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Identifying an accurate pre-screening tool in geriatric oncology

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Contents

Abstract

The use of comprehensive geriatric assessment (CGA) in cancer patients older than 70 is recommended. Three pre-screening instruments have been proposed: the abbreviated comprehensive geriatric assessment (aCGA), the Vulnerable Elders Survey (VES-13), and the Groningen frailty index (GFI). The objective of the study was to identify the most efficient pre-screening tool that accurately determines individuals who may benefit from the entire CGA. A total of 113 elderly cancer patients were assessed by means of the aCGA, VES-13, GFI and the full CGA. The sensitivity, specificity of the three instruments was calculated, using the results from the entire CGA as the gold standard for the GFI and the VES-13. The aCGA was assessed whether each sub-component reliably predicts impairment on each sub-component of the full CGA.

The majority of the participants were defined as being at risk of vulnerability: 68.14% had two or more impairments of the CGA or were cognitively impaired. The physical and disability questions are useful, but all other screening instruments miss too many cases.

Keywords: Geriatric oncology; Frail elderly; Geriatric assessment

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1. Introduction

There is a remarkable increase in the number of older patients with cancer. Persons over the age of 70 are the fastest growing proportion of the population. In addition, the most important risk factor for cancer is age [1]. Often, tumor diagnosis is made at a later stage compared with younger individuals, resulting from a restriction in screening programs and often an underestimation of symptoms [2]. Senior adults have been underrepresented in clinical trials, leading to a limited existence of evidence-based guidelines for treatment. Elderly patients are often treated with less intense and possibly suboptimal standard regimens, under the assumption that therapy is less effective and has more toxicity [3]. Furthermore, in senior adults, case complexity (related to possible existing co-morbidities and impaired functional status) and care complexity (related to the presence of multiple health care providers) are added up [4].

Senior citizens represent a inhomogeneous group. Within a decade of age, there is a substantial variety in life expectancy, capacity to live independently, and burden of co-morbidities. Thus, treatment choices should not be ascertained by calendar age per se. Just as when staging the tumor, its size and spread, clinicians need to determine the functional age of the patient and anticipate the functional response to treatment [5].

The International Society of Geriatric Oncology (SIOG) recommends the use of comprehensive geriatric assessment (CGA) in cancer patients older than 70 [6]. The CGA is a multidisciplinary evaluation of an older individual's functional status, cognition, psychological status, social support, nutritional status, co-morbidity, and review of the medications being taken [5,7]. Several instruments have been developed to assess the different components. Common measures of functional status, which investigate the necessary abilities enabling independence in everyday life, are activities of daily living (ADL) and instrumental activities of daily living (IADL). The mini-mental state examination (MMSE) investigates orientation, short-term memory, recall, and language and praxis function. A score less than 24 points suggests 'probable cognitive impairment' [8]. Emotional status is assessed by means of the geriatric depression scale (GDS), a validated screening tool for depression. The GDS-15 measures emotional factors present in depression and does not rely on somatic symptoms that confound the diagnosis of depression [9].

In more than 50% of patients older than 65 years, the CGA detects unexpected difficulties, which may lead to premature discontinuity of the cancer treatment [5]. Therefore, CGA may serve the decision-making process by identifying patients who are fit for treatment [5].

Unfortunately, the CGA is time-consuming. Exhaustion of both the patient and his physician frequently lead to the abandonment of the CGA [10]. A two-step approach is a pragmatic alternative, using a less time- and manpower-consuming pre-screening tool [11]. Pre-screening is a process in which a brief assessment is conducted to determine whether further screening is indicated. It is a short evaluation that is not intended to be diagnostic, and does not replace, but rather optimizes screening by selecting those senior patients who may benefit from an intensive survey [12]. Several pre-screening instruments have been proposed.

The abbreviated comprehensive geriatric assessment (aCGA) combines the items of the CGA that are most predictive of the total rating score of each scale [13]. The aCGA is developed to determine whether patients should undergo the ADL, IADL, GDS and MMSE based on cut-off point scores [12]. A cut-off point of two out of the selected four GDS items indicates insisting on the use of the full GDS. In the event of any detected impairment, the full ADL or IADL should be administered. Concerning the MMSE, a score of six or lower out of a maximum score of eight indicates cognitive screening with the complete MMSE [12]. The aCGA is not a complete pre-screening instrument with clear cut-offs such as the two described below, but was designed to conduct the CGA more efficiently.

