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Original Article

Comparison of the prognostic value of eight nutrition-related tools in older patients with cancer: A prospective study



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ABSTRACT

Objectives: The primary objective of the present study was to evaluate and compare the ability of eight nutrition-related tools to predict 1-year mortality in older patients with cancer.

Design, setting and participants: We studied older patients with cancer from the ELCAPA cohort and who had been referred for a geriatric assessment at one of 14 participating geriatric oncology clinics in the greater Paris area of France between 2007 and 2018.

Measurements: The studied nutrition-related tools/markers were the body mass index (BMI), weight loss (WL) in the previous 6 months, the Mini Nutritional Assessment, the Geriatric Nutritional Risk Index (GNRI), the Prognostic Nutritional Index, the Glasgow Prognostic Score (GPS), the modified GPS, and the C-reactive protein/albumin ratio.
Results: A total of 1361 patients (median age: 81; males: 51%; metastatic cancer: 49%) were included in the analysis. Most of the tools showed a progressively increase in the mortality risk as the nutrition-related risk category worsened (overall p-values <0.02 for all) after adjustment for age, outpatient status, functional status, severe comorbidities, cognition, mood, cancer treatment strategy, tumour site, and tumour metastasis. All the models were discriminant, with a C-index ranging from 0.748 (for the BMI) to 0.762 (for the GPS). The concordance probability estimate ranged from 0.764 (WL) to 0.773 (GNRI and GPS).

Conclusion: After adjustment for relevant prognostic factors, all eight nutrition-related tools/markers were independently associated with 1-year mortality in older patients with cancer. Depending on the time or context of the GA, physicians do not always have the time or means to perform and assess all the tools/markers compared here. However, even when some information is missing, each nutritional tool/marker has prognostic value and can be used in the evaluation.

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1. Introduction

Malnutrition is highly prevalent among older people and patients with cancer. The risk of developing malnutrition is multifactorial, commonly associated with inadequate nutrient intake (due to the effects of cancer, and the side effects of anticancer therapies, which can cause taste and smell alterations, a loss in appetite, swallowing and absorption disorders), an altered metabolism (frequently due to the presence of systemic inflammation [1–3]), and enhanced catabolism (due to the effects of the tumour itself) [4–6]. It has been well established that malnutrition is associated with poor clinical outcomes, worse treatment responses, low quality of life, and elevated morbidity and mortality rates in patients with cancer [1,7–10]. Accordingly, an assessment of malnutrition is essential when choosing care options and personalized treatments. This assessment is complicated by differences in definitions and overlap between the term “malnutrition” and other terms, such as “undernutrition”, “weight loss” (WL), “cachexia”, and “sarcopenia” [11]. In patients with cancer [12,13], markers of systemic inflammation (e.g. C-reactive protein (CRP)) should also be taken into account during a nutritional assessment [12].

Malnutrition can occur even in the absence of apparent weight loss, or prior to losing fat mass. It may also be masked by obesity, resulting in underdiagnosis [6,14]. The Global Leadership Initiative on Malnutrition (GLIM) recently suggested the use of three phenotypic criteria (non-volitional WL, low body mass index, and reduced muscle mass) and two etiologic criteria (reduced food intake or assimilation, and inflammation or disease burden) for the diagnosis of malnutrition [11]. However, muscle mass measurements are not available in most institutions. With the emergence of these new diagnostic criteria involving body composition measurements, the diagnosis of malnutrition is challenging. The GLIM consensus statement also describes a two-step approach in which validated screening tools are applied initially to identify at-risk individuals.

Several malnutrition screening tools have been described in the literature [14–16]. Some are based on clinical variables and others are biochemical markers, purely nutritional markers, or combined nutrition-inflammation markers. Although the screening tools’ diagnostic performance has often been evaluated, it is also important to investigate the ability to predict poor clinical outcomes – especially in older patients with cancer. A recent systematic review [17] of the relationship between malnutrition and clinical outcomes in older adults with cancer identified 15 nutritional risk markers and described their associations with the mortality rate and the incidence of complications following chemotherapy or surgery; there were four “objective indexes” (the Prognostic Nutritional Index [PNI], the Controlling Nutritional Status Score [CONUT], the Nutritional Risk Index [NRI], and the Geriatric Nutritional Risk Index [GNRI]), four anthropometric markers (the body mass index [BMI], WL, mid-arm circumference, and calf circumference), two measures of muscle strength (hand-grip strength, and the lean skeletal muscle mass determined by computed tomography), three biochemical markers (haemoglobin, albumin, and CRP), and measures of food and fluid intake. Other tools (i.e. the Glasgow Prognostic Score [GPS], the modified GPS [mGPS], and the CRP/albumin ratio) that combine nutritional and inflammatory markers (i.e. albumin and CRP) have been linked to nutritional status and poor survival in patients with cancer [13,18,19]. Lastly, tools combining nutritional variables with other clinical variables that may lead to malnutrition have been proposed to assess nutritional risk status in older people. For example, the Mini Nutritional Assessment (MNA) combines an anthropometric assessment, a general assessment (including cognition, depression, and polypharmacy), dietary habits, and the self-assessment of nutritional and health status.

To the best of our knowledge, the abilities of the various nutrition-related tools to predict overall survival in older patients with cancer have not previously been compared. Therefore, the primary objective of the present study was to compare eight frequently used nutrition-related tools/markers with regard to the prediction of 1-year overall mortality in a large population of older patients with cancer.

