**Dieses Dokument ist eine Zweitveröffentlichung (Verlagsversion) /
This is a self-archiving document (published version):**

Leopold Hentschel, Anke Rentsch, Felicitas Lenz, Beate Hornemann, Jochen Schmitt,
Michael Baumann, Gerhard Ehninger, Markus Schuler

**A Questionnaire Study to Assess the Value of the Vulnerable Elders
Survey, G8, and Predictors of Toxicity as Screening Tools for Frailty
and Toxicity in Geriatric Cancer Patients**

Erstveröffentlichung in / First published in:

Oncology Research and Treatment. 2016, 39 (4), S. 210 – 216 {Zugriff am: 19.05.2020}. Karger.
ISSN 2296-5262.

DOI: <https://doi.org/10.1159/000445365>

Diese Version ist verfügbar / This version is available on:

<https://nbn-resolving.org/urn:nbn:de:bsz:14-qucosa2-706009>

„Dieser Beitrag ist mit Zustimmung des Rechteinhabers aufgrund einer (DFGgeförderten) Allianz- bzw. Nationallizenz frei zugänglich.“

This publication is openly accessible with the permission of the copyright owner. The permission is granted within a nationwide license, supported by the German Research Foundation (abbr. in German DFG).

www.nationallizenzen.de/

A Questionnaire Study to Assess the Value of the Vulnerable Elders Survey, G8, and Predictors of Toxicity as Screening Tools for Frailty and Toxicity in Geriatric Cancer Patients

Leopold Hentschel^a Anke Rentsch^a Felicitas Lenz^b Beate Hornemann^a Jochen Schmitt^c
Michael Baumann^{a,d} Gerhard Ehninger^{a,b} Markus Schuler^{b,e}

^aUniversity Cancer Center, University Hospital Carl Gustav Carus, Technical University Dresden, Dresden, Germany;

^bDepartment of Internal Medicine I, University Hospital Carl Gustav Carus, Technical University Dresden, Dresden, Germany;

^cCenter for Evidence-Based Healthcare, University Hospital Carl Gustav Carus, Technical University Dresden, Dresden, Germany;

^dDepartment of Radiotherapy and Radiation Oncology, University Hospital Carl Gustav Carus, Technical University Dresden, Dresden, Germany;

^eDepartment of Internal Medicine II, HELIOS Klinikum Emil von Behring, Berlin, Germany

Keywords

Comorbidity · Frailty · Geriatric assessment · Screening · Toxicities

Summary

Background: The aim of this study was to identify an appropriate screening instrument for the identification of frail elderly patients in a tertiary cancer center. In order to improve cancer care for older patients, the use of a geriatric assessment (GA) has been proposed to identify frail patients or those who are at a higher risk for chemotherapy-related toxicities. In busy clinical routine, an appropriate screening instrument could be used to spare time- and resource-consuming application of GA. **Patients and Methods:** We administered the Vulnerable Elders Survey (VES-13), G8 questionnaire, and Predictors of Toxicity (POT) as well as a GA at the first visit of 84 consecutive patients at a single Comprehensive Cancer Center. Analysis for patients' characteristics as well as sensitivity, specificity, and positive and negative predictive value (npv) was conducted. **Results:** The median age of the patients was 73 years (range 63–93 years), 61.9% were male, most (63%) suffered from gastrointestinal tumors, 39.3% had a multiple cancer diagnosis, and 53.6% had metastasis. 30 (35.7%) individuals were classified as 'frail' by the GA. Sensitivity of G8 was 38.3%, and the npv was 63.8%. Sensitivity for VES-13 was 57.1%, and npv was 76.3%. Sensitivity of POT was 72.7%, and the

npv was 80.6%. **Conclusion:** For the first time, the VES-13, G8, and POT are compared in a sample of older German patients. The POT seems to be a sufficient screening tool to identify frail patients in a tertiary referral cancer center and helps to save time and resources compared with a complete GA.

© 2016 S. Karger GmbH, Freiburg

Introduction

Cancer is the predominant cause of death in the elderly population and presents health challenges as cancer rates continue to rise [1, 2]. In order to improve cancer care for older patients with a high risk of enhanced treatment-induced morbidity, international consensus guidelines and position papers on the use of a geriatric assessment (GA) have been created [3–5]. However, older patients are under-represented in clinical trials, resulting in difficulties with incorporating evidence-based clinical decision making for this heterogeneous group of patients [6]. As data are based on younger patients, survival estimates might have to be adjusted [7], making it more difficult to discuss the advantages and disadvantages of treatment in elderly patients. Therefore, cancer therapy and decision making about treatment for older patients exhibit several difficulties, especially, when considering general health status, comorbidities, polypharmacy, and functional and cognitive status.