The Vulnerable Elders Survey (VES-13) is a 13-item screening tool that asks elderly people to report their age, physical status, functional capacity, and their self-estimated health. In a US sample, a score of $\geq$3 identified 32% of individuals as being vulnerable [14]. These vulnerable elderly had a four times greater risk of functional deterioration or death over 2 years than those with a score less than three [14,15]. The clear cut-off point makes the VES-13 a practical instrument; nevertheless, patients may overestimate their own physical competences.

The Groningen frailty index (GFI) is a simple tool that screens for diminished abilities and resources in physical, cognitive, social and psychological functioning. A score of four or more indicates a higher risk for frailty [16]. Thus, like the VES-13, a distinct cut-off point is an advantage of the GFI.

In order to identify the most efficient pre-screening tool that accurately determines individuals who may benefit from the entire CGA, we conducted a study among elderly Flemish and Dutch cancer patients. The objective was to compare the results of three selected pre-screenings tools, currently insufficiently validated, using the results from the entire CGA as the gold standard.

2. Methods

2.1. Participants

Eligible patients were 70 years of age or over, with a diagnosis of cancer (any stage), who were actively receiving treatment or not, and who speak Dutch. Patients with severe cognitive impairment were excluded. Patients were recruited at the oncology wards of the Virga Jesse Hospital (Hasselt), Hospital Zuid Oost-Limburg (Genk), the academic hospital of Maastricht and from general practice. Informed

consent was obtained from all participants. The study was approved by the ethical review board of the Medical School of the Catholic University of Leuven and the ethical review boards of all participating hospitals.

2.2. Data collection

The interviews were conducted by trained medical staff. All patients were assessed by means of the aCGA, VES-13, GFI, and the full CGA. Furthermore, from all participants, clinical information was obtained using a standardized questionnaire, including demographics (age, sex, height and weight), baseline tumor characteristics, details of their medical history and medication use.

A list of the different components that compiled the CGA is provided in the Appendix A.

2.3. Statistical analysis

The sensitivity (the probability that the test correctly classifies vulnerable patients as positive), specificity (the probability that the test correctly classifies fit patients as negative), negative predictive value (the proportion of patients with a negative test result who are not vulnerable) and the positive predictive value (the proportion of patients with a positive test result who are vulnerable) of the pre-screening instruments were calculated, using the results from the full CGA as the gold standard. For the cognitive part of the aCGA, the full MMSE was used as the gold standard. Being at risk of vulnerability was defined as having impairment in two or more domains (ADL and IADL) or being cognitively impaired (MMS ≤ 24). A negative predictive value close to 100% indicates that testing negative is reassuring as to absence of vulnerability [17]. A low negative predictive value is more likely to result from poor sensitivity than poor specificity [17].

To facilitate an overall comparison among the three screening instruments, we created an aggregated performance of the aCGA. Being at risk of vulnerability was defined by the necessity to administer the full MMSE, the ADL, the IADL or the MMSE.

All statistical analyses were performed using STATA version 8.0 software [18].

3. Results

3.1. Patient characteristics

A total of 113 patients were recruited. Table 1 shows the demographic distribution of the participants. The mean age of the patients was 77 years; 60% were male. The majority of the participants lived with their partner (58%); 34% lived alone. Prostate cancer was the most common diagnosis, accounting for 32% of the patients; while breast cancer and colon cancer were equally prevalent (15%).

Table 1
Demographic and clinical characteristics of the participants.

Variable	*N*	%
Gender		
Male	68	60
Female	45	40
Age in years (mean ± SD)		77 ± 4
Living situation		
With partner	66	58
Alone	38	34
Nursing home	5	4
With children	4	4
Months since cancer diagnosis (mean ± SD)		79 ± 141
Cancer diagnosis		
Prostate	36	32
Lung	13	11
Breast	17	15
Colon	17	15
Other	30	27

3.2. Presence of ADL, IADL, cognitive impairment, depression, and co-morbidity

These results are shown in Table 2. The majority of the participants had no ADL impairment (39%); 31% were classified as having one ADL deficiency; 10% had two ADL impairments. However the majority demonstrated dependency in three or more IADL domains (51%); 23% of the participants had no IADL impairments, 10% had a deficiency in one IADL domain, 16% in two domains.

