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Accuracy of the G-8 geriatric-oncology screening tool for identifying vulnerable elderly patients with cancer according to tumour site: The ELCAPA-02 study☆,☆☆

Evelyne Liuu[a,*], *Florence Canouï-Poitrine*[b,c], *Christophe Tournigand*[d], *Marie Laurent*[a,b], *Philippe Caillet*[a,b], *Aurelie Le Thuaut*[b,c,e], *Helene Vincent*[f], *Stephane Culine*[g], *Etienne Audureau*[b,c], *Sylvie Bastuji-Garin*[b,c,e,1], *Elena Paillaud*[a,b,1], *on behalf of the ELCAPA Study Group*[2]

[a]AP-HP, hôpital Henri-Mondor, Department of Internal Medicine and Geriatrics, Onco-Geriatric Clinic, F-94010 Créteil, France
[b]Université Paris Est Créteil (UPEC), LIC EA 4393, F-94010 Créteil, France
[c]AP-HP, hôpital Henri-Mondor, Department of Public Health, F-94010 Créteil, France
[d]AP-HP, hôpital Henri-Mondor, Department of Medical Oncology, F-94010, France
[e]AP-HP, hôpital Henri-Mondor, Clinical Research Unit (URC-Mondor), F-94010 Créteil, France
[f]AP-HP, hôpital Paul-Brousse, Department of Geriatrics, F-94804 Villejuif, France
[g]AP-HP, hôpital Saint-Louis, Department of Medical Oncology, F-75010 Paris, France

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ABSTRACT

Background/Objective: G-8 screening tool showed good screening properties for identifying vulnerable elderly patients with cancer who would benefit from a comprehensive geriatric assessment (CGA). We investigated whether tumour site and metastatic status affected its accuracy.

Materials and Methods: Design: Cross-sectional analysis of a prospective cohort study. Setting: Geriatric-oncology clinics of two teaching hospitals in the urban area of Paris. Participants: Patients aged 70 or over (n = 518) with breast (n = 113), colorectal (n = 108), urinary-tract (n = 89), upper gastrointestinal/liver (n = 85), prostate (n = 69), or other cancers (n = 54). Measurements: Reference standard for diagnosing vulnerability was the presence of at least one abnormal test among the Activities of Daily Living (ADLs), Instrumental ADL, Mini-Mental State Examination, Mini Nutritional Assessment, Cumulative Illness Rating Scale-Geriatrics, Timed Get-Up-and-Go, and Mini-Geriatric Depression Scale. Sensitivity, specificity and likelihood ratios of G-8 scores ≤ 14 were compared according to tumour site and patient characteristics.

Results: Median age was 80; 48.2% had metastases. Prevalence of vulnerability and abnormal G-8 score was 84.2% (95% confidence interval [95% CI], 81–87.3) and 79.5% (95% CI, 76–83).

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☆☆ Collaborators: Isabelle Baumgaertner, Noel Boudjema, Muriel Carvalho-Verlinde, Marie Chaubet, Jean-Leon Lagrange, Nicolette Reynald, and Iradj Sobhani.

* *Corresponding author at:* Service de Médecine Interne et de Gériatrie, hôpital Henri-Mondor, 51, avenue du Maréchal de Lattre de Tassigny, 94010 Créteil Cedex, France. Tel.: +33 1 49 81 27 13; fax: +33 1 49 81 27 17.
E-mail address: evelyne.liuu@hmn.aphp.fr (E. Liuu).

[1] SBG and EP contributed equally to this article.

[2] The ELCAPA Study Group was composed of three oncologists (S. Culine, C. Tournigand, and M. Chaubet), one radiotherapist (J.L. Lagrange), five geriatricians (P. Caillet, M. Laurent, E. Liuu, E. Paillaud, and H. Vincent), two epidemiologists (F. Canouï-Poitrine and S. Bastuji-Garin), one pharmacist (M. Carvahlo-Verlinde), one bio-statistician (A. Le Thuaut), one clinical research medical doctor (N. Reynald), and one clinical research assistant (N. Boudjema).

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The G-8 was 86.9% sensitive (95% CI, 83.4–89.9) and 59.8% specific (95% CI, 48.3–70.4). G-8 performance varied significantly (all p values < 0.001) across tumour sites (sensitivity, 65.2% in prostate cancer to 95.1% in upper gastrointestinal/liver cancer; and specificity, 23.1% in colorectal cancer to 95.7% in prostate cancer) and metastatic status (sensitivity and specificity, 93.8% and 53.3% in patients with metastases vs. 79.5% and 63.3% in those without, respectively). Differences remained significant after adjustment on age and performance status.

Conclusion: These G-8 accuracy variations across tumour sites should be considered when using G-8 to identify elderly patients with cancer who could benefit from CGA.

