Obesity survival paradox in cancer patients: Results from the Physical Frailty in older adult cancer patients (PF-EC) study

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Abstract

Background & aims: the obesity survival paradox is an emergent issue in oncology, but its existence remains unclear particularly in older cancer patients. We aimed to assess the obesity survival paradox in older cancer patients.

Methods: all consecutive cancer outpatients 65 years and older referred for geriatric assessment (GA) before a decision on cancer treatment between November 2013 and September 2016 were enrolled in the PF-EC cohort study. The main outcome was 6-month mortality. A Cox univariate and multivariate proportional hazard regression models were performed with baseline GA, oncological variables (cancer site, extension and treatment modalities) and C-reactive protein (CRP). We assessed the prognostic value of body mass index categories (i.e. malnutrition < 21, 21 ≤ normal weight ≤ 24.9, 25 ≤ overweight ≤ 29.9 and obesity ≥ 30 kg/m^2) in the whole study population and according to the metastatic status.

Results: 433 patients with a mean age of 81.2 ± 6.0 years were included, 51% were women, 44.3% had digestive cancers, 18% breast cancer and 14.5% lung cancer and 45% metastatic cancers. Eighty-eight of these patients (20.3%) were obese at baseline. Mortality rate was 17% during the 6-month follow-up period. After adjustment for sex, gait speed, Mini-Mental State Examination, cancer site and exclusive supportive care, obesity (compared to normal weight) was independently and negatively associated with 6-month mortality only in metastatic patients (aHR 0.17, 95% CI [0.03–0.92], *P* = 0.04).

Conclusion: our study confirms the obesity survival paradox in older cancer patients only in the metastatic group.

Keywords: *cancer, metastasis, obesity survival paradox, geriatric assessment, older people.*

Background

The prevalence of obesity (body mass index (BMI) ≥ 30 kg/m^2) is increasing worldwide, with about 40% of people between 65-74 years old and 30% over 75 years old being obese [1]. Moreover, 60% to 70% of newly diagnosed cancers concern older patients [2]. Obesity is a major risk factor of morbidity in older people. It is associated with an increased risk of cancers (breast, colon, uterine, leukaemia), cardiovascular morbidity (stroke, myocardial infarction), disability, number of medications, metabolic syndrome and osteoarthritis, and it decreases mobility and quality of life [1]. Obesity is also a well-known risk factor of mortality in middle-aged people, but recent studies have demonstrated that this association is not seen for adults aged 65 and over. This is termed the "obesity survival paradox" [1].

Over the past decade, the obesity survival paradox has been specifically observed in cancer patients with local and metastatic disease in several studies [3]: patients treated for colorectal [4,5] and renal cancer [6,7], patients with lymphoma undergoing autologous haematopoietic cell transplantation [8] and metastatic patients requiring radiotherapy [9].

To our knowledge, only one study has assessed the obesity survival paradox specifically in older cancer patients. In this recent study, the association between BMI and overall survival (OS) during a 10-year follow-up was assessed in 97 patients 60 years and over with acute myeloid leukaemia before chemotherapy [10]. Median age was 68 years, the median OS was 316 days and 32% of patients were obese. A BMI <25 kg/m^2 compared to obesity (≥ 30 kg/m^2) was an independent predictor of mortality (HR = 2.14, 95% CI, 1.21–3.77).

The older cancer population is heterogeneous in comorbidities, physical reserves, functional status and socioeconomic environment [11]. Geriatric assessment (GA) is therefore recommended by the International Society of Geriatric Oncology (SIOG) [12] to detect vulnerabilities likely to lead to poor outcomes and treatment complications [13–15].

To date, no studies have assessed the obesity survival paradox in older cancer patients after adjustment for GA domains, and the existence of the obesity survival paradox in such patients remains unclear. We postulated that obesity was positively associated with OS in older cancer patients. We aimed to assess the existence of the obesity survival paradox in older cancer patients of the whole study population and according to the metastatic status.

Methods

Study design and population

The Physical Frailty in Elderly Cancer patients (PF-EC) survey is an open prospective observational two-centre cohort study that started in November 2013. All consecutive patients aged 65 years and over referred for geriatric assessment in two university hospitals in the greater Paris area of France, Avicenne Hospital in Bobigny and Jean Verdier Hospital in Bondy, were included. Patients were referred by oncologists, radiotherapists, surgeons, or other specialists when a new diagnosis of cancer was highly suspected or confirmed histologically and when frailty was suspected, during the two weeks before a cancer treatment decision.

For the present analysis, we included all outpatients, regardless of cancer type, stage or treatment, who presented up to September 30, 2016. The inclusion date was the date of the first geriatric oncology visit.

Informed consent was obtained from the patients before inclusion. The study was approved by the local ethics committee (CLEA, Avicenne Hospital, Bobigny, France).

Data collection:

In this study, we followed the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) recommendations for the reporting of observational epidemiological studies [16].