2. Methods

2.1. Population

The Elderly Cancer Patient (ELCAPA) prospective multicentre cohort study includes patients aged 70 or over with a solid or hematologic cancer and who have been referred for a geriatric assessment (GA) at one of 19 geriatric oncology units in the greater Paris area of France [20]. The study inclusion date was the date of the first consultation at the geriatric oncology unit. All the study patients provided their written, informed consent before inclusion. The study protocol was approved by the independent ethics committee (*CPP Ile-de-France I*, Paris, France; approval reference: 2019 mai-MS121). The survey was registered at ClinicalTrials.gov (NCT02884375).

In the present study (ELCAPA-34), we evaluated patients recruited between January 2007 and January 2018 at 14 centres and for whom complete data for each of the nutrition-related tools and follow-up were available.

2.2. Data collection

A geriatrician performed an extensive GA (including a comprehensive clinical examination) during a consultation at the geriatric oncology unit. After the GA, the cancer treatment strategy was chosen in a multidisciplinary team meeting. The strategy comprised one or more of the following: surgery, chemotherapy, radiotherapy, hormone therapy, targeted therapy, immunotherapy, and supportive care. Data were collected prospectively at the time of the first GA. The following sociodemographic and cancer-related variables were recorded: age, sex, the social environment (living alone or not), patient status (inpatient or outpatient), tumour site, and metastatic status. Functional status was evaluated using the Eastern Cooperative Oncology Group performance status (ECOG-PS), the Activities of Daily Living (ADL) scale (a score of 5 or less out of 6 was considered to be abnormal) and the Instrumental Activities of Daily Living (IADL) scale (a score of less than 8 out of 8 was considered to be abnormal). Impaired mobility was defined as a timed get-up-and-go (TUG) test completion time of more than 20 s. Inability to perform the TUG test was also recorded. Falls in the previous 6 months were documented. Severe comorbidities were defined as grade 3–4 on the Cumulative Illness Rating Scale for Geriatrics (CIRS-G). Polypharmacy was defined as taking five or more medications per day [21]. Cognitive status was assessed using the Mini Mental State Examination (MMSE): a score below 24 out of 30 was considered to indicate cognitive impairment. Mood was assessed using four items from the Geriatric Depression Scale (mini-GDS): a score of 1 or more was considered to indicate a risk of depression [22]. Laboratory data (i.e. serum CRP, serum albumin, and the lymphocyte count) were collected at the time of the GA (± 10 days).

2.3. Nutrition-related tools

We studied the following nutrition-related tools: BMI, WL in the previous six months, the MNA, the GNRI, the PNI, the GPS, the mGPS, and the CRP/albumin ratio. The corresponding equations, formulas, categories, and cut-offs are described in [Table 1](#).

2.4. Outcome

The primary outcome was 1-year overall mortality, defined as the time interval between the GA and death or last follow-up. Vital status was determined from medical charts or via the French national vital records register (*Répertoire National d'Identification des Personnes Physiques*).

2.5. Statistical analysis

The patient’s characteristics were described using summary statistics. Categorical variables were described as the number (percentage), and

Table 1
Description of the eight nutrition-related tools studied.

Tools	Description and formulas	Cut-offs	Categories
BMI	BMI = current weight (kg)/height ² (m) Categorized according to the classification of the World Health Organization and prior studies [11,57,58].	<22 kg/m ² 22 to <25 kg/m ²	Underweight Normal weight
Weight loss	Percentage of body weight loss in the previous 6 months (WL): WL = 100% - [current weight (kg)/weight 6 months before GA (kg)]. [11]	25 to <30 kg/m ² ≥30 kg/m ² ≤5% 5 to 10% >10%	Overweight Obese Minimal weight loss Moderate weight loss Severe weight loss
MNA [59]	Questionnaire of 18 items (anthropometric assessment, general assessment, dietetic habits evaluation, self-assessment of nutritional and health status). Each question rate: from 0 to 2 or 3 points. Overall score range: 0–30 points.	<17: 17 to 23.5: ≥24:	Malnourished Risk for malnutrition Well nourished
GNRI [60]	GNRI = [1.489 × albumin (g/L)] + [41.7 × (current weight/ideal weight)] Ideal weight (Lorentz equations) ^a : For men: height (cm) - 100 - [(height (cm) - 150)/4] For women: height (cm) - 100 - [(height (cm) - 150)/2.5]	<82: 82 to <92: 92 to ≤ 98: >98:	Major nutrition-related risk Moderate nutrition-related risk Low nutrition-related risk No nutrition-related risk
PNI [61]	PNI = 10 × serum albumin (g/dl) + 0.005 × total lymphocyte count (per mm ³).	>40: <40:	Severe malnutrition Moderate malnutrition
GPS [62]	Both normal CRP (≤10 mg/L) and albumin (≥35 g/L) levels Abnormal CRP (>10 mg/L) or abnormal albumin (<35 g/L) levels	0: 1: 2:	Well nourished Normal score Abnormal score
mGPS [63]	Both abnormal CRP (>10 mg/L) and albumin (<35 g/L) levels Normal CRP level (≤10 mg/L) Abnormal CRP (>10 mg/L) and normal albumin (≥35 g/L)	0: 1: 2:	Abnormal score Normal score Abnormal score
CRP/albumin ratio	Both abnormal CRP (>10 mg/L) and albumin (<35 g/L) levels The CRP/Albumin ratio was divided in tertiles.	≤0.08: 0.08 to 0.50: >0.50:	Abnormal score Low Intermediate High

Abbreviations: BMI, body mass index; CRP, C-Reactive Protein; MNA, mini nutritional assessment; GNRI, geriatric nutritional risk index; PNI, prognostic nutritional index; GPS, Glasgow prognostic score; mGPS, modified GPS.