1. Introduction

The management of elderly patients with cancer is becoming a major public health issue in industrialised countries due to the ageing of the population and the steady increase in cancer incidence with advancing age.[1] Patients older than 65 years account for 60% of all cancers and 70% of cancer deaths.[2] Elderly patients with cancer exhibit variable degrees of co-morbidities, physical reserve limitations, and disability that require specific management strategies. The Comprehensive Geriatric Assessment (CGA) is a multidimensional tool for identifying health problems in elderly patients.[3] The CGA followed by appropriate multidisciplinary interventions can help to optimise cancer treatment strategy, improve treatment completion and survival, and reduce adverse outcomes.[4–8]

However, the CGA is time-consuming. Screening tools are therefore used[9–15] to identify vulnerable elderly patients with cancer who are most likely to benefit from the CGA. A recent review compared the performance of seven geriatric screening tools (abbreviated CGA [aCGA], Vulnerable Elders Survey-13 [VES-13], Geriatric 8 [G-8], Groningen Frailty Index [GFI], Triage Risk Screening Tool [TRST], Fried Frailty Criteria, and Barber).[16] A validation study in elderly patients with head-and-neck cancer[17] and conference abstracts of four studies in elderly patients with various tumour sites suggested that the G-8 may be the most sensitive among these screening tools.[16,18–22] In particular, the ONCODAGE project,[18] a large multicentre prospective study in 1425 elderly patients with solid cancer at various sites or lymphoma, suggested high sensitivity of the G-8 when considering the CGA as the reference exam.

However, in previous studies the performance of the G-8 was estimated globally without any stratification by tumour site or metastatic status. Given the nature of the items explored by the G-8 — food intake, weight loss, motor skills, neuropsychological status, body mass index, number of medications, self-rated health, and age,[9] it is likely that one given tumour may differentially impact the G-8 dimensions, and thus might modify the performance of the G-8 to detect vulnerability. In addition, assessing this potentially varying accuracy is of crucial importance within the field of oncology, where oncologists and centres enrolling patients are often specialized in the treatment of one given tumour site (e.g. breast, digestive tract, urologic, hematologic) and for whom average diagnostic performance is not relevant. Finally, according to the Standards for the Reporting of Diagnostic accuracy studies (STARD), estimates of variations in diagnostic accuracy across subgroups of participants, readers, or centres are essential when developing a new diagnosis/screening test.[23] We hypothesized that G-8 accuracy might vary according to tumour site and metastatic disease status. To test this hypothesis, we assessed G-8 accuracy by tumour site and metastatic disease status in a large cohort of elderly patients with cancer.

2. Patients and Methods

2.1. Study Design and Population

We performed a cross-sectional analysis of data from the prospective open ELCAPA (ELderly CAncer PAtient) cohort of consecutive in- and out-patients aged 70 years or older who had histologically documented cancer and were referred to one of two geriatric-oncology clinics in teaching hospitals in the urban area of Paris, France. Inclusion started in January 2007. Study inclusion occurred on the day of the first geriatric-oncology visit. For the present study, we selected all patients with solid cancer recruited between January 2007 and December 2011 who had complete CGA and G-8 data. Informed consent was obtained from all study patients prior to inclusion. The protocol was approved by the appropriate ethics committee (CPP Ile-de-France I, Paris, France).

2.2. Study Data

The following data were abstracted from the database: baseline patient characteristics, age, sex, tumour site, metastatic disease status, Eastern Cooperative Oncology Group Performance Status (ECOG-PS), and CGA. At inclusion in the cohort, each patient underwent the multidimensional CGA, which has been described in detail in a prior study.[24] The CGA uses validated tests and scores to assess nine domains according to international recommendations: functional status (Activity of Daily Living, ADL,[25] and Instrumental Activities of Daily Living, IADLs), mobility (Timed Get-Up-and-Go test, GUG),[26] nutritional status (MNA),[27] cognitive status (Mini-Mental State Examination MMSE),[28] mood (Mini-Geriatric Depression Scale, mini-GDS),[29] co-morbidities (Cumulative Illness Rating Scale for Geriatrics, CIRS-G),[30] polypharmacy (number of medications), social environment, and urinary and/or faecal incontinence. All items of these tests were recorded in the standardized ELCAPA Case-Report Form and the final scores were implemented prospectively in the data set. The CGA was performed by a senior geriatrician specialized in oncology (PC). The G-8 score, which was not available in the database, was collected retrospectively from

the standardized ELCAPA Case-Report Form between January and March 2012 by a geriatrician (EL), who was blinded to CGA results.