Cancer and demographic data: Demographic data (age, sex), tumour characteristics (site, extension: local, locally advanced or metastatic/diffuse) and Eastern Cooperative Oncology Group Performance Status (ECOG-PS) were obtained at the first geriatric oncology visit as part of the GA. Cancer treatment modalities were categorised as exclusive supportive care or not and were collected during the 6-month follow-up.

Body mass index

Weight and height were measured at the first geriatric oncology visit to calculate body mass index (BMI) which was categorised in four classes according to the World Health Organization and the French nutritional guidelines: BMI < 21 (malnutrition), 21.0 ≤ BMI ≤ 24.9 (normal weight), 25.0 ≤ BMI ≤ 29.9 (overweight) and BMI ≥ 30 (obesity). Obesity was described as moderate (30.0 ≤ BMI ≤ 34.9), severe (35.0 ≤ BMI ≤ 39.9) or morbid (BMI ≥ 40.0) [17,18].

Geriatric assessment

At the first geriatric oncology visit, each patient underwent GA following the recently updated recommendations of the International Society of Geriatric Oncology [19]. Comorbidities were assessed by the Cumulative Illness Rating Scale-Geriatric (CIRS-G) [20]. A total score dichotomised by a median of 14, or the presence of at least one grade 3 (severe) or grade 4 (very severe) comorbidity excluding the current cancer, was considered to indicate impairment. Polypharmacy was defined as taking five or more drugs a day. Dependency was defined by an Activities of Daily Living (ADL) score of less than or equal to 5/6 or a four-item simplified (use of telephone, transports, medications, and money management) Instrumental ADL (IADL) that was less than 4/4 [21,22]. Mobility was assessed by gait speed (GS) measured over a short distance (4 m) in metres/second (m/s) [23]. A slow GS was defined as < 0.8 m/s because this threshold has shown a strong and independent association with early death in older cancer patients [23,24]. Repeated falls were defined as at least two falls in the previous year. Depressed mood was defined as a Mini-Geriatric Depression Scale

(Mini-GDS) score of at least 1/4 [25]. Cognitive impairment was defined by a Mini-Mental State Examination (MMSE) score of less than 24/30 [26].

Muscle weakness

Maximum hand grip strength (kilograms) measured twice for each hand using a CAMRY hand-held dynamometer (model EH101) was used to assess muscle weakness (MW) at the first geriatric oncology visit. MW was defined by the thresholds adjusted for gender and BMI derived from the frailty phenotype established by Fried *et al.* [27].

Covariate

Inflammation was assessed by C-reactive protein (CRP) level measured by immunoturbidimetric assay during the first 3 weeks after the GA. Abnormal CRP was defined as $\geq$ 10 mg/l [28].

Outcomes

The primary outcome was overall 6-month mortality following the GA to assess predictors of early death. Vital status was determined by telephoning patients or their family or from medical records.

Statistical analysis

We used numbers for descriptive data, proportions for qualitative variables and means with SDs or medians with interquartile (IQR) range (25^{th}-75^{th}) for quantitative variables. Comparisons between obese and non-obese and then between metastatic and non-metastatic patients were carried out using the chi-square test or Fisher's exact test for qualitative variables and the Student *t* test or Wilcoxon's test for quantitative variables as appropriate. We assessed correlation by using the Spearman rho test as appropriate for categorical variables. Multicollinearity between variables was defined as a rho test ≥ 0.50.

Baseline factors associated with obesity were analysed by univariate and multivariate logistic analyses. Variables yielding *P* values less than 0.2 in the univariate analysis were considered for inclusion in the multivariate analysis.

Survival curves were plotted according to the Kaplan-Meier method. Comparisons according to BMI categories in the whole study population and in patient subsets according to the metastatic status were performed by the log-rank test. Cox univariate and multivariate proportional hazard regression models were performed with baseline characteristics associated with 6-month mortality. Model assumptions were verified. Continuous variables were shown per their standard deviations. Variables yielding *P* values less than 0.2 in the univariate analysis were considered for inclusion in the multivariate analyses. We conducted a stratified analysis in patient subsets according to the metastatic status. All analyses were adjusted for sex, gait speed, cancer-site, cancer-extension and supportive care.

All tests were two-sided at a significance level of 0.05. Multiple imputation was performed to handle missing data for MMSE (MICE package using predictive mean matching method as appropriate for numeric variables). The data were analysed using R statistical software version 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria, http://www.R-project.org).

Results

Patients

Of the 457 consecutive older cancer outpatients aged 65 and over who were referred for GA up to September 30, 2016, and were potentially eligible, 433 were finally eligible for this study (Figure 1).

Baseline characteristics of patients (Table 1)

Median age was 82 (IQR 77–85) years. The majority were women, had solid tumours (95%), local (20%) and locally advanced (35%) cancer. Colorectal and breast cancer were the two most common types, whereas urological malignancies were uncommon (4.8%). Obesity affected 20.3% (88/433) of patients, of whom 70 (79.5%) were moderately obese, 15 (17%) were severely obese and 3 (3.5%) morbidly obese. Geriatric assessment showed that most patients had significant impairment in several domains: two-thirds of patients had severe comorbidities, polypharmacy and muscle weakness. IADL dependency was more frequent than ADL dependency and concerned two-thirds of patients. More than half of patients had slow gait speed and cognitive impairment. Less than half of patients had depressive mood and CRP ≥ 10 mg/l. Repeated falls were uncommon.