Table 1. Overview of geriatric assessment (GA) and its measures

Dimension	Instrument	Dimension impaired
Cognition	search of electronic patient files	file contains record of dementia
Psychological distress	NCCN Distress Thermometer	answer ≥ 5
IADL	Instrumental Activities of Daily Living	sum score < 8
Nutritional status	Mini-Nutritional Assessment	sum score ≤ 7
Polypharmacy	single item: 'Do you take more than 3 different kinds of medication per day?'	'yes'
Mobility/falls	single item: 'Did you fall during the last 6 months'	'yes'

Geriatric medicine uses the concept of frailty, despite the lack of an agreed upon definition [8, 9]. Hamaker et al. [9] summarize the characterization of frailty by Rockwood and Mitnitski [10] and Ferrucci et al. [8] as follows: 'a state of decreased physiological reserves, arising from cumulative deficits in several physiological systems and resulting in diminished resistance to stressors'. This more holistic definition conflicts with the original definition by Fried et al. [11], which encompasses criteria such as weight loss, walk time, and kilocalories expended during physical activity as well as cut-offs for these measures. Thus, while Fried emphasizes more measurable physiological aspects, Hamaker focuses on less specific and thereby also less measurable aspects to define frailty.

Despite the differences in defining frailty in terms of creating an effective assessment tool, conducting a geriatric assessment has proven to help predicting toxicity and morbidity [12, 13] and provides better information compared to the performance status judged by the physician [13, 14]. Some screening instruments have been developed to serve as an alternative to a time-consuming gold-standard GA, in order to identify patients at risk. Among others, both the questionnaires G8 and the Vulnerable Elders Survey (VES-13) have been evaluated in routine oncologic practice [3, 15, 16] and used in several studies [3, 9, 17, 18]. Heterogeneous reporting is found concerning the superiority of one instrument versus the other. While some data indicate no differences [9], others show that the sensitivity of the G8 is higher than that of the VES-13 and vice versa for specificity [18]; however, both the G8 and VES-13 are superior to most other screening measures [3].

Hurria et al. [19, 20] developed and evaluated the Predictors of Toxicity (POT), a primarily self-administered questionnaire derived from geriatric domains to directly predict toxicity in elderly people undergoing chemotherapy. Similarly, both the G8 and the VES-13 have also been used to predict treatment-related toxicity [21]. Additionally, single domains from the GA have been identified to be of prognostic value for toxicities in elderly patients undergoing chemotherapy [12, 22, 23].

Patients presenting at our tertiary cancer center are often diagnosed with advanced disease [24]. Stage at diagnosis depends on the respective entity, and the predominant tumor sites in this study were gastrointestinal, seldom diagnosed at a localized stage [25]. Besides predicting functional decline and overall survival [26, 27] as well as quality of life [28], one of the most important aims of a screening instrument in routine use is to predict toxicity from systemic cancer treatment in an attempt to improve cancer care.

Ultimately, even if VES-13 and G8 were developed to screen for frailty and POT was developed for predicting the different construct of chemotherapy-related toxicities, all of the above tools aim to identify vulnerable patients. A comparison of the G8, VES-13, and POT is both necessary and interesting before implementing them in routine oncologic use in a tertiary referral cancer center, especially since no formal comparison of the most widely used instruments exists in older German patients.

Patients and Methods

Patients and Procedure

Patients were screened as part of their routine care at their first respective appointment for treatment of hematologic or oncologic diseases at the Comprehensive Cancer Center. As the applied questionnaires were part of routine admission procedure, all consecutive patients who consented to participate were eligible. This paper describes a subsample of patients older than 63 years. A GA and 3 geriatric screening instruments VES-13, G8, and POT were administered as part of the routine admission questionnaire on the patients' first visit to the hospital. A printed form was handed out to the patients, and the questionnaire was self-administered. Additional information was derived from the patients' files by medical documentarists. Patient data was obtained as part of the routine admission procedure, wherein patients consented to provide answers on the used questionnaires and to their data being processed and analyzed. No data of a sole individual is shown, all results are presented as merged data.

For the VES-13, complete data were obtained for analysis of psychometric parameters in 59 (70.2%) patients; for the G8, data could be used for 63 (75.0%) patients, and for the POT, 57 (67.9%) patients could be included. 39 (46.2%) patients completed all 3 instruments, 25 (29.8%) patients completed 2 instruments, 12 (14.3%) patients completed 1 screening. 8 patients did not answer enough questions for calculation of any screening instrument.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Ethical approval was obtained from the responsible ethics committee, and patients signed informed consent prior to study inclusion.

Geriatric Assessment

There is no consensus on the type, measurement, and cut-off of specific domains to be included in a GA [29–31]. Most studies aiming to conduct a GA differ in the actual construct being measured [9]. The GA in this study included measures of 6 domains: cognition, psychological distress, instrumental activities of daily living (IADL), nutritional status, polypharmacy, and falls. These domains were assessed as patient-reported outcomes based on well-established questionnaires and by manually searching the patients' previous health records.