Using the MMSE to assess cognitive status, 85% of the participants scored good (score ≥ 24), 11% as mildly cognitively impaired and 3% as poor (score ≤ 18). Twenty-six percent of the participants were scored mildly depressed on the geriatric depression scale; 4% were scored majorly depressed; 69% had a normal score.

Table 2
Patient characteristics.

	%
ADL dependency	
ADL independent	39
Impairment in one ADL domain	31
Impairment in two ADL domains	10
Impairment in three or more ADL domains	20
IADL dependency	
IADL independent	23
Impairment in one IADL domain	10
Impairment in two IADL domains	16
Impairment in three or more IADL domains	51
Cognitive impairment	
No cognitive impairment	85
Mildly cognitively impaired	11
Poor cognitive status	3
Depression	
Major	4
Mild	26

Table 3
Summary statistics for diagnostics testing for GFI, VES-13, and aCGA.

	Sensitivity (95% CI) True-positive	Sensitivity (95% CI) False-negative	Positive predictive value (95% CI) False-positive	Negative predictive value (95% CI) True-negative
GFI	39% (28–51%)	86% (70–95%)	86% (70–95%)	40% (29–51%)
	30	47	5	31
Vs ADL[a]	47% (30–65%)	76% (65–85%)	46% (29–63%)	77% (66–86%)
	16	18	19	60
Vs IADL[a]	39% (28–51%)	86% (71–95%)	86% (70–95%)	41% (30–53%)
	30	46	5	32
VES-13	61% (49–72%)	78% (61–90%)	85% (73–93%)	48% (35–62%)
	47	30	8	28
Vs ADL[a]	76% (59–89%)	63% (52–74%)	47% (34–61%)	86% (75–94%)
	26	8	29	50
Vs IADL[a]	67% (55–77%)	89% (75–97%)	93% (82–98%)	57% (43–70%)
	51	25	4	33
aCGA				
GDS	69% (38–90%)	92% (85–97%)	53% (28–77%)	96% (90–99%)
	9	4	8	92
Cognitive status	23% (7–50%)	100% (96–100%)	100% (40–100%)	88% (80–93%)
	4	13	0	96
ADL	97% (86–100%)	47% (35–58%)	48% (36–60%)	97% (85–100%)
	37	1	40	35
IADL	92% (84–97%)	69% (52–84%)	87% (77–93%)	81% (62–92%)
	71	6	11	25
Aggregated	51% (39–62%)	97% (85–100%)	97% (87–100%)	48% (36–60%)
	39	38	1	35

[a] Performance against impairment in two or more domains (ADL/IADL) of the full CGA.

The large majority of the participants (76%) had one or more co-morbidities; 24% had no medical history. Cardiovascular diseases were the most frequent co-morbidities (31%), followed by diabetes mellitus (19%), and arthritis and other joint problems (10%).

Only two participants (1.8%) had no functional dependence in ADL and IADL, no serious co-morbidities, and no cognitive impairment.

The majority of the participants were defined as being at risk of vulnerability: 68% had two or more impairments of the CGA or were cognitively impaired. Thirty-two percent were not at risk of vulnerability.

3.3. Results of the pre-screening instruments

These results are shown in Table 3. The mean GFI score for the group was 4.2 (standard deviation: 2.55). The GFI classified 31% of the participants as being at high risk of vulnerability. The sensitivity of the GFU was poor in 39%; likewise, the negative predictive value was fair (40%).

The mean VES-13 score for the group was 3.77 (standard deviation: 2.77). The VES-13 classified 49% of the participants as being vulnerable. The sensitivity of the VES-13 was moderate (61%) with a lower negative predictive value (48%).

Two of the four items of the GDS selected for the aCGA were answered positively in 15% of the patients. The aCGA indicated the necessity of administering the complete ADL and IADL in 34% and 72% of the participants, respectively. The sensitivity of the different parts of the aCGA varied (69% for the GDS part, 23% for the cognitive part, 97% for the ADL part and 92% for the IADL). However, the negative predictive values were high for the cognitive part (88%) and the IADL domain (81%) and excellent for the GDS and ADL parts (96% and 97%, respectively).