Comparison between obese and non-obese patients

In univariate analysis, male sex, locally-advanced cancer (compared to local cancer), total CIRS-G and grade 3 comorbidity, polypharmacy, ADL dependency and slow gait speed were the variables positively and significantly associated with obesity. Metastatic cancer (compared to local cancer) and CRP ≥ 10 mg/l were the variables negatively and significantly associated with obesity. In multivariate analysis, breast cancer, total CIRS-G and slow gait speed were positively and independently associated with obesity. CRP ≥ 10 mg/l was negatively and independently associated with obesity. Moreover, when multivariate analysis included ADL or IADL as covariate instead of slow gait speed, ADL (*P* = 0.10) and IADL (*P* = 0.74) were not independently associated with obesity.

Comparison between metastatic and non-metastatic patients

Metastatic patients did not differ by mean age (*P* = 0.06), proportion of exclusive supportive care (*P* = 0.94), total comorbidities (*P* = 0.46), polypharmacy (*P* = 0.61), ADL and IADL (*P* = 0.09 and 0.77 respectively), gait speed (*P* = 0.45), muscle strength (*P* = 0.68), mini-GDS (*P* = 0.90) and MMSE (*P* = 0.19). In contrast, metastatic patients had more aggressive cancers (lung, pancreas and bile ducts) (*P* < 0.0001), a lower BMI (*P* = 0.01) with a smaller proportion of obese patients (16%), were more frequently men (*P* < 0.0001) and had significantly higher CRP levels (*P* = 0.01).

Predictors of overall 6-month mortality

Mortality rate during the 6-month follow-up after the initial GA was 17% (95% CI, 13.8–21%). Median overall survival was not reached.

Kaplan-Meier survival analysis plotted by BMI category alone showed no significant difference between obesity and other categories (i.e. normal weight, overweight and malnutrition) in the whole study population (Figure 2). However, there was a trend towards a protective effect of obesity on 6-month mortality (*P* log rank test = 0.06).

In univariate analysis (Table 2), breast cancer and haematological malignancies (compared to colorectal cancer) were negatively associated with 6-month mortality. In contrast, male gender, lung, liver, pancreas and bile ducts, gynaecological malignancies, oesophageal and gastric and other cancers (compared to colorectal cancer), locally-advanced and metastatic cancer, exclusive supportive care, slow gait speed, muscle weakness, cognition impairment and CRP ≥ 10mg/l, were positively associated with 6-month mortality. Age, comorbidities, BMI categories and depressed mood were not significantly associated with 6-

month mortality. Because of the multicollinearity between GS, ADL/IADL and ECOG-PS, we used only GS as clinical variable of functional status in multivariate analyses [29]. Because of the multicollinearity between total CIRS-G total and grade 3 comorbidity and polypharmacy, we used only the CIRS-G total score as clinical variable to assess the burden of comorbidities in multivariate analyses. Due to the non-linear association between BMI and survival, we compared BMI categories to normal weight to perform our analyses.

In multivariate analysis (Figure 3), BMI categories were still not independently associated with 6-month mortality in the whole study population or in non-metastatic patients. In metastatic patients, obesity compared to normal weight was the only BMI category independently and negatively associated with 6-month mortality after adjustment for sex, gait speed, MMSE, cancer site and exclusive supportive care.

Discussion

In this cohort of consecutive older outpatients with currently untreated cancer at various sites and stages, obesity defined by BMI ≥ 30 kg/m^2 compared to normal weight was not independently associated with 6-month mortality in the whole study population or in non-metastatic patients. In the stratified analysis, obesity was independently and negatively associated with 6-month mortality in metastatic patients after adjustment for sex, gait speed, MMSE, cancer site and exclusive supportive care. Breast cancer, comorbidities and slow gait speed were the variables independently and positively associated with obesity. In contrast, inflammation defined by CRP levels ≥ 10 mg/l was independently and negatively associated with obesity.