Details on the measurements and scoring of each of these dimensions can be obtained from table 1. Previously published cut-off values for the identification of frail dimensions were used whenever available: the Distress Thermometer [32] for assessing psychological distress, the Short-Form Mini-Nutritional Assessment [33] for nutritional status, and the IADL of Lawton and Brody [34]. If no such score was available (polypharmacy, falls, diagnosis of cognitive impairment such as dementia), a positive record in the patient's file was set as identifying a dimension as being frail. There is no consensus on how many dimensions of a GA should be impaired for classifying a patient as frail; studies use several different criteria [29–31]. Frailty was defined as 2 or more of the dimensions included in our GA being identified as 'impaired' [9], in order to specify a cut-off value to prevent patients being casually classified as frail and to avoid ceiling effects.

Screening Measures

Vulnerable Elders Survey – VES-13

Screening was conducted using the VES-13, a well-established and validated 13-item screening tool, to identify the risk for death or functional decline in the geriatric population. This instrument was first tested in a sample of more than 6,200 people aged 65 years or older with different diseases. Patients exceeding or equaling the cut-off of 3 points are at a 4.2 times higher risk of death or functional decline in the next 2 years compared to those below the cut-off [35, 36]. We applied the same cut-off in our study.

Geriatric Screening Tool – G8

The G8 was introduced by Bellera et al. [16] in 2012 as a physician-assessed tool to identify geriatric cancer patients for whom the administration of a time-consuming comprehensive GA would be beneficial. Patients can fill in this instrument with the assistance of a healthcare professional as described by Soubeyran et al. [18], even if the G8 was not developed as a self-administered tool. The G8 consists of 7 items based on the Mini-Nutritional Assessment [33] and a single item covering the patient's age. This instrument was first tested in more than 360 cancer patients aged 70 years or older. Patients falling below the cut-off of 14 points are recommended to complete a GA [16]. This cut-off was also applied in our study. Currently, there are no studies reporting test-retest reliability or interrater reliability. Soubeyran et al. [18] reported a Cohen's kappa of 0.65 between G8 and the respective items of a separately assessed Mini-Nutritional Assessment.

Predictors of Toxicity – POT

The POT was used as a screening system for chemotherapy-related toxicities. The POT consists of different items and parameters covering geriatric conditions (i.e., falls, liver or kidney disease), laboratory values (i.e., albumin, hemoglobin), activities of daily living, and tumor-related information (i.e., dosage of chemotherapy, type of cancer). Answers were provided by healthcare professionals using both laboratory data and patient files. This instrument was first tested in 500 tumor patients. According to the patients' scores, ranging from 0 (indicating low risk) to 23 (indicating high risk), patients are classified into groups indicating low (0–5 points), intermediate (6–9 points), or severe risk (10–23 points) for side effects [20]. In this study, every patient with a score equal to or above 9 points was considered frail.

Furthermore, the performance status developed by the Eastern Cooperative Oncology Group (ECOG) was assessed [37]. This measure describes a patient's level of functioning, i.e., caring for him-/herself, physical ability, and daily activity. It ranges from 0 ('fully active') to 5 ('dead') and is assessed by a healthcare professional.

Statistical Analysis

We conducted analyses for sensitivity, specificity, positive and negative predictive value of the screening-tools and our GA, as well as their respective 95% confidence intervals (CI) by using Excel 2010 (Microsoft, Redmond, WA, USA)

Table 2. Patient characteristics

Characteristics	
Median age (range), years	73 (63–93)
	Patients, n (%)
Sex	
Female	32 (38.1)
Male	52 (61.9)
ECOG score	
0	24 (28.6)
1	22 (26.1)
2	3 (3.6)
3	2 (2.4)
4	0 (0.0)
Not available	33 (39.3)
Multiple cancer diagnosis	
Yes	33 (39.3)
No	51 (60.7)
Patients with metastases	
Yes	45 (53.6)
No	39 (46.4)
Cancer type (n = 125 ICD diagnoses ^a)	
Gastrointestinal	64 (51.2)
Mesothelial and soft tissue	6 (4.8)
Male genital organs	4 (3.2)
Malignant neoplasm of the breast	6 (4.8)
Malignant neoplasms, primary, of lymphoid, hematopoietic, and related tissues	3 (2.4)
Melanoma and other skin	11 (8.8)
Neoplasms of uncertain or unknown behavior	7 (5.6)
Respiratory and intrathoracic organs	7 (5.6)
Urinary tract	8 (6.4)
Other	9 (7.2)

^aMultiple diagnoses per patient were counted separately.

and SPSS 22 (IBM Corp., Armonk, NY, USA) [38]. Sensitivity measures the number of patients with a positive screening among all frail patients. Specificity measures the number of patients with a negative screening among all healthy patients. Positive predictive outcome describes the number of frail patients among all patients screened positive. Negative predictive outcome describes the number of healthy patients among all patients screened negative.

Furthermore, we used for each screening tool separate receiver operating characteristic (ROC) curves to analyze the diagnostic performance of all 3 screening tools against the GA. The area under the curve (AUC) was calculated as a measure of overall predictive quality of the respective instrument.