2.2.1. *Abnormal Reference Exam*

The reference standard for diagnosing vulnerability was an abnormal result on at least one of seven validated tests included in the CGA, namely, ADL ≤ 5, IADL ≤ 7, MMSE ≤ 23, mini-GDS ≥ 1, MNA ≥ 23.5, CIRS-G: at least one comorbidity grade 3 or 4 and GUG ≥ 20 s. The tests for the reference exam were from the G-8 development study except depressed mood assessment as GDS-15 which was replaced by the mini-GDS in our study.[9] Similarly, chosen cut-offs were used in the G-8 development study and corresponded to validated thresholds of the original tests for MMSE, mini-GDS, MNA and GUG.[9]

We performed two sensitivity analyses: 1) vulnerability was defined as abnormal results on at least two of the seven tests; and 2) we included in the analysis patients with at least one altered CGA domain, even if other CGA parameters were missing.

2.2.2. *G-8 Screening Tool*

The G-8 has eight items, taking into account nutritional data, motor skills, neuropsychological status, medication, self-rated health, and age.[9] Seven of these items were selected from the Mini Nutritional Assessment (MNA) questionnaire.[27] We used the cut-offs identified in the construction sample as indicating vulnerability with a need for a CGA, namely, a G-8 score ≤ 14.[9]

2.3. *Statistical Analysis*

Patient and cancer characteristics, reference test scores, and G-8 item scores were described as numbers and percentages for qualitative variables and as medians with 25th and 75th percentiles (quartile 1 to quartile 3, Q1–Q3), for quantitative variables.

2.3.1. *Overall Accuracy of the G-8 Score*

G-8 score accuracy was evaluated in the overall study population based on sensitivity and specificity with their 95% confidence intervals (95% CIs) and percentage of correctly classified patients. The positive likelihood ratio (PLR) and negative likelihood ratio (NLR) were also estimated. A LR expresses the odds that a given result of a diagnostic test (positive or negative) would be expected in a patient with (as opposed to one without) a target disorder. By contrast with predictive values, LR is independent of prevalence.

2.3.2. *G-8 Accuracy According to Tumour Site and Other Factors Associated with G-8 Accuracy*

To investigate whether G-8 accuracy differed across tumour site, we considered six sites: colon/rectum, breast, prostate, urinary tract, liver and upper gastrointestinal tract, and other disease sites (unknown primary, lung, sarcoma, skin, head-and-neck, brain, small intestine, penis, endometrial, ovarian and germinal). Patient characteristics, reference test scores, and G-8 items were compared across these six groups using Pearson's chi-square test for qualitative variables and the nonparametric Kruskal–Wallis test for quantitative variables. G-8 accuracy was then assessed for each site separately and the results were compared across sites.

Factors affecting the G-8 sensitivity were defined as those that affected the likelihood of an abnormal G-8 among patients with an abnormal reference exam. Factors affecting G-8 specificity were defined as factors affecting the likelihood of a normal G-8 score in patients with a normal reference exam. Univariate and multivariate age-adjusted logistic regression analyses were performed to identify factors that independently influenced sensitivity or specificity, i.e. predicting false negatives or false positives, respectively. Odds ratios (ORs) were estimated with their 95% CIs.

All tests were two-tailed. p-Values lower than 0.05 were considered significant. For pairwise comparisons among tumour-site groups, a Bonferroni's correction was applied. No multiple imputation was performed for missing data. The data were analysed using STATA statistical software (STATA 2005, release 11.0; College Station, TX, USA). This observational study is reported according to the STARD checklist for diagnostic accuracy studies.[23]

3. Results

Of the 773 ELCAPA cohort patients with solid cancer, 518 were included in the ELCAPA-02 study (Fig. 1). Missing data were due to unavailable data regarding the extensive IADL test (8 items) (only the short IADL test [4 items] was available) leading to unavailable reference exam. Compared to patients that were included, patients with missing data for reference tests or G-8 (n = 255) more often had digestive cancer (colon/rectum, upper gastrointestinal tract, and liver) and an ECOG-PS ≥ 2. Neither age nor the proportion of patients with metastatic disease differed significantly between the two groups (data not shown). Table 1 lists the main patient characteristics. Median age was 80 years (25–75th percentiles: 76–84) and 52.1% were men. The most common tumour sites were the breast (21.8%) and colon/rectum (20.8%). Overall, 67% (n = 348) of the study population were outpatients. As expected, outpatients were less likely to have metastases (38% vs. 70%, p < 0.001), colorectal cancer (18% vs. 27%, p < 0.001), liver or upper gastrointestinal tract cancer (11% vs. 28%, p < .001), ECOG-PS ≥ 2 (33% vs. 71%, p < 0.001), impaired CGA parameters (at least one impaired score 78% vs. 96%, p < 0.001) and abnormal G-8 (71% vs. 97%, p < 0.001) when compared to inpatients.

Overall, 436 patients (84.2%; 95% CI, 81–87.3) had at least one abnormal reference test and 412 patients (79.5%; 95% CI, 76–83) had a G-8 score ≤ 14. Moreover, 29.6% of patients with an abnormal G-8 had a normal MNA test.