The average time to complete the three screening instruments was 15 min while it took 30 min more to administer the full CGA.

4. Discussion

In our study, the physical and disability questions were useful, but all other screening instruments missed too many cases.

Elderly patients should be treated holistically, receiving attention to all existing medical, psychological, and social issues [10]. Non-uniformity of the aging process makes an individualized approach to disease management relevant to the treatment of the elderly cancer patient. Any patient over 70 should receive some sort of evaluation. However, it is difficult for the oncologist to decide who should have a CGA [19]. Using a short pre-screening tool will save time. The most important characteristic of a short pre-screening tool is the ability to exclude the possibility of vulnerability, with a high negative predictive value [20]. False-negative results will lead to false reassurance about the absence of vulnerability. Pre-screening tools should be simple and quick to administer. They provide elementary information on the patient's problems; positive results indicate the need for a more complete geriatric evaluation [20].

The presence of the vulnerability may then be determined by the full CGA. Screening for vulnerability will help to distinguish those elderly patients who may benefit from current cancer treatment in terms of a survival advantage from those at a higher risk of developing complications, comprising treatment tolerance, and/or being too vulnerable or frail to receive aggressive therapy [21]. The CGA may help to determine whether the cancer itself would cause symptoms or complications during the remaining life expectancy beyond what is already present due to causes other than the cancer [19]. Integrating an assessment at serial time points of the continuum of cancer care (before, during and after treatment) will define the short- and long-term impact of the cancer therapy on functional and cognitive decline [7]. Integrating an intervention plan, based on a geriatric assessment, improves quality of life, survival or participation in cancer treatment decisions [20].

The main strength of our study is the heterogeneous sample of the participants, increasing the generalization of the results. However, in interpreting our results, some limitations need to be considered. As the CGA, used as the gold standard, does not have a clear cut-off point, the different categories had to be defined empirically. We decided to use the definition "at risk of vulnerability" of Rodin and Mohile [5]. We acknowledge that the definition is open to discussion. Possible selection bias may have been introduced following a loss of patients who could not have been interviewed because of a very high age or seriousness of their disease. Selection bias may lead to an underestimation of vulnerability. However, a study comparing the results of the VES-13 with the CGA in prostate cancer patients defined 60% of the patients as being impaired on ≥2 tests within the CGA [22]. In our study, this was slightly higher (68.14%). The sensitivity of the VES-13 in prostate cancer patients was higher than in our study (72.7% and 61.04%, respectively)

Self-reported data may reflect respondent bias. Finally, the cross-sectional design does not allow the course of vulnerability over the continuum of cancer care to be observed.

In summary, the current study demonstrated the validity of the aCGA and the VES-13 as pre-screening instruments in elderly cancer patients in Flanders and the Netherlands.

Reviewers

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Appendix A.

Components of the CGA and the different pre-screening instruments used:

Geriatric domain	Instrument/scale	Number of questions	Cut-off points associated with increased risk of vulnerability
Functional status			
Activities of daily living	Barthel Index [23]	10	2[a]
Instrumental activities of daily living	Lawton Scale [24]	9	2[a]
Cognition	Mini-mental state examination [8]	30	≤24
Psychological state	Geriatric depression scale [9]	15	≥8
Pre-screening instruments			
aCGA [13]		GDS: 4	2
		ADL: 3	1
		IADL: 4	1
		MMS: 4	6
VES-13 [14]		13	≥3
GFI [16]		15	≥4

[a] Cut-off point used in our study.

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Biographies

Eliane Kellen received her M.D. degree from the University of Leuven. The topic of her Ph.D. dissertation concerned the interaction between gene and environmental risk factors for the development of bladder cancer. Her main interests include primary and secondary prevention of cancer. She is (co-)author of several publications in top-rated cancer journals.

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Marjan Van Dijk received her M.D. degree from the University of Amsterdam. She was trained as a specialist in Internal Medicine and Hematology in the academic hospitals of Utrecht and Amsterdam. Her dissertation contained clinical, epidemiological, physiological and molecular studies on autosomal dominant polycystic kidney disease. She now works as an oncologist with a special interest in neuro-oncology.

Ilse Verdonck received her Master of Nursing degree from the University of Leuven. The topic of her dissertation concerned the involvement of home care nurses in euthanasia in Flanders.

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