Results

Sample Description

A total of 84 consecutive geriatric patients of a German cancer center were included from 04/2013 to 06/2013 in this cross-sectional cohort study. For this sample, 'geriatric' was defined as being 63 years of age or older. Patient characteristics are summarized in table 2. The median age of the study patients was 73 years (range 63–93 years). 61.9% were male. Almost 40% had a multiple cancer diagnosis, and more than 50% had metastatic disease.

Table 3. Prevalence of geriatric impaired dimensions

Domain	Patients with impaired dimension (assessable patients)		
	overall	female	male
Cognition	2 (83)	1 (32)	1 (51)
Psychological distress	48 (70)	20 (26)	28 (44)
Instrumental activities of daily living	23 (47)	13 (25)	10 (22)
Nutritional status	1 (63)	1 (27)	0 (36)
Polypharmacy	29 (84)	13 (32)	16 (52)
Falls	4 (84)	1 (32)	3 (52)
	Patients with CGA classification, n (% of total)		
	overall	female	male
Classification as 'frail' by geriatric assessment	30	17 (20.2)	13 (15.5)
Classification as non-frail by geriatric assessment	54	15 (17.9)	39 (46.4)
Mean count of impaired dimensions		1.5	1.1

Table 4. Diagnostic parameters of the Vulnerable Elders Survey (VES-13), G8 questionnaire, and Predictors of Toxicity (POT)

	VES-13 (n = 59), % (95% CI)	G8 (n = 63), % (95% CI)	POT (n = 57), % (95% CI)
Sensitivity	57.1 (44.5–69.8%)	38.3 (25.9–50.7%)	72.7 (61.2–84.3%)
Specificity	79.2 (68.8–89.5%)	62.5 (50.1–74.9%)	65.2 (52.9–77.6%)
Positive predictive value	61.2 (48.7–73.6%)	37.0 (24.6–49.3%)	54.6 (41.6–67.5%)
Negative predictive value	76.3 (65.4–87.1%)	63.8 (51.6–76.1%)	80.6 (70.4–90.9%)

Frail Patients

Frailty was defined as equaling or exceeding 2 'impaired' dimensions. Out of 84 patients, 30 (35.7%) individuals were classified as 'frail' by the GA. Among those, a complete GA was available in 21 patients. In non-frail patients, a full GA was available in 16 individuals. 22 persons had 2 impaired dimensions, 7 individuals held 3 impaired dimensions, and 1 patient held 4 impaired dimensions. At least 5 out of 6 dimensions of the GA were available for 65 (77.4%) patients. Of all the patients classified as frail, 13 (43.3%) were male and 17 (56.7%) female. Overall, female patients seemed to have more impaired dimensions (mean 1.5) than their male counterparts (mean 1.1; $t(54) = 2.01$) ($p < 0.05$). Details on which dimensions were impaired can be obtained from table 3. The mean age of the patients classified as frail was 72.2 years, whereas patients not classified as frail were on average 73.4 years old, a difference that failed to reach statistical significance ($t(82) = 1.08$; $p = 0.370$). The ECOG performance status was obtained in 51 patients (20 frail and 31 non-frail) and was ECOG = 0 in 24 patients, ECOG = 1 in 22 patients, ECOG = 2 in 3 patients, and ECOG = 3 in 2 patients. Patients classified as frail received a higher averaged ECOG status ($= 0.850$) than the non-frail group ($= 0.548$), a difference that failed to reach statistical significance ($t(49) = 1.72$; $p = 0.172$).

Predictive Value of Screening Instruments

The 3 geriatric screening instruments were assessed for their sensitivity, specificity, positive predictive value, and negative predictive value for identifying patients as 'frail' using a GA.

As seen in table 4, the sensitivity of VES-13 was 57.1% (95% CI 44.5–69.8%), specificity was 79.2% (95% CI 44.5–69.8%), the posi-

tive predictive value was 62.1% (95% CI 48.7–73.6%), and the negative predictive value was 76.3% (95% CI 65.4–87.1) based on the analysis of 59 patients. Out of these, 35 (59.3%) patients exceeded the cut-off. The mean VES-13 score was 5.4 (standard deviation (SD) 2.7) for patients being classified as frail by the GA, whereas patients that were being classified as non-frail had a mean score of 3.1 (SD 2.6), a difference that was highly significant ($p = 0.002$).

As demonstrated in table 4, the sensitivity of the G8 was 38.3% (95% CI 25.9–50.7%), specificity was 62.5% (95% CI 50.1–74.9%), the positive predictive value was 37.0% (95% CI 24.6–49.3%), and the negative predictive value was 63.8% (95% CI 51.6–76.1%) based on the analysis of 63 patients. Of these, 47 (74.6%) patients scored below the cut-off. The mean G8 score was 11.9 (SD 2.4) for patients being classified as frail by the GA. Persons being classified as non-frail had a mean score of 13.3 (SD 2.0), a difference that was highly significant ($p = 0.025$).