Our findings are consistent with a large retrospective study by Tsang *et al.* [9]. In this study, 4,010 metastatic cancer patients requiring a radiotherapy with a median age of 59.6 years (range: 18.4–94) and with an ECOG-PS 0-1 were included. The median follow-up time was 24.4 months (range 0.13–164.1). Obesity (BMI ≥ 30 kg/m^2) compared to normal weight was independently associated with overall survival (HR 0.67, CI 95%, 0.56–0.80). In agreement with these authors, one of the main explanations of the obesity paradox in metastatic cancer patients arises from the inverse association between BMI and fatty acid synthase (FASN) expression. FASN is an oncogene that encodes for rate-limiting enzymes involved in fatty acid synthesis, a process essential for tumour growth and which is overexpressed in several malignancies [9]. Hakimi *et al.* showed that FASN is significantly downregulated in obese patients with renal cell carcinoma and has a beneficial effect on cancer-specific survival [7]. However, in our study we observed the observation of obesity survival paradox only in metastatic patients and this deserves discussion. Metastatic status is related to a high malignant potential that requires higher levels of energy [9]. One of the main energy sources for malignant cells arises from elevated adipose tissue lipolysis and increasing fatty acid oxidation [9]. Accordingly, there is probably a greater fat loss in metastatic patients due to aggressive tumour behaviour with higher energy demand. This probably could explain the significantly lower BMI in metastatic patients in our cohort, in which obese patients had an advantage in overall survival due to higher fat reserves.

In a recent multicentre prospective observational study that included 1,306 consecutive older patients hospitalised in an emergency department (mean age 85 ± 6 years) geriatric assessment was carried out in all patients [30]. Obesity (BMI ≥ 30 kg/m^2) was found in 19.6% and was negatively and independently (after adjustment for age, mobility disorders, dementia syndrome, dependency and comorbidities) associated with overall 1-year (HR 0.8, 95% CI, 0.6–1.0, *P* = 0.05) and 2-year (HR 0.8, 95% CI, 0.6–1.0, *P* = 0.03) survival. Among these obese patients, 12.9% had cancer. In agreement with the authors of this study, we support the existence of two distinct subtypes of obesity, as has been suggested in the literature [31]: metabolically healthy obesity (MHO) and metabolically unhealthy obesity (MUO). About 20-30% of obese patients may have MHO, which is characterised by the absence of metabolic complications of obesity, by low inflammation and low disability [31]. This approach could explain in part the obesity survival paradox. Accordingly, there was probably a natural selection of MHO in our cohort since it comprised older people with significant comorbidities and no significant disability which they survived until recently developing a cancer.

More recently, a multicentre prospective cohort study conducted in 6,662 community-dwelling older women aged 75 and older confirmed the obesity survival paradox [32]. The risk of death during the 5-years follow-up of frail women (frailty defined by the Fried model) compared with not-frail normal weight women, decreased with increase of BMI after adjustment for age, cardiovascular drugs, hospital admission in the last 12 months and functional status: HR (frail-underweight) = 2.04 [1.23–3.39]; HR (frail-normal weight) = 3.07

[2.21–4.26]; HR (frail-overweight) = 1.83 [1.31–2.56]; HR (frail-obese) = 1.76 [1.15–2.70]; $P < 0.001$. However, the obesity survival paradox in cancer patients remains debatable. Obesity survival paradox observation may involve methodological biases such as reverse causality, confounding, detection bias, or collider bias [33]. The non-obese population may include patients who had lost weight as a result of more severe illness, while BMI is not an optimal measure of body fat and obese older patients may be affected by selective survival bias. Nevertheless, several authors have argued that such biases may not solely explain the obesity paradox [33,34].

The strengths of our study are the study design and the internal consistency with other large studies (ONCODAGE, ELCAPA) conducted in older cancer patients (age, cancer site, cancer extension at inclusion). Moreover, to our knowledge, this is the first study that confirmed the obesity survival paradox in older cancer patients after adjustment for several geriatric domains.

However, our study has several limitations. Firstly, because of the small size of the severe and morbid obesity subgroups we were unable to determine the prognostic value of obesity in these patients. Secondly, the history of weight loss was not considered in our study, and this probably limited the association between obesity and digestive cancers related to obesity (oesophageal, gastric, colorectal or pancreatic cancers). Digestive cancers often lead to a major weight loss before diagnosis. Thirdly, due to the short follow-up time, we were unable to confirmed the obesity survival paradox in non-metastatic patients.

Finally, our results suggest that in older cancer patients, BMI probably does not yield sufficient understanding of the heterogeneous nature of obesity. A more comprehensive approach would include on the one hand, an estimation of body composition in obese patients (particularly with assessment of abdominal adiposity) and on the other hand, the history of weight loss [35,36].

Conclusion:

We confirmed the obesity survival paradox in older cancer patients only in the metastatic subgroup. This result may be linked with the downregulation of fatty acid synthase expression in obese patients, an oncogene that is overexpressed in metastatic disease.