^a Ideal weight = 1 when current weight exceeded ideal weight.

continuous variables were described as the median [interquartile range (IQR)]. Age was dichotomized at 82, using the Youden optimal cut-off. Comparisons between included patients and non-included patients were based on Student's *t*-test or Wilcoxon's rank sum test for continuous variables and the chi-squared test or Fisher's exact test for categorical variables, as appropriate.

The follow-up time was quantified in a reverse Kaplan-Meier estimation [23]. Overall survival was calculated using the Kaplan-Meier method and compared across groups with a log-rank test. Trends analyses were performed using the log-rank test for trend. Crude hazard ratios (HRs) with their 95% confidence intervals (CIs) were estimated in an unadjusted Cox proportional hazards analysis. Main known prognostic factors (i.e. cancer site, advanced disease, cancer treatment, inpatient status, ADL, IADL, TUG, severe comorbidities, depression, age, sex, performance status [10,24–26], social characteristics (living alone) and other GA components (polypharmacy, MMSE, history of falls) were considered for univariate analyses. We tested the interaction between the tumour site and metastatic status, in light of our previous observations in the ELCAPA cohort [26]. Then, we built a multivariate model for each nutrition-related tool/marker. To build the baseline multivariate model, factors associated ($p < 0.05$) with 1-year overall mortality in the univariate analysis were included in a multivariable Cox model. After a stepwise backward procedure, only factors independently associated with 1-year mortality were kept in the model. Multicollinearity was tested using the variance inflation factor. To assess the contribution of the nutrition-related tools, each one was added separately to the baseline model. The proportional hazards assumption was tested by calculating Schoenfeld residuals and was met.

We compared the prognostic value of the models built for each nutrition-related tool by calculating the Akaike information criterion (AIC) [27] and calibration and discrimination indices. The discriminative ability of each prognostic model was assessed using Harrell's concordance index (C-index) [28], the Gönen and Heller concordance probability estimate (CPE) [29], and the R². Higher discrimination ability

corresponded to higher indices (up to 1). The C-index CIs were computed using the bootstrap method with 1000 replicates. Good discrimination was defined as a C-index and a CPE ≥ 0.70. Calibration of the Cox models was assessed by the Grönnesby and Borgan test [30] ($P > 0.20$ for a good fit). We compared the AIC of the baseline model with the AIC of the models with the nutrition-related tool and expressed the difference as the Δ AIC. A larger Δ AIC corresponded to a better fit.

2.6. Sensitivity analyses

We performed subgroup analyses by metastatic status and by four main cancer sites (breast, colorectal, prostate and other urological cancers), for which adjusted HRs and the main calibration and discriminatory indices (Grönnesby and Borgan, CPE and C-index) were calculated. For cancer sites with low number of patients and events, univariate cox analyses were performed and crude HRs were calculated. Main calibration and discriminatory indices were computed.

In the main analysis (comparison of the eight nutrition-related tools/markers), we included only patients who had full datasets for all tools/markers. In order to test the robustness of our results, we evaluated the ability of each individual tool/marker to predict survival. For each analysis, we included patients with full data for the corresponding tool - even when data for the other tools were missing.

All statistical tests were two-tailed, and the threshold for statistical significance was set to $p < 0.05$. The analyses were performed using R software (version 4.0.2) [31] and its tidyverse [32], survival [33] and other packages [34–39].

3. Results

3.1. Characteristics of the study participants

In all, 1361 of 3783 patients were included in the analysis (Supplementary Figure S1). When compared with the patients not

Table 2
Baseline characteristics of the study population (N = 1361).

		N	%
Age (y)	median [IQR]	81 [77–85]	
Sex	female	673	49.5
Living alone, <i>missing n = 4</i>		527	38.8
Patient status	Inpatients	288	21.2
Tumour site, <i>missing n = 3</i>	Breast	265	19.5
	Colorectal	190	14.0
	Pancreas	76	5.6
	Upper digestive tract/liver	121	8.9
	Prostate	170	12.5
	Urinary tract	209	15.4
	Lung	91	6.7
	Haematological	57	4.2
	Others ^a	179	13.2
Cancer extension ^b , <i>missing n = 88</i>	Local	551	45.3
	Metastatic/x	665	54.7
Cancer treatment strategy, <i>missing n = 200</i>	Curative	559	48.1
	Palliative therapy	412	35.5
	Supportive care alone	190	16.4
ECOG-PS, <i>missing n = 3</i>	0–1	709	52.2
	2–4	649	47.8
Severe comorbidities, <i>missing n = 77</i>	CIRS-G: ≥ 1 grade 3–4	825	64.3
Polypharmacy, <i>missing n = 54</i>	≥ 5 medications/d	875	66.9
Impaired MMSE, <i>missing n = 162</i>	score < 24	300	25.0
Impaired mini-GDS, <i>missing n = 87</i>	score ≥ 1	419	32.9
Impaired ADL, <i>missing n = 3</i>	score $\leq 5/6$	355	26.1
Impaired IADL, <i>missing n = 30</i>	score < 8/8	827	62.1
Timed get-up-and-go test, <i>missing n = 121</i>	≤ 20 s	842	67.9
	> 20 s/not able to perform the test	398	32.1
Falls (previous 6 months), <i>missing n = 14</i>	≥ 1 fall	388	28.8
Nutrition-related tools/markers			
Body mass index (kg/m ²)	< 22	363	26.7
	22 to <25	352	25.8
	25 to <30	468	34.4
	≥ 30	178	13.1
Weight loss in the previous 6 months	$\leq 5\%$	939	69.0
	5 to 10%	212	15.4
	> 10%	210	15.6
Mini Nutritional Assessment	< 17	205	15.1
	17 to 24	586	43.1
	≥ 24	570	41.8
Geriatric Nutritional Risk Index	< 82	201	14.8
	82 to 92	283	20.8
	92 to 98	311	22.8
	> 98	566	41.6
Prognostic Nutritional Index	< 40	391	28.7
	40 to 45	324	23.8
	> 45	646	47.5
Glasgow Prognostic Score	0	623	45.8
	1	370	27.2
	2	368	27.0
Modified Glasgow Prognostic Score	0	762	56
	1	231	17
	2	368	27
C-reactive protein/albumin ratio	≤ 0.08	444	32.6
	0.08–0.50	453	33.3
	> 0.50	464	34.1