As shown in table 4, the sensitivity of POT was 72.7% (95% CI 61.2–84.3%), specificity was 65.2% (95% CI 52.9–77.6%), the positive predictive value was 54.6% (95% CI 41.6–67.5%), and the negative predictive value was 80.6% (95% CI 70.4–90.9%) based on the analysis of 57 patients. Of these, 11 (19.3%) patients exceeded the cut-off. The mean POT score was 10.8 (SD 3.2) for patients being classified as frail by the GA, whereas patients classified as non-frail had a mean score of 8.4 (SD 2.7), a difference that was highly significant ($p = 0.004$).

Compared Predictive Performance

The ROC curves of the VES-13 (AUC = 0.733), the G8 (AUC = 0.350), and the POT (AUC = 0.725) are presented in figure 1 a–c.

Fig. 1. Receiver operating characteristic analysis of **a** the Vulnerable Elders Survey (VES-13), **b** G8 questionnaire, and **c** Predictors of Toxicity (POT) (straight black line = area under the curve; dashed line = reference line of 'no discrimination').

Discussion

To our knowledge, this study is the first to compare the predictive qualities of G8, VES-13, and POT in a prospective trial in a sample of elderly cancer patients in Germany. Our study reports on a patient group referred to a tertiary cancer center. Therefore, the results provide useful information applicable to everyday situations in a tertiary cancer center when trying to evaluate the predictive characteristics of these geriatric screening instruments and their feasibility in oncology practice.

Compared with a full GA and the other screening tools, the G8 shows limited predictive qualities. Ultimately, the predictive quality of the G8 in our study was below that reported by others (sensitivity of 92% [31] and 85% [16]). When comparing those results, we found some differences regarding the study population. First, the percentage of patients with an abnormal screening score presented in the other studies was much higher (76–82%) as compared to our study population (36%). In a further step, we looked in more detail at the different cut-off values for G8 used in other studies. Bellera et al. [16] proposed a value of ≤ 14 as the preferred cut-off for identification of elderly frail patients as we did in our study. In contrast, Baitar et al. [31] used a different approach and calculated the predictive parameters for different cut-offs of G8. Applying the same procedure for explorative reasons, an alternative G8 cut-off of ≤ 11 produces the best sensitivity of 73% and a specificity of 73%. A third difference concerns the age of the study populations: The median age of the population of Bellera et al. [16] was 77 years, whereas the median age in our group was 73 years. Patients with gastrointestinal cancer comprised 38% in that study, while our study indicated a higher rate of 51.2%. Another substantial difference was the rate of hematologic patients (30%) compared to our study (2%). Moreover, the G8 predominately relies on malnutrition, which might limit the predictive quality for patients that are compromised in that way while others could be overlooked. In conclusion, the differences in accuracy could be ascribed to the fact that our patient population does not compare well with the others. Since tumor location and histology can impact the ability to detect patients at risk [21, 39], a more detailed definition of the target population might be needed in order to achieve maximum accuracy.

The VES-13 shows moderate sensitivity and a moderate positive predictive outcome, as well as good specificity and negative predictive outcome. Interestingly, the accuracy for the VES-13 was very comparable to the data reported by others [17, 18, 29, 40]. The AUC of the VES-13 was bigger than that of the G8 and comparable to the AUC found by Luciani et al. [15], but smaller than that found by Mohile et al. [41]. When comparing these 2 screening instruments for frailty, the VES-13 is more sensitive than the G8 in identifying frail patients. Although the sensitivity is not as high as the minimal acceptable sensitivity of 85% predefined by Smets et al. [42], it is well in line with the results of several studies reviewed by Decoster et al. [3]. For identifying patients not in need of a further assessment based on a GA, the VES-13 is also more specific than the G8. These findings are in contrast to those reported by Soubeyran et al. [18] who observed a superiority of the G8 regarding sensitivity. For typical patients of a tertiary cancer center, the VES-13 seems to be a sufficient screening tool to identify frail patients; however, it is still only slightly better than identifying patients by chance. More importantly, the combination of both instruments (VES-13 and G8), as tested by others [40, 43], did not show superior results in our group (data not shown).

The POT, which was developed and introduced much more recently, shows a high sensitivity and moderate positive predictive outcome as well as good specificity and a high negative predictive value. Therefore, the POT seems to be a promising instrument not

only in predicting chemotherapy-associated toxicities but also in detecting patients in geriatric oncology that are at risk in general. This would be another reason to choose the POT over other screening instruments since it can be used to predict toxicity further on in the course of treatment.

We also observed a difference in ECOG status in patients classified as frail by the GA. These patients have a worse ECOG status than those classified as non-frail. This effect failed to reach significance, which is strikingly interesting, as ECOG performance status is frequently used as a criterion for chemotherapy dosage [14] and for frailty screening [44]. Additionally, Wildes et al. [45] found that ECOG is not significantly associated with grade III or IV toxicities or mortality prediction. Therefore, besides other relevant factors for dosage of chemotherapy, a GA or an appropriate screening could contribute to decision making about the dosage of chemotherapy in frail patients beyond the ECOG.