Conflicts of interest

None declared

Authors' contributions

Conception and design: FP, TA, FCP, VL, GS, EP

Acquisition of data: FP, TA, BD, PW, NG, LZ

Analysis and interpretation of data: FP, TA, FCP, BD, LZ, EP

Drafting the article: FP, FCP, EP

Reviewing the article: FP, TA, FCP, BD, VL, PW, NG, GS, LZ, EP

Final approval: FP, TA, FCP, BD, VL, PW, NG, GS, LZ, EP

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Figure 1. Flow the selection of patients

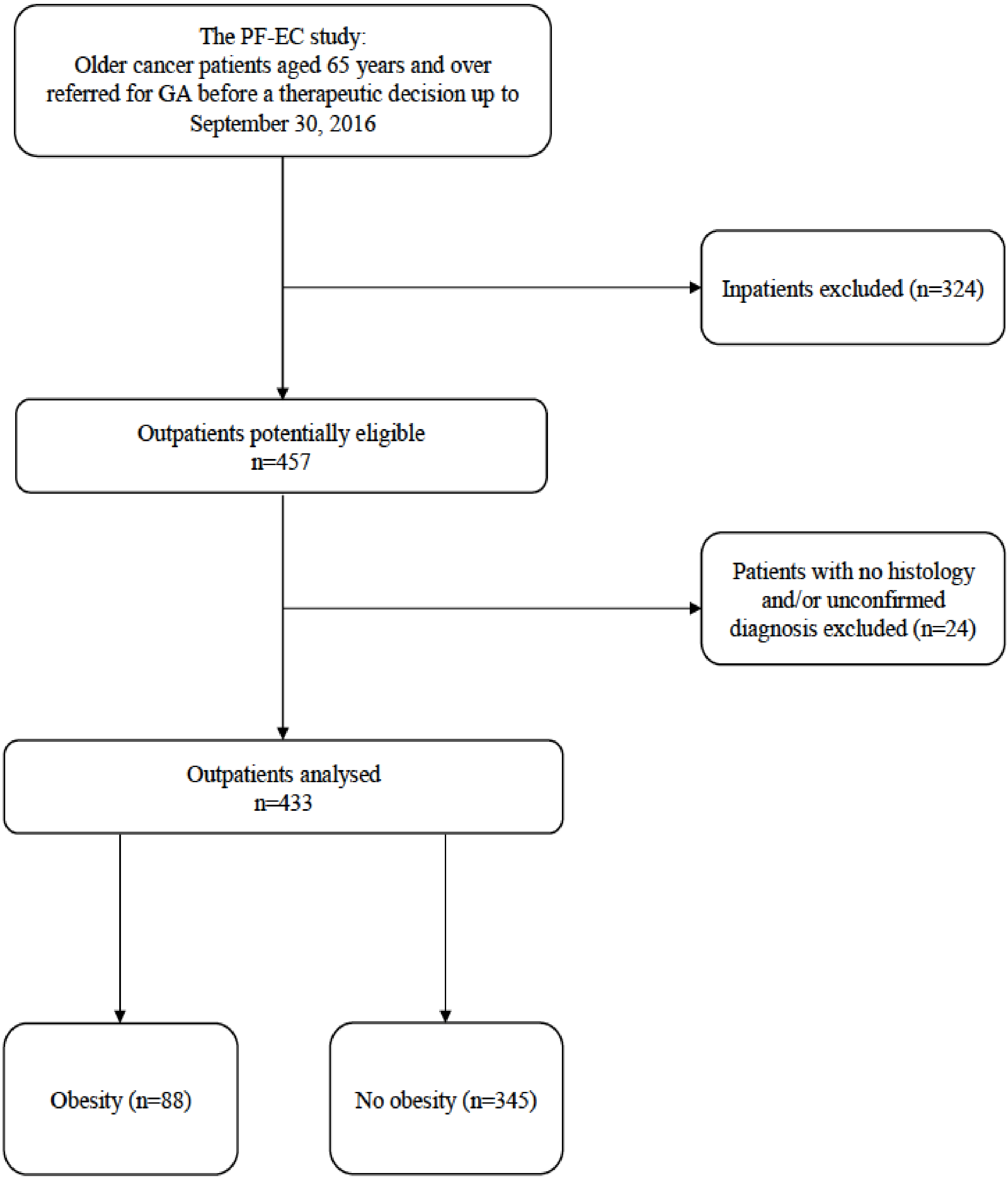

Table 1. Baseline characteristics of 433 consecutive older cancer outpatients and factors independently associated with obesity