ADL: activities of daily living; CIRS-G: Cumulative Illness Rating Scale for Geriatrics; ECOG-PS: Eastern Cooperative Oncology Group performance status; IADL: instrumental activities of daily living; Mini-GDS: Mini- Geriatric Depression Scale; MMSE: Mini-Mental State Examination.

^a Brain (n = 8), head and neck (n = 17), sarcoma (n = 14), thyroid (n = 6), ovary (n = 17), primary unknown origin (n = 24), uterus (n = 24), skin and soft tissues (n = 32), others (n = 37).

^b non-haematological.

included in the analysis, the included patients had significantly higher proportions of males (44% vs. 51%, respectively) and outpatients (66% vs. 79%). The included patients were slightly younger (mean \pm SD age: 81.3 \pm 5.8, vs. 81.8 \pm 5.7 for non-included patients) and less likely to have a cognitive disorder (25% vs. 29%, respectively), an impaired ADL score (26% vs. 31%), or an impaired IADL score (62% vs. 66%). Furthermore, the included patients had a better nutritional status, with higher MNA,

GNRI, and PNI scores, a lower CRP/albumin ratio, and a higher proportion of patients with normal GPS and mGPS scores.

The overall median [IQR] age at inclusion was 81 [77–85], 51% of the patients were men, and 79% were outpatients (Table 2). The most frequent cancers were digestive system cancers (29%), followed by urological cancers (28%) and gynaecological cancers (including breast cancer; 24%); 49% of the patients had metastases. The majority of the

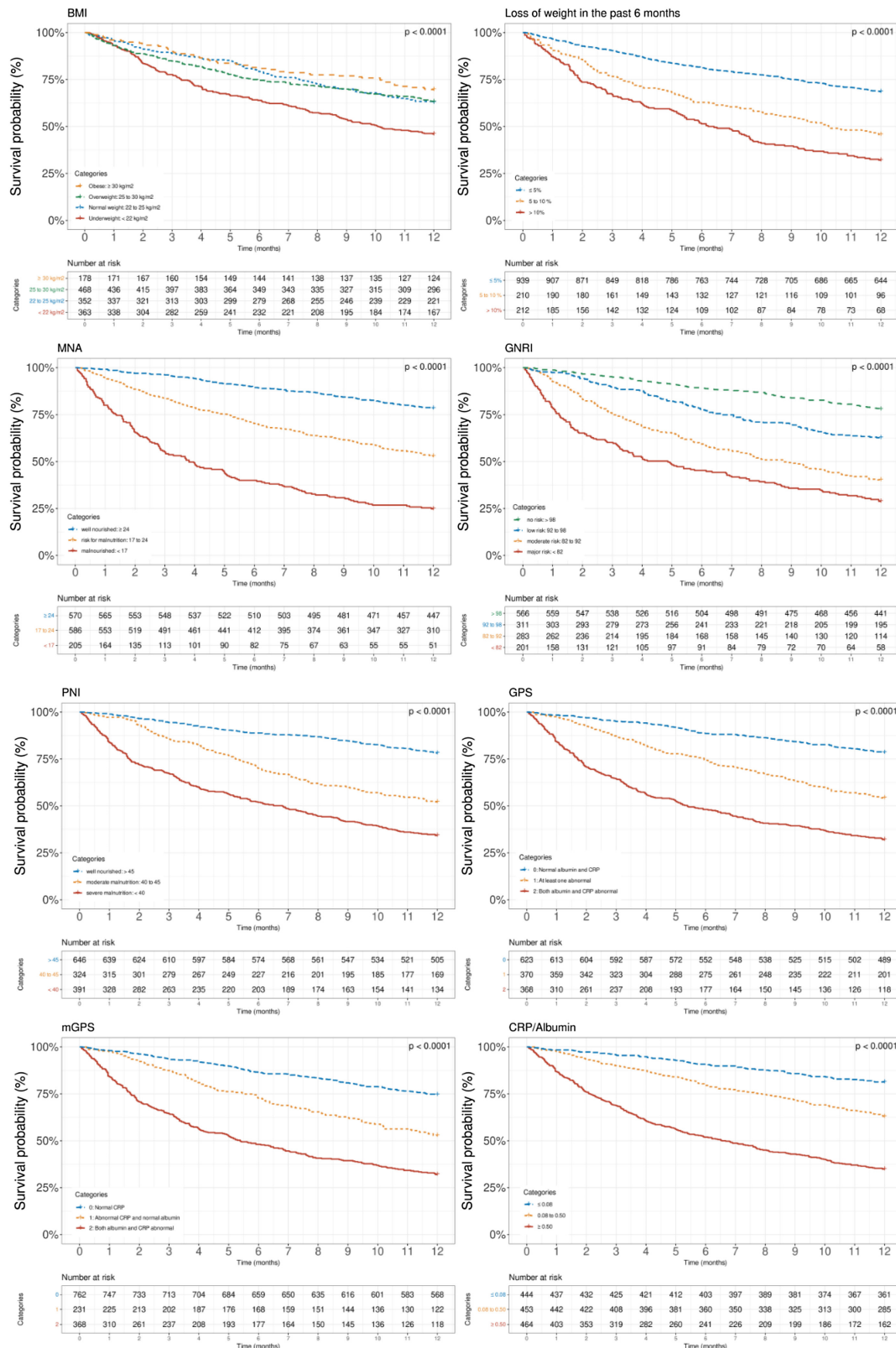


Fig. 1. Kaplan-Meier curves of 1-year overall survival among 1361 older patients with cancer, according to the categories of eight nutrition-related tools.