3.1. *Overall Accuracy of the G-8 Score*

Sensitivity was 86.9% (95% CI, 83.4–89.9), specificity was 59.8% (95% CI, 48.3–70.4), PLR was 2.16 (1.66–2.82), and NLR was 0.22 (95% CI, 0.16–0.30). In the sensitivity analysis using at least two abnormal reference tests to define vulnerability, sensitivity of the G-8 was significantly higher (93.4%; 95% CI, 90.6–95.9) and specificity slightly lower (52.9%; 95% CI, 44.8–60.9).

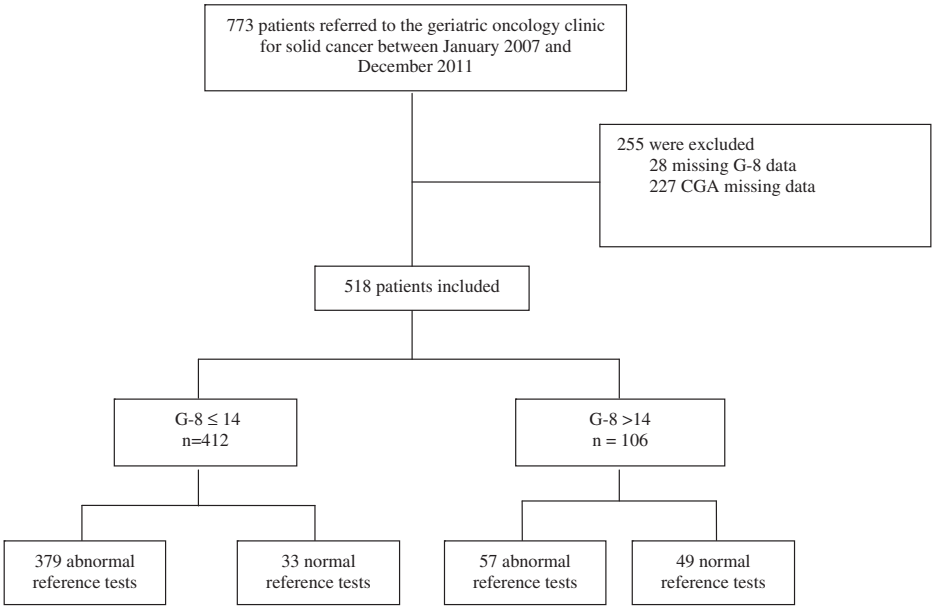

Fig. 1 – Flow chart: the ELCAPA-02 study. Abbreviations: CGA, Comprehensive Geriatric Assessment.

Table 1 – Characteristics of ELCAPA-02 patients (n = 518).

	n (%)
Male gender	270 (52.1)
Age in years, median (25–75th percentile)	80 (76–84)
ECOG-PS ≥ 2 (n = 485)	222 (45.8)
Tumour site	
Breast	113 (21.8)
Colorectal	108 (20.8)
Urinary tract	89 (17.2)
Liver or upper gastrointestinal tract	85 (16.4)
Prostate	69 (13.3)
Other sites [a]	54 (10.4)
Metastasis (n = 500)	241 (48.2)
CGA parameters	
ADL ≤ 5	142 (27.4)
IADL ≤ 7	313 (60.4)
MMSE ≤ 23	118 (22.8)
Mini-GDS ≥ 1	170 (32.8)
MNA ≤ 23.5	295 (57.0)
Get up & go > 20 s	202 (39.0)
CIRS-G: At least one grade 3/4 co-morbidity	262 (50.6)
Abnormal CGA (at least one abnormal score)	436 (84.2)
Total G-8, median (25–75th percentile)	12 (9–14)
Total G-8 ≤ 14	412 (79.5)

Abbreviations: ECOG-PS, Eastern Cooperative Oncology Group Performance Status; ADLs, Activities of Daily Living; IADLs, Instrumental Activities of Daily Living; MMSE, Mini Mental State Examination; Mini-GDS, Mini Geriatric Depression Scale; MNA, Mini Nutritional Assessment; CIRS-G, Cumulative Illness Rating Scale for Geriatrics.

Note: Missing ECOG-PS data: 33 patients; missing disease status data: 18 patients.

[a] Unknown, 15; lung, 11; sarcoma, 8; skin, 6; head & neck, 4; brain, 4; small intestine, 2; penis, 1; endometrial, 1; ovarian, 1; and germinal, 1.

The PLR was 2.2 (95% CI, 1.7–2.8) and NLR was 0.2 (95% CI, 0.2–0.3). The G-8 false negative patients (n = 57) had the following profile: 52.6% had an impaired IADL test; 47.4%, an impaired CIRS-G; 26.3%, an impaired mini-GDS; 17.5%, an impaired GUG; 8.8%, an impaired MNA; 7%, an impaired ADL; and 5.3%, an impaired MMS.