Variables	All patients n = 433 (%)	Univariate analysis BMI ≥30 kg/m^2 n = 88 (20.3%)	BMI <30 kg/m^2 n = 345 (79.7%)	*P*[a]	Multivariate analysis aOR	95%CI	*P*
Age (years)							
Mean +/- SD	81.2 +/- 6.0	80.5 +/- 6.3	81.4 +/- 5.9	0.23			
Quartiles				0.69			
65-76	101 (23)	22 (25)	79 (23)				
77-81	115 (26)	24 (27)	91 (26.3)				
82-84	87 (21)	20 (23)	67 (19.4)				
85-103	130 (30)	22 (25)	108 (31.3)				
Sex (male)	212 (49)	33 (37.5)	179 (52)	0.01	0.98	0.51-1.88	0.96
Cancer site				0.08			0.38
Colorectal	81 (19)	13 (15)	68 (19.7)		1 (reference)		
Breast	79 (18)	27 (30.8)	52 (15)		2.62	1.11-6.17	
Lung	63 (14.5)	10 (11)	53 (15.3)		1.22	0.46-3.22	
Liver	61 (14)	14 (16)	47 (14)		1.55	0.63-3.80	
Pancreas and bile ducts	26 (6)	3 (3.4)	23 (6.6)		0.85	0.20-3.51	
Gynaecological malignancies	26 (6)	7 (8)	19 (5.5)		1.67	0.49-5.65	
Oesophageal and gastric	23 (5.3)	2 (2.3)	21 (6)		0.40	0.07-2.08	
Haematological malignancies	23 (5.3)	4 (4.5)	19 (5.5)		1.16	0.30-4.40	
Urological malignancies[b]	21 (4.9)	4 (4.5)	17 (4.9)		1.62	0.41-6.38	
Other[c]	30 (7)	4 (4.5)	26 (7.5)		0.82	0.22-2.96	
Cancer extension				0.04			0.16
Local	85 (20)	16 (18)	69 (20)		1 (reference)		
Locally advanced cancer	153 (35)	41 (47)	112 (32.5)		1.82	0.88-3.74	
Metastatic	195 (45)	31 (35)	164 (47.5)		1.13	0.52-2.40	
ECOG-PS ≥ 2 (yes)	195 (45)	47 (53)	148 (43)	0.08			

Exclusive supportive care (yes)	74 (17)	13 (15)	61 (18)	0.49				
Missing data = 8								
Comorbidities (CIRS-G)								
Total ≥ 14	215 (49.6)	59 (67)	156 (45)	0.0002	2.16		1.25-3.76	0.006
Grade 3 (severe) ≥ 1	263 (61)	65 (74)	198 (57)	0.004				
Grade 4 (very severe) > 1 (excluding current cancer)	95 (22)	24 (27)	71 (20.5)	0.17	1.34		0.72-2.49	0.34
Polypharmacy (yes)	283 (66)	70 (79.5)	213 (62)	0.0009				
Dependency								
ADL ≤ 5/6	138 (32)	41 (47)	97 (28)	0.0009				
IADL < 4	274 (63)	63 (72)	211 (61)	0.06				
Mobility								
Slow GS (<0.8 m/s)	235 (54)	63 (72)	172 (50)	0.0002	2.30		1.25-4.25	0.007
Muscle weakness (missing data = 8)	287 (67.5)	66 (75)	221 (64)	0.09	0.92		0.49-1.72	0.79
Repeated falls (missing data = 5)	72 (17)	19 (21.5)	53 (15)	0.16	1.15		0.60-2.20	0.66
Mood								
Mini-GDS ≥ 1/4	191 (44.5)	39 (44.3)	152 (44)	0.86				
Cognition								
MMSE < 24/30	237 (55)	55 (62.5)	182 (53)	0.10	1.18		0.67-2.08	0.55
Inflammation								
CRP (mg/l) ≥ 10	193 (44.5)	29 (33)	164 (47.5)	0.01	0.55		0.31-0.96	0.03

ADL: activities of daily living
BMI: body mass index
CIRS-G: Cumulative Illness Rating Scale-Geriatric
CRP: C-reactive protein
ECOG-PS: Eastern Cooperative Oncology Group Performance Status
GS: gait speed
IADL: instrumental activities of daily living
IQR: interquartile range (25th-75th)
Mini-GDS: Mini-Geriatric Depression Scale
MMSE: Mini-Mental State Examination

a Comparisons between obese and non-obese patients using the chi-square test or Fisher’s exact test for qualitative variables and Student *t* test or Wilcoxon’s test for quantitative variables.

b prostate = 12, urothelial = 4, kidney = 3, bladder = 2

c unknown primary site = 8, mesothelioma = 5, cutaneous epidermidis carcinoma = 4, anal = 3, sarcoma = 2, melanoma = 2, oral carcinoma = 2, duodenal = 2, thymoma = 1, non-differentiated carcinoma = 1.

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Table 2. Overall 6-month mortality in univariate Analysis

Variables	**Univariate analysis**	
	HR [95% CI]	***P*[a]**
BMI categories:		0.06
Normal Weight	1 (reference)	
Malnutrition	1.84 [0.94-3.60]	
Overweight	1.07 [0.61-1.88]	
Obesity	0.62 [0.28-1.36]	
Age (per 6.0 years increase)	1.01 [0.97-1.05]	0.41
Sex (male)	1.68 [1.05-2.70]	0.02
Cancer site		0.0001
Colorectal	1 (reference)	
Breast	0.39 [0.12-1.25]	
Lung	2.12 [0.95-4.73]	
Liver	1.21 [0.49-2.99]	
Pancreas and bile ducts	2.55 [0.97-6.69]	
Gynaecological malignancies	1.27 [0.40-4.07]	
Oesophageal and gastric	2.71 [1.03-7.12]	
Haematological malignancies	0.33 [0.04-2.62]	
Urological malignancies[b]	2.56 [0.93-7.06]	
Other[c]	3.14 [1.27-7.72]	
Exclusive supportive care (yes)	2.99 [1.81-4.94]	<0.0001
Cancer extension		<0.0001
Local	1 (reference)	
Locally advanced	4.15 [1.24-13.8]	
Metastatic	7.54 [2.34-24.2]	
Comorbidities (CIRS-G)		
Total ≥ 14	1.25 [0.78-1.99]	0.33
Grade 3 (severe) ≥ 1	1.03 [0.64-1.66]	0.88
Grade 4 (very severe) > 1 (excluding current cancer)	1.03 [0.63-1.88]	0.75