patients (64%) had at least one CIRS-G grade 3 or 4 comorbidity, and 67% were taking five or more medications per day. The median [IQR] levels of albumin and CRP were respectively 37 [32–41] g/L and 7.0 [2.5–30] mg/L. Depending on the tool, the proportion of patients with impaired nutritional status ranged from 27% (BMI $< 22 \text{ kg/m}^2$) to 58% (GNRI ≤ 98 or MNA < 24) (Table 2).

3.2. Survival analysis

The median follow-up time was 4.6 years (IQR: 2.5–7.5 years). The overall 1-year mortality rate was 40.6% [95% confidence interval (CI): 38%–43.2%], and the median mortality time was 1.5 years [95%CI: 1.4–1.7 years].

Table 3
Univariate analysis for 1-year mortality.

	Survivors (N = 808)		Deceased (N = 553)		Unadjusted hazard ratio	
	No. of Patients	%	No. of Patients	%	[95%CI]	P
Age (≥ 82 years old)	363	45	294	53	1.27 [1.08–1.50]	0.005
Sex, female	442	55	231	42	0.68 [0.57–0.80]	<0.001
Living alone	317	39	210	38	0.97 [0.82–1.15]	0.7
Inpatient status	98	12	190	34	2.76 [2.32–3.30]	<0.001
Tumour site * Cancer extension, ref: colorectal local	65	9	20	4	Ref. 1.00	<0.001
Colorectal metastatic	49	7	45	9	2.48 [1.47–4.20]	<0.001
Upper digestive tract and liver local	30	4	19	4	1.85 [0.99–3.47]	0.05
Upper digestive tract and liver local	13	2	46	9	5.16 [3.05–8.73]	<0.001
Pancreas local	15	2	12	2	2.09 [1.02–4.28]	0.043
Pancreas metastatic	10	1	32	6	6.19 [3.54–10.8]	<0.001
Breast or Prostate local	203	27	7	1	0.13 [0.05–0.30]	<0.001
Breast metastatic	73	10	30	6	1.34 [0.76–2.35]	0.3
Prostate metastatic	49	7	47	9	2.38 [1.41–4.02]	0.001
Urological malignancies local	61	8	38	7	1.79 [1.04–3.08]	0.03
Urological malignancies metastatic	38	5	57	11	3.46 [2.08–5.76]	<0.001
Haematological	28	4	29	6	2.75 [1.56–4.87]	<0.001
Lung local	16	2	12	2	2.03 [0.99–4.14]	0.05
Lung metastatic	17	2	42	8	4.84 [2.84–8.25]	<0.001
Others local	36	5	16	3	1.42 [0.73–2.73]	0.3
Others metastatic	46	6	69	13	3.52 [2.14–5.80]	<0.001
Cancer treatment strategy, ref: curative treatment	438	64	121	26	Ref. 1.00	<0.001
Palliative therapy	201	29	211	45	2.93 [2.34–3.67]	<0.001
Supportive care alone	48	7	142	30	6.22 [4.87–7.94]	<0.001
ECOG-PS, ref: 0–1	535	66	174	32	Ref. 1.00	<0.001
≥ 2	271	33	378	68	3.23 [2.70–3.87]	<0.001
Severe comorbidities (≥ 1 grade 3–4, CIRS-G)	422	56	403	76	2.16 [1.77–2.64]	<0.001
Polypharmacy (≥ 5 medications/d)	484	62	391	74	1.55 [1.27–1.88]	<0.001
Mini-Mental State Examination score (< 24)	152	21	148	31	1.51 [1.24–1.83]	<0.001
Mini- Geriatric Depression Scale (score ≥ 1)	200	26	219	43	1.83 [1.54–2.18]	<0.001
Activities of daily living score ($\leq 5/6$)	145	18	210	38	2.27 [1.91–2.69]	<0.001
Instrumental activities of daily living score ($< 8/8$)	430	54	397	74	2.12 [1.75–2.57]	<0.001
Get-up-and-go test, ref: ≤ 20 s	581	78	261	53	Ref. 1.00	<0.001
> 20 s/Not able to perform the test	166	22	232	47	2.06 [1.69–2.52]	<0.001
Falls in the previous 6 months (≥ 1)	203	25	185	34	1.43 [1.19–1.70]	<0.001
Nutrition-related tools						
Body mass index (kg/m^2), ref: 22 to < 25	221	27	131	24	Ref. 1.00	<0.001
< 22	167	21	196	35	1.71 [1.37–2.13]	<0.001
25 to < 30	296	37	172	31	1.02 [0.81–1.28]	0.9
≥ 30	124	15	54	10	0.79 [0.57–1.08]	0.14
Weight loss in the previous 6 months, ref: $\leq 5\%$	644	80	295	53	Ref. 1.00	<0.001
5 to 10%	68	8	144	26	2.11 [1.70–2.62]	<0.001
$> 10\%$	96	12	114	21	3.12 [2.56–3.81]	<0.001
Mini Nutritional Assessment, ref: ≥ 24	447	55	123	22	Ref. 1.00	<0.001
< 17	51	6	154	28	6.59 [5.19–8.37]	<0.001
17 to 24	310	38	276	50	2.66 [2.15–3.29]	<0.001
Geriatric Nutritional Risk Index, ref: > 98	441	55	125	23	Ref. 1.00	<0.001
< 82	58	7	143	26	5.65 [4.44–7.19]	<0.001
82 to 92	114	14	169	31	3.72 [2.95–4.70]	<0.001
92 to 98	195	24	116	21	1.88 [1.46–2.43]	<0.001
Prognostic Nutritional Index, ref: > 45	505	62	141	25	Ref. 1.00	<0.001
< 40	134	17	257	46	4.71 [3.83–5.79]	<0.001
40 to 45	169	21	155	28	2.63 [2.09–3.30]	<0.001
Glasgow Prognostic Score, ref: 0	489	61	134	24	Ref. 1.00	<0.001
1	201	25	169	31	2.49 [1.98–3.12]	<0.001
2	118	15	250	45	5.17 [4.19–6.39]	<0.001
modified Glasgow Prognostic Score, ref: 0	568	70	194	35	Ref. 1.00	<0.001
1	122	15	109	20	2.15 [1.70–2.71]	<0.001
2	118	15	250	45	4.26 [3.53–5.15]	<0.001
C-reactive protein/albumin ratio, ref: ≤ 0.08	361	45	83	15	Ref. 1.00	<0.001
0.08–0.50	162	20	302	55	2.21 [1.70–2.87]	<0.001
> 0.50	285	35	168	30	5.41 [4.24–6.91]	<0.001