Furthermore, our data indicated an unexpected finding. There was a non-significant difference between the age of frail (72.2 years) and non-frail (73.4 years) patients. The non-frail group was older than those classified as frail, indicating that in clinical routine, age should definitely not be used as an 'ultra-short' and easy-to-administer screening for frailty.

This study also has some limitations. Since it was carried out in the framework of the daily routine admission procedure at a tertiary cancer center and not as a predefined study, the GA could not solely use methodologically elaborated questionnaires due to both time and resource constraints. For example, we measured mobility with a single-item question instead of using standardized methods such as the Timed Up & Go test [46] or the 'Ten-meter Timed Walk Test' [47], and cognition was assessed by manual search of electronic patient files in our tumor documentation system instead of applying a more elaborate instrument such as those described by Lange et al. [48]. Ultimately, no consensus on 1 definitive GA exists, and therefore most studies differ in what exactly is being measured [9]. Thus, our study adds to the variety of different approaches of measuring the GA domains. Using single-item questions could contribute to sparing time and resources. The authors are aware that the rate of missing data is a further limitation. As this study was carried out in the framework of routine admission procedures, immediate examination of the data completion rate

was not always possible. Furthermore, time could have been limited by clinical routine, e.g. patients may have had to stop filling in the questionnaires in order to meet their appointment with a treating physician. Additionally, the low number of patients completing all 3 screening instruments limits their comparability. Further trials should focus on this as well as on data integrity by e.g. using electronic devices which were proven to be usable for data collection even in routine care [49–51].

Conclusion

In the search for an appropriate screening tool to identify vulnerable elderly patients without administering a complete GA, the data from our tertiary cancer center have indicated that the POT is the best available tool providing sufficient sensitivity and a high negative predictive value. Since single-item questions can already provide substantial knowledge in a risk assessment [52], it is a challenging and important task for future research to identify easy and quick to perform instruments in selected patient populations to detect frailty and potential harm of therapy.

Online Supplemental Material

Appendix I. VES-13, modified from [36].

Appendix II. G8 questionnaire, modified from [16].

Appendix III. POT questionnaire, modified from [20].

To access the online supplemental material, please refer to www.karger.com/?DOI=445365.

Acknowledgement

We thank Kay Menzel for his support in data collection.

Disclosure Statement

This study did not receive external funding. The authors declare that they have no conflict of interest.

References

- 1 Yancik R: Cancer burden in the aged: an epidemiologic and demographic overview. *Cancer* 1997;80:1273–1283.
- 2 Smith BD, Smith GL, Hurria A, Hortobagyi GN, Buchholz TA: Future of cancer incidence in the United States: burdens upon an aging, changing nation. *J Clin Oncol* 2009;27:2758–2765.
- 3 Decoster L, Van Puyvelde K, Mohile S, Wedding U, Basso U, Colloca G, et al.: Screening tools for multidimensional health problems warranting a geriatric assessment in older cancer patients: an update on SIOG recommendations. *Ann Oncol* 2015;26:288–300.
- 4 Pallis AG, Fortpied C, Wedding U, Van Nes MC, Penninckx B, Ring A, et al.: EORTC elderly task force position paper: approach to the older cancer patient. *Eur J Cancer* 2010;46:1502–1513.
- 5 Wildiers H, Heeren P, Puts M, Topinkova E, Janssen-Heijnen MLG, Extermann M, et al.: International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. *J Clin Oncol* 2014;32:2595–2603.
- 6 Van Bakkum ML, van Munster BC, Thunnissen PLM, Smorenburg CH, Hamaker ME: Current palliative chemotherapy trials in the elderly neglect patient-centered outcome measures. *J Geriatr Oncol* 2015;6:15–22.
- 7 Lamont EB, Schilsky RL, He Y, Muss H, Cohen HJ, Hurria A, et al.: Generalizability of trial results to elderly medicare patients with advanced solid tumors (alliance 70802). *J Natl Cancer Inst* 2015;107:336.
- 8 Ferrucci L, Guralnik JM, Studenski S, Fried LP, Cutler GB, Walston JD, et al.: Designing randomized, controlled trials aimed at preventing or delaying functional decline and disability in frail, older persons: a consensus report. *J Am Geriatr Soc* 2004;52:625–634.
- 9 Hamaker ME, Jonker JM, de Rooij SE, Vos AG, Smorenburg CH, van Munster BC: Frailty screening methods for predicting outcome of a comprehensive geriatric assessment in elderly patients with cancer: a systematic review. *Lancet Oncol* 2012;13:e437–e444.