Mobility:		
Slow GS (<0.8 m/s)	2.88 [1.69-4.92]	<0.0001
Muscle weakness (missing data = 8)	2.52 [1.35-4.71]	0.002
Mini-GDS ≥ 1/4	1.12 [0.70-1.79]	0.61
MMSE < 24/30	2.23 [1.34-3.71]	0.001
CRP (mg/l) ≥ 10	4.01 [2.37-6.78]	<0.0001

BMI: body mass index

CIRS-G: Cumulative Illness Rating Scale-Geriatric

CRP: C-reactive protein

GS: gait speed

IQR: interquartile range

Mini-GDS: Mini-Geriatric Depression Scale

MMSE: Mini-Mental State Examination

HR: hazard ratio.

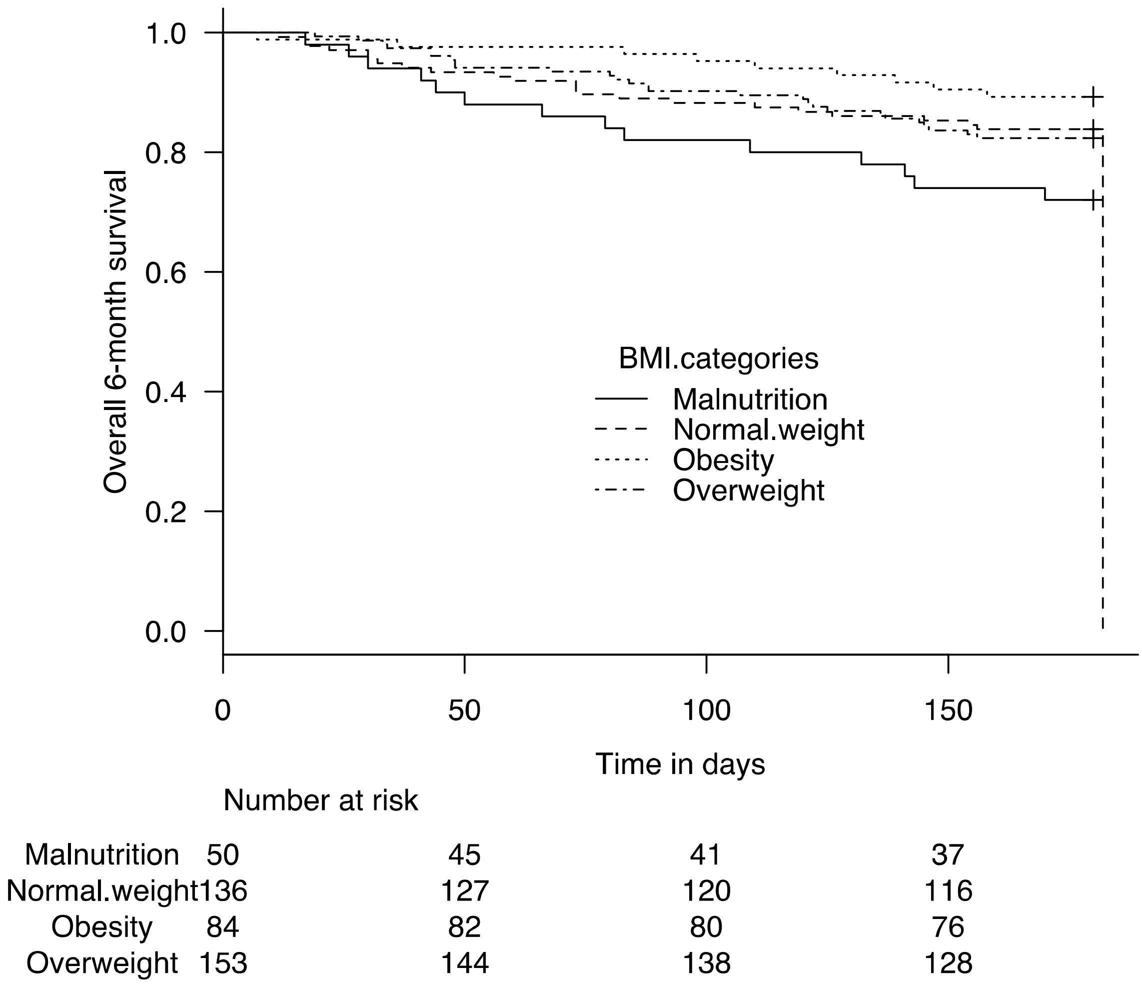
Continuous variables were shown per their standard deviations.

a log-rank test

b prostate = 12, urothelial = 4, kidney = 3, bladder = 2

c unknown primary site = 8, mesothelioma = 5, cutaneous epidermidis carcinoma = 4, anal = 3, sarcoma = 2, melanoma = 2, oral carcinoma = 2, duodenal = 2, thymoma = 1, non-differentiated carcinoma = 1.