CIRS-G: Cumulative Illness Rating Scale for Geriatrics; ECOG-PS: Eastern Cooperative Oncology Group performance status.

We observed a graded relationship between the categories and 1-year mortality, with the worse categories giving the highest mortality rates ($p < 0.02$ in an overall log-rank test; $p < 0.0001$ in a test for trend; Fig. 1).

In the univariate analysis, other factors associated with higher 1-year mortality were older age, male sex, inpatient status, tumour site

combined with cancer extension (colorectal, upper digestive tract, liver, prostate, and lung metastatic cancers; pancreas and urological cancers and haematological malignancies, compared with non-metastatic colorectal cancer), palliative therapy and supportive care alone, a poor ECOG-PS (≥ 2), severe comorbidities, polypharmacy, impaired MMSE,

mini-GDS, ADL and IADL scores, an impaired or failed TUG test, and falls in the previous 6 months (Table 3). A significant interaction was found between tumour site and metastatic status ($p = 0.010$); the negative effect of having metastatic disease differed from one type of tumour to another and was highest for pancreatic, upper digestive tract and liver cancers. We therefore created a composite variable comprising the tumour site and metastatic status.

With regard to the nutrition-related tools (Table 3), patients with a low BMI ($<22 \text{ kg/m}^2$) had higher mortality risk than patients having a normal BMI ($22\text{--}24.9 \text{ kg/m}^2$). Similarly, the mortality risk was higher in patients with substantial WL than in patients with minimal WL. Similar results were found for the other tools: patients with impaired nutritional risk status or abnormal scores had a higher risk of mortality than patients with no nutritional risk or a normal score.

Based on the literature, on univariate analyses and in order to avoid multicollinearity [40], we selected one variable for each geriatric dimension. The baseline model included the following independent prognostic factors: age (≥ 82 years old), impaired ADL score (<5), having at least one severe comorbidity (CIRS-G grades 3–4), a risk of a cognitive disorder (MMSE < 24), a risk of depression (mini-GDS ≥ 1), the cancer treatment strategy (curative treatment, palliative treatment, or supportive care alone), inpatient status, tumour site, and tumour extension (reference: local colorectal cancer). All the variance inflation factors were below 1.5.

In the multivariate analysis adjusted for the factors included in the baseline model, all the nutrition-related tools were independently associated with 1-year mortality (overall p -values < 0.02 for all) (Table 4). The increment in the risk of 1-year mortality in patients with impaired nutritional risk status ranged from 1.33 [95%CI: 1.02–1.75] for patients with WL between 5 and 10% (compared with patients with WL $\leq 5\%$) to 2.97 [2.10–4.20] for patients with a GNRI < 82 (a major nutrition-related risk, compared with patients with no nutrition-related risk: GNRI > 98).

3.3. Ability of each nutrition-related tool to predict 1-year mortality

The baseline model had good discriminative ability, with a CPE of 0.762 and a C-index of 0.749. It was well calibrated, with a Grönnesby and Borgan p -value of 0.63. Table 4 shows the prognostic performance of the eight multivariate models, one for each nutrition-related tool adjusted for the baseline model (i.e. the value of adding each nutrition-related tool to the baseline model). Except for models including the BMI and the CRP/albumin ratio, all the models were well calibrated ($p > 0.20$). All the models showed good discrimination (C-index and CPE ≥ 0.70).

All the nutrition-related tools improved the levels of calibration and discrimination, relative to the baseline model. The GNRI score showed the highest increment in discrimination, with a R^2 of 0.357 (compared with 0.328 in the baseline model) and a CPE of 0.773; it also gave the best fit, with the greatest ΔAIC (34.2). The GPS ($R^2 = 0.352$, CPE = 0.773 and

Table 4
Predictive ability of 8 nutrition-related tools for 1-year mortality in older patients with cancer.