3.2. *G-8 Accuracy According to Tumour Site and Other Factors Associated with G-8 Accuracy*

Baseline characteristics, prevalence of metastatic disease and CGA parameters differed significantly across tumour sites (Table 2). The proportion of patients with an abnormal reference exam ranged from 66.7% in the prostate group to 95.3% in the upper gastrointestinal/liver group ($p < 0.001$). The prevalence of a G-8 score ≤ 14 varied from 44.9% in the prostate group to 92.9% in the upper gastrointestinal/liver group and 94% in the other-site group ($p < 0.001$). The prevalence of patients with an abnormal reference exam or a G-8 score ≤ 14 differed significantly between the groups with and without metastases (87.6% vs. 81%, $p = 0.047$; and 88% vs. 71.4%, $p < 0.001$; respectively). Fig. 2 showed a discrepancy between the proportions of abnormal CGA and G-8 in the group of patients with non-metastatic prostate cancer. In the other subgroups, there were similar proportions of patients with an abnormal CGA and G-8. Among G-8 items, severe anorexia and weight loss >3 kg were significantly more common in the colon/rectum, upper gastrointestinal/liver, and other site groups than in the three remaining groups. Moreover, the proportion of patients aged 80 years or less (a characteristic assigning 2 points in the G-8 score) was higher in the prostate group (78.3%) than in the other five sites (42.6%

Table 2 – Baseline characteristics and CGA parameters according to tumour site in the ELCAPA-02 study (n = 518).

	Breast	Colorectal	Urinary Tract	Liver and upper GI tract	Prostate	Other sites [a]	p value [b]
	n = 113	n = 108	n = 89	n = 85	n = 69	n = 54	
Median age, years (25–75th percentile)	79 (75–84)	81 (77–86)	80 (77–84)	80 (77–84)	77 (75–79)	82 (78–86)	<0.001
ECOG-PS ≥ 2 (n = 485)	39 (36.4)	45 (43.7)	39 (45.9)	43 (53.7)	18 (31.0)	38 (73.1)	<0.001
Metastasis (n = 500)	39 (36.1)	63 (58.9)	34 (40.5)	39 (48.7)	28 (41.8)	38 (70.4)	<0.001
CGA parameters							
ADL ≤ 5	18 (15.9)	30 (27.8)	23 (25.8)	29 (34.1)	16 (23.2)	26 (48.1)	0.001
IADL ≤ 7	47 (41.6)	82 (75.9)	56 (62.9)	54 (63.5)	29 (42.0)	45 (83.3)	<0.001
MMSE ≤ 23	27 (23.9)	21 (19.4)	18 (20.2)	21 (24.7)	11 (15.9)	20 (37.0)	0.1
Mini-GDS ≥ 1	34 (30.1)	32 (29.6)	24 (27.0)	38 (44.7)	16 (23.2)	26 (48.1)	0.001
MNA ≤ 23.5	45 (39.8)	66 (61.1)	50 (56.2)	69 (81.2)	22 (31.9)	43 (79.6)	<0.001
Get up & go > 20 s	40 (35.4)	48 (44.4)	32 (36.0)	35 (41.2)	17 (24.6)	30 (55.6)	0.01
CIRS-G: at least one grade 3/4 co-morbidity	46 (40.7)	57 (52.8)	44 (49.4)	52 (61.2)	29 (42.0)	34 (63.0)	0.02
Abnormal CGA (at least one impaired score)	85 (75.2)	95 (88.0)	78 (87.6)	81 (95.3)	46 (66.7)	51 (94.4)	<0.001
Abnormal G-8 (total score ≤ 14)	80 (70.8)	95 (88.0)	76 (85.4)	79 (92.9)	31 (44.9)	51 (94.4)	<0.001

Data are n (%) unless otherwise indicated. Note: Missing ECOG-PS data: 33 patients; missing disease status data: 18 patients.
Abbreviations: GI, Gastro-Intestinal; BMI, Body Mass Index; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; ADLs, Activities of Daily Living; IADLs, Instrumental Activities of Daily Living; MMSE, Mini Mental State Examination; Mini-GDS, Mini Geriatric Depression Scale; MNA, Mini Nutritional Assessment; CIRS-G, Cumulative Illness Rating Scale for Geriatrics.
[a] Unknown, 15; lung, 11; sarcoma, 8; skin, 6; head & neck, 4; brain, 4; small intestine, 2; penis, 1; endometrial, 1; ovary, 1; and germinal, 1.
[b] Pearson's chi-square test, Fisher's exact test, or Kruskal–Wallis test as appropriate.

to 51.3%). No difference was found for self-reported health status or number of drugs (data not shown).