- 10 Rockwood K, Mitnitski A: Frailty defined by deficit accumulation and geriatric medicine defined by frailty. *Clin Geriatr Med* 2011;27:17–26.
- 11 Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al.: Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56:M146–M157.
- 12 Aparicio T, Jouve J-L, Teillet L, Gargot D, Subtil F, Le Brun-Ly V, et al.: Geriatric factors predict chemotherapy feasibility: ancillary results of FFCO 2001–02 phase III study in first-line chemotherapy for metastatic colorectal cancer in elderly patients. *J Clin Oncol* 2013;31:1464–1470.
- 13 Extermann M, Aapro M, Bernabei R, Cohen HJ, Droz J-P, Lichtman S, et al.: Use of comprehensive geriatric assessment in older cancer patients: recommendations from the task force on CGA of the International Society of Geriatric Oncology (SIOG). *Crit Rev Oncol Hematol* 2005;55:241–252.
- 14 Tucci A, Ferrari S, Bottelli C, Borlenghi E, Drera M, Rossi G: A comprehensive geriatric assessment is more effective than clinical judgment to identify elderly diffuse large cell lymphoma patients who benefit from aggressive therapy. *Cancer* 2009;115:4547–4553.
- 15 Luciani A, Ascione G, Bertuzzi C, Marussi D, Codecà C, Maria GD, et al.: Detecting disabilities in older patients with cancer: comparison between comprehensive geriatric assessment and Vulnerable Elders Survey-13. *J Clin Oncol* 2010;28:2046–2050.
- 16 Bellera CA, Rainfray M, Mathoulin-Pélissier S, Mertens C, Delva F, Fonck M, et al.: Screening older cancer patients: first evaluation of the G-8 geriatric screening tool. *Ann Oncol* 2012;23:2166–2172.
- 17 Monfardini S, Basso U, Fiduccia P, Brunello A, Baretta Z, Soldà C, et al.: Can the short screening test Vulnerable Elders Survey 13 (VES-13) substitute for the time-consuming comprehensive geriatric assessment (CGA) to identify vulnerable/frail elderly breast cancer patients. *ASCO Annual Meeting* 2010. *J Clin Oncol* 2010;28(15 suppl):abstr 9114.
- 18 Soubeyran P, Bellera C, Goyard J, Heitz D, Curé H, Rousselot H, et al.: Screening for vulnerability in older cancer patients: the ONCODAGE Prospective Multicenter Cohort Study. *PLoS ONE* 2014;9:e115060.
- 19 Hurria A, Gupta S, Zauderer M, Zuckerman EL, Cohen HJ, Muss H, et al.: Developing a cancer-specific geriatric assessment. *Cancer* 2005;104:1998–2005.
- 20 Hurria A, Togawa K, Mohile SG, Owusu C, Klepin HD, Gross CP, et al.: Predicting chemotherapy toxicity in older adults with cancer: a prospective multicenter study. *J Clin Oncol* 2011;29:3457–3465.
- 21 Stokoe JM, Pearce J, Sinha R, Ring A: G8 and VES-13 scores predict chemotherapy toxicity in older patients with cancer. *J Geriatr Oncol* 2012;3:S81.
- 22 Falandry C, Brain E, Bonnefoy M, Mefti F, Jovenin N, Rigal O, et al.: Impact of geriatric risk factors on pegylated liposomal doxorubicin tolerance and efficacy in elderly metastatic breast cancer patients: final results of the DOGMES multicentre GINECO trial. *Eur J Cancer* 2013;49:2806–2814.
- 23 Extermann M, Boler I, Reich RR, Lyman GH, Brown RH, DeFelice J, et al.: Predicting the risk of chemotherapy toxicity in older patients: the Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score. *Cancer* 2012;118:3377–3386.
- 24 Trautmann F, Hentschel L, Hornemann B, Rentsch A, Baumann M, Ehninger G, et al.: Electronic real-time assessment of patient-reported outcomes in routine care—first findings and experiences from the implementation in a comprehensive cancer center. *Support Care Cancer* 2016;Epub ahead of print.
- 25 Siegel R, DeSantis C, Virgo K, Stein K, Mariotto A, Smith T, et al.: Cancer treatment and survivorship statistics, 2012. *CA Cancer J Clin* 2012;62:220–241.
- 26 Hoppe S, Rainfray M, Fonck M, Hoppenreys L, Blanc J-F, Ceccaldi J, et al.: Functional decline in older patients with cancer receiving first-line chemotherapy. *J Clin Oncol* 2013;31:3877–3882.
- 27 Kenis C, Decoster L, Van Puyvelde K, De Grève J, Conings G, Milisen K, et al.: Performance of two geriatric screening tools in older patients with cancer. *J Clin Oncol* 2014;32:19–26.
- 28 Pottel L, Lycke M, Boterberg T, Pottel H, Goethals L, Duprez F, et al.: G-8 indicates overall and quality-adjusted survival in older head and neck cancer patients treated with curative radiochemotherapy. *BMC Cancer* 2015;15:875.
- 29 Kellen E, Bulens P, Deckx L, Schouten H, Van Dijk M, Verdonck I, et al.: Identifying an accurate pre-screening tool in geriatric oncology. *Crit Rev Oncol Hematol* 2010;75:243–248.