Models	Adjusted Hazard Ratios [95% CI]	P-value	Calibration		Discriminant ability		
			Goodness of fit (Grönnesby and Borgan)	ΔAIC	CPE	Harrell's C index [95%CI]	R^2
Baseline ^a	Ref		0.63	4633.5	0.762	0.749 [0.727–0.7725]	0.328
Baseline + nutrition-related tool:							
BMI							
<22 kg/m ²	1.56 [1.18–2.06]	0.026	0.12	3.8	0.766	0.748 [0.7265–0.771]	0.335
22 to <25 kg/m ²	Ref						
25 to <30 kg/m ²	1.26 [0.94–1.67]						
$\geq 30 \text{ kg/m}^2$	1.28 [0.87–1.88]						
Weight loss (<6 months)							
$\leq 5\%$	Ref						
5 to 10%	1.33 [1.02–1.75]						
>10%	1.51 [1.15–1.98]						
MNA							
<17	2.69 [1.88–3.85]	<0.0001	0.52	24.9	0.769	0.758 [0.737–0.780]	0.349
17 to 24	1.57 [1.20–2.05]						
≥ 24	Ref						
GNRI							
<82	2.97 [2.10–4.20]	<0.0001	0.24	34.2	0.773	0.76 [0.737–0.783]	0.357
82 to 92	2.04 [1.50–2.77]						
92 to 98	1.37 [1.01–1.86]						
>98	Ref						
PNI							
<40	2.11 [1.58–2.83]	<0.0001	0.62	23.8	0.772	0.759 [0.738–0.782]	0.348
40 to 45	1.75 [1.32–2.31]						
>45	Ref						
GPS							
0	Ref						
1	1.65 [1.25–2.17]						
2	2.36 [1.76–3.17]						
mGPS							
0	Ref						
1	1.54 [1.15–2.05]	<0.0001	0.60	25.5	0.771	0.760 [0.739–0.784]	0.349
2	2.05 [1.57–2.68]						
CRP/albumin ratio							
≤ 0.08	Ref						
0.08–0.50	1.51 [1.09–2.08]	<0.0001	0.15	25.7	0.772	0.760 [0.738–0.782]	0.349
>0.50	2.31 [1.67–3.18]						

AIC: Akaike Information Criterion; BMI: Body Mass Index; CI: Confidence Interval; CPE, concordance probability estimate; CRP: C-reactive protein; GNRI: Geriatric Nutritional Risk Index; GPS: Glasgow Prognostic Score; mGPS: modified Glasgow Prognostic Score; MNA: Mini Nutritional Assessment; PNI: Prognostic Nutritional Index.

^a Age (≥ 82 years old) + ADL (<5) + CIRS-G grade 3–4 (≥ 1 comorbidity) + MMSE (<24) + mini-GDS (≥ 1) + cancer treatment decision + outpatient status + cancer site * cancer extension.

Δ AIC = 29.8) performed almost as well as the GNRI. Since these two tools were based on albumin, we performed the same analysis on serum albumin alone (<35 g/L vs ≥ 35 g/L). Hypoalbuminemia (<35 g/L) was also independently associated with 1-year mortality (aHR = 1.69, 95% CI: 1.33–2.15) but presented a lower improvement of fit (Δ AIC = 15.8) and of discrimination ($R^2 = 0.341$ and CPE = 0.768). CRP alone gave much the same performance as albumin (data not shown).

3.4. Sensitivity analyses

Sensitivity analyses of patients with the specific nutrition-related tool available gave much the same calibration and discrimination results as the main analyses (**Supplementary Table 1**). However, models including the BMI or the CRP/albumin ratio were better calibrated than in the main analysis.

Analyses of metastatic status subgroups (**Supplementary Table 2**) produced contrasting results. In the metastatic subgroup ($n = 484$), the GNRI gave the largest increment in discrimination, with a C-Harrell of 0.717 [95%CI: 0.687–0.744] and a CPE of 0.724 (compared with a C-Harrell of 0.699 [95%CI: 0.670–0.727] and a CPE of 0.702 in the baseline model). In the non-metastatic subgroup ($n = 393$), the GPS gave the largest increment in discrimination, with a C-Harrell of 0.779 [95%CI: 0.744–0.820] and a CPE of 0.784 (compared with a C-Harrell of 0.761 [95%CI: 0.722–0.790] and a CPE of 0.774 in the baseline model). With regard to the four main cancer sites, the tools with the highest discriminant power were WL in the previous 6 months and BMI in patients with colorectal cancer, the CRP/albumin ratio in patients with breast cancer, the mGPS in patients with prostate cancer, and the PNI, the GPS and the CRP/albumin ratio in patients with other urological cancers (**Supplementary Table 3**). In the univariate analyses regarding the four cancer sites with low number of patients, the tools with the highest discriminant power were the MNA and GNRI in patients with haematological malignancies or upper digestive tract and liver cancers, the PNI and GPS in patients with pancreas cancer, and WL in patients with lung cancer (**Supplementary Table 4**).

4. Discussion

Our results showed that all eight nutrition-related tools studied (BMI, WL, MNA, GNRI, PNI, GPS, mGPS, and the CRP/albumin ratio) were independently associated with 1-year mortality in a large population of older patients with cancer. This is consistent with the literature data and confirmed that malnutrition increases the risk of death in older adults with cancer. Indeed, a recent meta-analysis found that malnutrition was associated with a two-fold increased risk of death in this type of patient population [41].

Each of the eight nutrition-related tools analysed here had previously been found to be predictive of mortality. For example, the GNRI was developed to predict morbidity and mortality in hospitalized older patients and has demonstrated prognostic value in various clinical conditions, including heart failure [42], chronic haemodialysis [43], and cancer [44,45]. In comparison with other nutrition-related tools (i.e. the short-form MNA, a nutrition risk score, the Malnutrition Universal Screening Tool, and the Malnutrition Screening Tool), the GNRI identified the nutritional risk in patients undergoing haemodialysis [46] more accurately than the other tools when using a malnutrition-inflammation score as reference for malnutrition. A meta-analysis of 13 studies involving 8046 adult patients with cancer (median age: 68; range: 37–113) found that a low GNRI was associated with poor overall survival (HR = 1.95, 95%CI: 1.49–2.56) when compared with a high baseline GNRI [44]. The disparity in the strength of these associations between the literature and our present results might be due to differences in the study country (with 1 in Korea, 9 in Japan, and 5 in China, vs. our study in France), the GNRI cut-off, and the age range.