Sensitivity, specificity, and proportion of correctly classified patients differed significantly across tumour sites (all p-values < 0.001) (Table 3). Pairwise analyses showed that G-8 sensitivity was significantly lower in the prostate cancer group compared to the four others (p < 0.001 in all pairwise comparisons with a 0.003 significance threshold after Bonferroni's correction), with the exception of the breast group. G-8 sensitivity in the group with breast cancer was significantly lower than in the upper gastrointestinal/liver and other-site groups (p = 0.002 for both comparisons). In age-adjusted multivariate analysis, G-8 sensitivity in patients in the prostate group remained significantly lower than G-8 sensitivity in patients in the colon/rectum group (taken as the reference) (Table 4). Sensitivity was significantly higher in patients in the metastatic group and in patients with ECOG-PS ≥ 2 compared to patients in the non-metastatic group and patients with ECOG-PS < 2 (p < 0.001 for both comparisons) in univariate and multivariate analyses (Tables 3 and 4). Specificity was significantly higher in the prostate group than in the colon/rectum, breast, and urinary-tract groups (p < 0.001

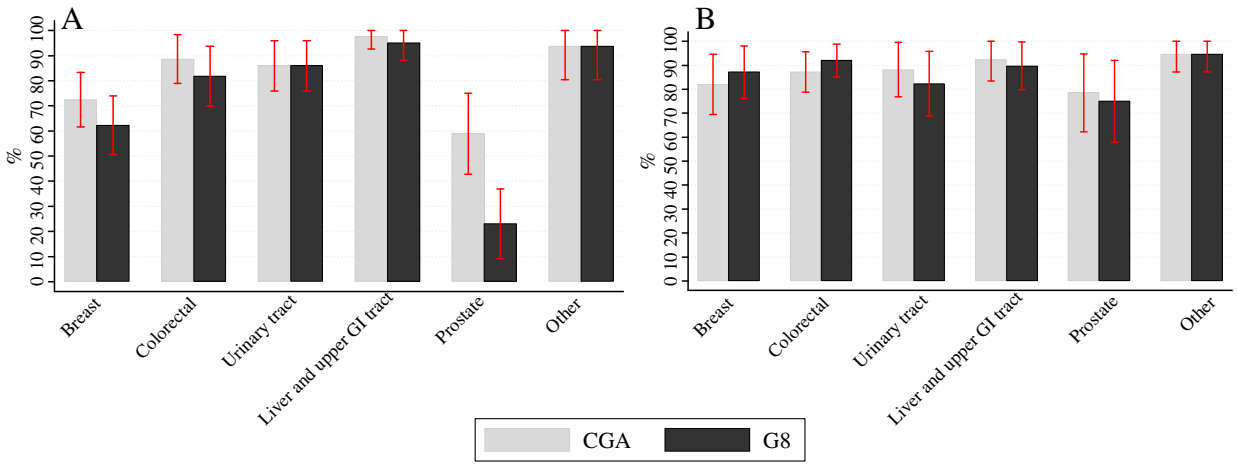

Fig. 2 – Proportion of abnormal CGA and G-8 according to tumour site and metastatic status (A: without metastases; B: with metastases). Abbreviations: CGA, Comprehensive Geriatric Assessment; GI, Gastro-Intestinal; G-8, Geriatric 8.

Table 3 – Accuracy of the G-8 screening tool according to tumour site, metastatic status and performance status in the ELCAPA-02 study.

	G-8	CGA		Sensitivity (%)	Specificity (%)	Positive likelihood ratio	Negative likelihood ratio	Correctly classified
		Abnormal[b]	Normal					
		n	n					
Breast	Abnormal	67	13	78.8 (68.6–86.9)	53.6 (33.9–72.5)	1.7 (1.1–2.6)	0.4 (0.2–0.7)	82 (72.6)
n = 113	Normal	18	15					
Colorectal	Abnormal	85	10	89.5 (81.5–94.8)	23.1 (5.0–53.8)	1.2 (0.9–1.6)	0.5 (0.1–1.4)	88 (81.5)
n = 108	Normal	10	3					
Urinary	Abnormal	70	6	89.7 (80.8–95.5)	45.5 (16.7–76.6)	1.7 (1.0–2.8)	0.2 (0.1–0.6)	75 (84.3)
tract	Normal	8	5					
n = 89								
Upper GI	Abnormal	77	2	95.1 (87.8–98.6)	50.0 (6.8–93.2)	1.9 (0.7–5.1)	0.1 (0.03–0.4)	79 (92.9)
and liver	Normal	4	2					
n = 85								
Prostate	Abnormal	30	1	65.2 (49.8–78.6)	95.7 (78.1–99.9)	15 (2.2–103.2)	0.4 (0.2–0.6)	52 (75.4)
n = 69	Normal	16	22					
Other	Abnormal	50	1	98.0 (89.6–100)	66.7 (9.4–99.2)	2.9 (0.6–14.6)	0.03 (0.00–0.2)	52 (96.3)
sites[a]	Normal	1	2					
n = 54								
Metastasis								
Yes,	Abnormal	198	14	93.8 (89.7–96.7)	53.3 (34.3–71.7)	2.0 (1.4–3.0)	0.1 (0.06–0.2)	198 (76.4)
n = 241	Normal	13	16					
No,	Abnormal	167	18	79.5 (73.4–84.8)	63.3 (48.3–76.6)	2.2 (1.5–3.2)	0.3 (0.2–0.5)	214 (88.8)
n = 259	Normal	43	31					
ECOG-PS								
<2	Abnormal	145	32	75.9 (69.2–81.8)	55.6 (43.4–67.3)	1.7 (1.30–2.2)	0.4 (0.3–0.6)	185 (70.3)
n = 263	Normal	46	40					
≥2	Abnormal	212	1	96.8 (93.5–98.7)	66.7 (9.4–99.2)	2.9 (0.6–4.4)	0.05 (0.02–0.1)	214 (96.4)
n = 222	Normal	7	2					