- 30 Molina-Garrido MJ, Guillen-Ponce C: Comparison of two frailty screening tools in older women with early breast cancer. *Crit Rev Oncol Hematol* 2011;79:51–64.
- 31 Baitar A, Van Fraeyenhove F, Vandebroek A, De Droogh E, Galdermans D, Mebis J, et al.: Evaluation of the Groningen Frailty Indicator and the G8 questionnaire as screening tools for frailty in older patients with cancer. *J Geriatr Oncol* 2012;4:32–38.
- 32 Mehnert A, Müller D, Lehmann C, Koch U: Die deutsche Version des NCCN Distress-Thermometers: Empirische Prüfung eines Screening-Instrumentes zur Erfassung psychosozialer Belastung bei Krebspatienten. *Zeitschrift für Psychiatrie, Psychologie und Psychotherapie* 2006;54:213–223.
- 33 Rubenstein LZ, Harker JO, Salvà A, et al.: Screening for undernutrition in geriatric practice: developing the Short-Form Mini-Nutritional Assessment (MNA-SF). *J Gerontol A Biol Sci Med Sci* 2001;56:M366–M372.
- 34 Lawton MP, Brody EM: Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist* 1969;9:179–186.
- 35 Min LC, Elliott MN, Wenger NS, Saliba D: Higher Vulnerable Elders Survey Scores Predict Death and Functional Decline in Vulnerable Older People. *J Am Geriatr Soc* 2006;54:507–511.
- 36 Saliba D, Elliott M, Rubenstein LZ, Solomon DH, Young RT, Kamberg CJ, et al.: The Vulnerable Elders Survey: a tool for identifying vulnerable older people in the community. *J Am Geriatr Soc* 2001;49:1691–1699.
- 37 Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, et al.: Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol* 1982;5:649–655.
- 38 IBM SPSS Statistics for Windows, version 22.0. New York, NY, IBM Corporation, 2013.
- 39 Dubruielle S, Bron D, Roos M, Vandenbossche S, Meuleman N, Maerevoet M, et al.: The respective usefulness of the G8 and a comprehensive geriatric assessment (CGA) to predict intolerance to chemotherapy and survival of fit and vulnerable older patients with hematological malignancies. *J Geriatr Oncol* 2013;4:S56.
- 40 Soubeyran P, Bellera C, Goyard J: Validation of the G8 screening tool in geriatric oncology: the ONCODAGE project. *J Clin Oncol* 2011;29(suppl):abstr 9001.
- 41 Mohile SG, Bylow K, Dale W, Dignam J, Martin K, Petrylak DP, et al.: A pilot study of the vulnerable elders survey-13 compared with the comprehensive geriatric assessment for identifying disability in older patients with prostate cancer who receive androgen ablation. *Cancer* 2007;109:802–810.
- 42 Smets IHGJ, Kempen GJIM, Janssen-Heijnen MLG, Deckx L, Buntinx FJVM, van den Akker M: Four screening instruments for frailty in older patients with and without cancer: a diagnostic study. *BMC Geriatr* 2014;14:26.
- 43 Pottel L, Boterberg T, Pottel H, Goethals L, Van Den Noortgate N, Duprez F, et al.: Determination of an adequate screening tool for identification of vulnerable elderly head and neck cancer patients treated with radio(chemo)therapy. *J Geriatr Oncol* 2012;3:24–32.
- 44 Owusu C, Koroukian SM, Schluchter M, Bakaki P, Berger NA: Screening older cancer patients for a Comprehensive Geriatric Assessment: a comparison of three instruments. *J Geriatr Oncol* 2011;2:121–129.
- 45 Wildes TM, Ruwe AP, Fournier C, Gao F, Carson KR, Piccirillo JF, et al.: Geriatric assessment is associated with completion of chemotherapy, toxicity, and survival in older adults with cancer. *J Geriatr Oncol* 2013;4:227–234.
- 46 Podsiadlo D, Richardson S: The timed 'Up & Go': a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc* 1991;39:142–148.
- 47 Dean CM, Richards CL, Malouin F: Walking speed over 10 metres overestimates locomotor capacity after stroke. *Clin Rehabil* 2001;15:415–421.
- 48 Lange M, Rigal O, Clarisse B, Giffard B, Sevin E, Barillet M, et al.: Cognitive dysfunctions in elderly cancer patients: a new challenge for oncologists. *Cancer Treat Rev* 2014;40:810–817.
- 49 Atreja A, Rizk M: Capturing patient reported outcomes and quality of life in routine clinical practice: ready for prime time? *Minerva Gastroenterol Dietol* 2012;58:19–24.
- 50 Kallen MA, Yang D, Haas N: A technical solution to improving palliative and hospice care. *Support Care Cancer* 2011;20:167–174.
- 51 Hilarius DL, Kloeg PH, Gundy CM, Aaronson NK: Use of health-related quality-of-life assessments in daily clinical oncology nursing practice. *Cancer* 2008;113:628–637.
- 52 Pergolotti M, Deal AM, Williams GR, et al.: Health related quality of life (HRQOL) in older adults with cancer: the potential of a single-item screen. *ASCO Annual Meeting* 2015. *J Clin Oncol* 2015;33(suppl):abstr 9533.