Figure 2. Kaplan-Meier survival plotted by BMI category following GA in 433 older cancer outpatients



P value (log-rank) = 0.06

BMI: body mass index

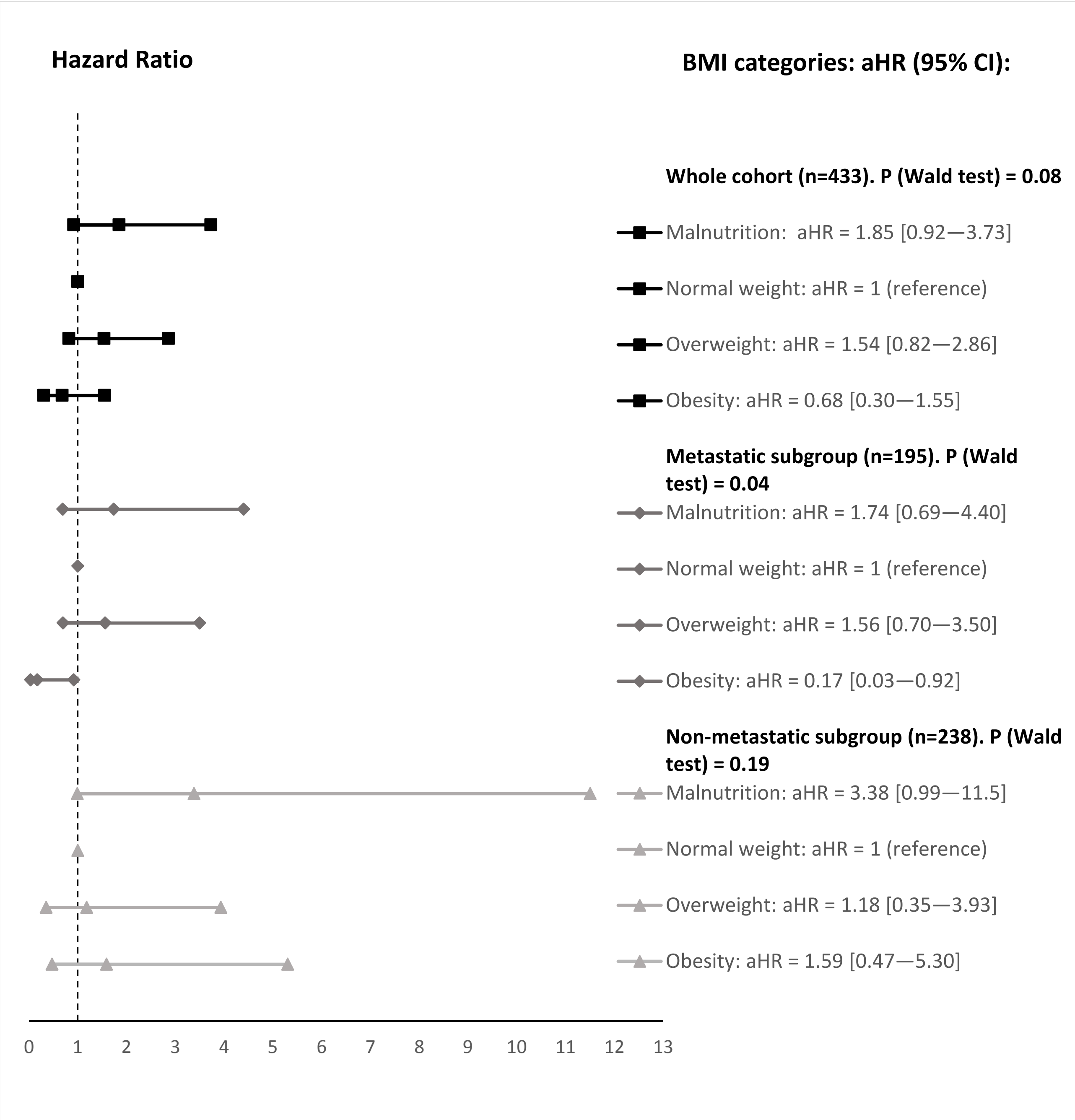
Malnutrition: BMI < 21 kg/m^2

Normal weight: 21 < BMI < 25 kg/m^2

Overweight: 25 < BMI < 30 kg/m^2

Obesity: BMI ≥ 30 kg/m^2

Figure 3. Forest plot of adjusted hazard ratio[a] for body mass index (BMI) categories for prediction of 6-month mortality in older cancer patients after geriatric assessment



[a] BMI categories were adjusted for sex, slow gait speed, MMSE, cancer site and exclusive supportive care.