Abbreviations: GI, Gastro-Intestinal; CGA, Comprehensive Geriatric Assessment; ECOG-PS: Eastern Cooperative Oncology Group Performance Status.

[a] Unknown 15, lung 11, sarcoma 8, skin 6, head & neck 4, brain 4, small intestine 2, penis 1, endometrial 1, ovary 1 and germinal 1.

[b] At least one abnormal score; # G-8 score ≤ 14.

for all three comparisons) in univariate and multivariate analyses (Tables 3 and 4). There was no significant interaction between metastatic disease status and tumour site. NLR was lower in metastatic group than in non metastatic whereas PLR was similar.

When including patients with at least one impaired CGA item even if other CGA parameters were missing (n = 642), results concerning accuracy were similar in each subgroup defined by tumour site, metastatic disease status and ECOG-PS (data not shown).

4. Discussion

We showed that G-8 accuracy varied significantly according to tumour site, metastatic disease status, and performance status. The G-8 sensitivity was particularly low in patients with prostate cancer, and the G-8 specificity was particularly low in those with colorectal cancer. Moreover, our results confirmed the overall high sensitivity of the G-8 and acceptable NLR: thus, a G-8 score > 14 indicates a very low likelihood of vulnerability as assessed by the CGA.[31] Specificity and PLR were only fair, so that a high proportion of patients with G-8 scores ≤ 14 had no vulnerability detected by the CGA.[31]

Our study population was of the same age and had a similar proportion of patients with metastasis than earlier studies.[9,18–22] It differed by the proportion of non-Hodgkin's lymphoma (0% in our patients, 30% in the development cohort,[9] and 7.9% in the ONCODAGE cohort),[19] breast cancer (21.8%, 0%, and 53.7%, respectively), and scheduled treatments (chemotherapy in the development cohort versus chemotherapy, radiotherapy, surgery, targeted therapy, and supportive care both in our patients and those of ONCODAGE cohort). Our study was consistent with data obtained in the development cohort and three validation studies in patients with various tumour sites,[8,18–22] showing high sensitivity (77% to 92%) and fair specificity (39% to 65%). We reported the PLR and NLR instead of predictive values because these diagnostic indices are not influenced by the prevalence of the abnormality of the reference test.[32,33] Indeed earlier studies showed marked differences in prevalence of abnormal reference tests (44% to 94%); similarly we showed also marked differences between tumour sites in our cohort. We found similar frequency of impaired G-8 scores (79.5%) as compared to the development study (82%). A screening instrument that classifies four-fifths of a population as "at risk of vulnerability" and who therefore would need a complete CGA is questionable. Above all, as pointed out by Bellera et al.,[9] we do not yet know if patients with only one abnormal questionnaire do necessarily need interventions by a geriatrician in all cases.

Table 4 – Multivariate analysis of factors associated with increased sensitivity and specificity of the G-8 screening tool: the ELCAPA-02 study.

	Sensitivity Patients with abnormal CGA (n = 436)		Specificity Patients with normal CGA (n = 82)	
	Adjusted OR [95% CI]	p	Adjusted OR [95% CI]	p
ECOG-PS ≥ 2 (n = 485)	4.58 [1.87–11.25]	0.001	–	–
Metastasis (n = 500)	2.91 [1.35–6.29]	0.01	–	–
Tumour site				
Breast	0.54 [0.20–1.50]	0.02	3.49 [0.70–17.45]	0.03
Colorectal	1		1	
Urinary tract	1.15 [0.38–3.49]		4.52 [0.63–32.10]	
Liver and upper GI tract	2.91 [0.71–11.98]		5.77 [0.46–72.80]	
Prostate	0.33 [0.11–0.99]		83.9 [6.60–1064]	
Other sites [a]	3.32 [0.38–29.04]		11.99 [0.68–211.27]	

Sensitivity is defined by abnormal G-8 score among patients with abnormal reference test (CGA), and specificity by normal G-8 score in patients with normal reference test.
Odds ratios were estimated using logistic regression analysis simultaneously adjusted for age and all variables in the table.
Abbreviations: OR, odds ratio; 95% CI, 95% confidence interval; GI, gastrointestinal; CGA, Comprehensive Geriatric Assessment; ECOG-PS, Eastern Cooperative Oncology Group Performance Status.
[a] Unknown 15, lung 11, head & neck 4, brain 4, skin 6, penis 1, sarcoma 8, small intestine 2, endometrial 1, ovary 1, and germinal 1.