The GPS was similar to the GNRI in terms of improved prediction of 1-year mortality and includes the albumin and CRP levels; it therefore captures biochemical information about nutrition and inflammation. Like the mGPS and the CRP/albumin ratio, the GPS adds prognostic value (relative to clinical and geriatric information alone) for the estimation of survival in older patients with cancer [47]. In a meta-analysis of studies of adult patients with cancer, the weighted average HR for an incremental increase in the GPS and mGPS was 2.0 in patients with operable or inoperable cancers [48]; we found similar results. The PNI is based on the albumin level and the lymphocyte count and reportedly helps to predict survival and the occurrence of postoperative complications in patients with oesophageal [49], gastric [50], colorectal [51] or lung cancer [52]. The PNI reflects the patient's inflammation and antitumor immunity status and so might not reflect nutrition alone [53]. In patients with oesophageal or lung cancer, the association between PNI and overall survival [49,52] was about as strong as in our study. In contrast to the above-mentioned biochemical markers, the MNA is based entirely on clinical information. It is widely used in clinical settings [54] and as a “semi-gold standard” for the validation of other nutritional tools [55], even though it includes additional information on overall health status. The association between a low MNA and a higher risk of early death documented in older (over-70) patients undergoing first-line chemotherapy [24] was similar to that observed in our study. The MNA performed similarly to the other nutrition-related tools and especially the GNRI and GPS. However, in a study of newly institutionalized older people, the GNRI has previously been described as a better predictor of all-cause mortality than the MNA [56].

Our analyses of cancer subgroups produced disparate results. The highest increment in discrimination was given by the GNRI in the metastatic subgroup and the GPS in the non-metastatic subgroup. Both tools take the serum albumin level into account, while the GNRI additionally accounts for WL and the GPS additionally accounts for the serum CRP level. This might reflect the important role of WL in patients with metastatic cancer, while the CRP might better reflect inflammation and the cancer's aggressiveness of patients with non-metastatic cancer.

4.1. Strengths and limitations

Our study had a number of strengths, including its prospective design, the large sample size, the various types of cancer studied, and the data on metastatic status; this enables us to access a broad range of clinical situations. Furthermore, our baseline model included variables from several distinct geriatric dimensions. We also assessed the prognostic performance of a variety of nutrition-related tools and estimated several calibration and discrimination indices. The study also had some limitations. The results should be extended to other older patients with cancer with caution because the patients in our study had all been referred by a physician for a GA; this might have introduced selection bias. The non-inclusion of patients lacking a complete dataset (i.e. data for all the nutrition-related tools) might also have been a source of selection bias; nonetheless, the fact that our sensitivity analyses gave similar results for each tool underlines the robustness of our findings. Lastly, we could not evaluate some other pertinent nutrition-related tools because they were not recorded in our dataset.

4.2. Implications for practice

Depending on the time or context of the GA (during a convention hospital stay, during a consultation, in a day hospital, and before or after first-line treatment (surgery or otherwise)), physicians do not always have the time or means to perform and assess all the tools/markers compared here. However, if the patient has been identified as being at risk of malnutrition, anthropometric markers should be monitored at each assessment (weight loss and BMI) in accordance with GLIM phenotypic criteria (GLIM 2019). These patients should also be made aware of the

need to monitor their weight regularly at home. To assess the prognosis and severity of malnutrition during follow-up, GNRI may be preferred, as it only requires measurement of albumin levels in addition to anthropometric markers. This is reinforced by our study, which shows the good prognostic performance of this score. However, this should be confirmed by further studies with repeated measures of GNRI. Still, even when some information is missing, each nutritional tool/marker has prognostic value and can be used in the evaluation.

In conclusion, all eight nutrition-related tools tested here (the BMI, WL in the previous 6 months, the MNA, the GNRI, the PNI, the GPS, the mGPS, and the CRP/albumin ratio) were independently associated with 1-year mortality in older patients with cancer after adjustment for known prognostic factors. The one-year mortality risk increased progressively with tools' values worsened.

Ethical standard

The study protocol was approved by the independent ethics committee (*CPP Ile-de-France I*, Paris, France; approval reference: 2019 mai-MS121). All the study patients provided their written, informed consent before inclusion.

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Declaration of interest

None.

CRedit authorship contribution statement

Rémi Valter: Formal analysis, Writing - original draft. **Elena Paillaud:** Project administration, Writing - review & editing. **Pascaline Boudou-Rouquette:** Investigation, Writing - review & editing. **Nadia Oubaya:** Methodology, Writing - review & editing. **Amélie Arégu:** Resources, Writing - review & editing. **Emmanuelle Lorisson:** Investigation, Writing - review & editing. **Etienne Brain:** Investigation, Writing - review & editing. **Godielieve Rochette de Lempdes:** Resources, Writing - review & editing. **Axelle Histe:** Data curation, Software. **Marie Laurent:** Resources, Writing - review & editing. **Florence Canoui-Poitrine:** Conceptualization, Project administration, Validation, Writing - review & editing. **Philippe Caillet:** Project administration, Resources, Writing - review & editing. **Amaury Broussier:** Methodology, Writing - review & editing. **Claudia Martinez-Tapia:** Conceptualization, Supervision, Writing - review & editing.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.jnha.2024.100188>.

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