, Writing – original draft, Writing – review & editing.

Cheryl P. Bruijnen: Resources, Data curation, Investigation, Writing – review & editing. **Frederiek van den Bos:** Supervision, Writing – review & editing. **Marielle H. Emmelot-Vonk:** Conceptualization, Investigation, Resources, Supervision, Writing – review & editing. **Remco de Bree:** Conceptualization, Resources, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

Appendix A. Supplementary Data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jgo.2024.101776.

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