We showed for the first time significant differences in G-8 accuracy according to tumour site, metastatic disease status, and performance status. Two reasons may explain these results. First, recruitment may have varied across tumour sites, as referral of patients with cancer to geriatric-oncology clinics may have differed across medical specialties, leading to recruitment bias. However, the geriatric-oncology clinic physicians work closely with all the cancer specialists. They saw elderly patients with cancer on both an inpatient and an outpatient basis consultation and attended all multidisciplinary meetings, during which they participated in therapeutic decisions. Moreover, we adjusted our multivariate model for age, metastatic disease status, and performance status, which differed across groups. Finally, our results concerning the global accuracy of the G-8 were fully in accordance with previous studies.

Second, the association between tumour site and G-8 accuracy found in our study may be ascribable to a residual confounding factor not investigated by the oncologic or geriatric adjustment variables. However, a real difference in G-8 accuracy across tumour sites seems likely. Indeed, the relatively low sensitivity in the prostate group is consistent with the delayed development of nutritional abnormalities in prostate cancer, leading to a relatively high rate of false-negative G-8 results. Conversely, the low specificity of the G-8 in colorectal cancer may be attributable to the higher mean age in this group, leading to a high false-positive rate. A recent study in patients with head-and-neck cancer found similar sensitivity to that reported in other validation studies in patients with various tumour sites, contrasting with considerably higher specificity (75%). This result may be ascribable to the younger patient age (median, 72 years) compared to other studies.[17]

Our results suggest ways for optimising G-8 screening performance. G-8 items could be weighted differentially according to tumour site and/or metastatic disease status. Another possibility could be to add an item on functional status or severe co-morbidities to increase G-8 sensitivity in cancers that have little or delayed effects on nutritional status (e.g., prostate cancer). Concerning functional status, one could suggest that more subtle indicators of frailty, such as dependency on IADLs should be part of a screening instrument since they precede many times the development of bolder deficiencies. These possibilities deserve to be investigated.

Our study has several strengths. We used a large cohort, independent from the one used to develop the G-8, and the investigators had no role in developing the G-8. We included patients with tumours at various sites and performed the first comparison of G-8 accuracy across subgroups after adjustment for potential confounders. Several limitations should also be kept in mind. About 60% of all elderly patients with cancer were referred to the geriatric-oncology clinics. Therefore, generalisation to the overall population of elderly patients with cancer should be viewed with caution. G-8 scores were recorded retrospectively; however, misclassification is unlikely, as the observer who determined the G-8 score was blinded to CGA results and had no role in performing CGAs. G-8 development was based on the MNA questionnaire: since all of G-8 elements (except age) come from the MNA, and this test is one of the 7 instruments considered for defining the reference exam (CGA), an abnormal G-8 will likely have abnormal CGA. It leads to an incorporation bias, which means that the tested score is included in the reference test. Lastly, size of the subgroups by tumour site was relatively small leading to large 95% confidence intervals.

In conclusion, our results suggest that G-8 accuracy varies according to tumour site, metastatic disease status, and performance status. In particular, sensitivity was low in patients with prostate cancer and specificity was low in patients with colorectal cancer. These G-8 accuracy variations across tumour sites should be considered when using the G-8 to identify

elderly patients with cancer who could benefit from CGA and suggested ways for optimising screening performance of G-8.

Disclosures and Conflict of Interest Statements

The authors declare no conflict of interest.

Sponsor's Role

The National Cancer Institute had no role in the design, methods, subject recruitment, data collections, analysis and preparation of the paper.

Author Contributions

Concept and design: E. Liuu, F. Canouï-Poitrine, C. Tournigand, M. Laurent, P. Caillet, A. Le Thuaut, H. Vincent, S. Culine, E. Audureau, S. Bastuji-Garin and E. Paillaud.
Data collection: E. Liuu, P. Caillet and H. Vincent.
Analysis and interpretation of data: E. Liuu, F. Canouï-Poitrine, C. Tournigand, M. Laurent, P. Caillet, A. Le Thuaut, H. Vincent, S. Culine, E. Audureau, S. Bastuji-Garin and E. Paillaud.
Manuscript writing and approval: E. Liuu, F. Canouï-Poitrine and E. Paillaud.

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