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Geriatric assessment findings independently associated with clinical depression in 1092 older patients with cancer: the ELCAPA Cohort Study

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Abstract

***Objective*: We aim to assess the prevalence and associated factors of clinical depression in older patients with cancer.**

***Methods*: We studied a prospective cohort of cancer patients aged ≥70 years and referred to geriatric oncology clinics between 2007 and 2012. A multidimensional geriatric assessment was performed before choosing the cancer-treatment strategy. Clinical depression was diagnosed by senior geriatricians by a semi-structured interview. It encompassed criteria of the Diagnostic and Statistical Manual of Mental Disorders (fourth edition) and of the International Classification of Diseases (10th edition). Multivariate logistic regression was performed.**

***Results*: Of 1121 consecutive patients, 1092 had available data (mean age, 80.4 years; women, 48.8%; metastases, 51.3%; cancer location: colorectal 21.1%, breast 16.8%, kidney, bladder or urinary tract 14.0%, and prostate 11.4%). The overall prevalence of clinical depression was 28.4% (95% confidence interval, 25.7–31.2). Factors independently associated with clinical depression by multivariate analysis adjusting for all following factors plus gender, and metastasis were impaired mobility (adjusted odds ratio [aOR], 2.35; 1.59–3.46), impaired functional status defined as Eastern Cooperative Oncology Group Performance Status ≥ 2 (aOR, 2.39; 1.66–3.43) or as activities of daily living < 6 (aOR, 2.43; 1.73–3.41), inpatient status (aOR, 1.68; 1.20–2.37), inadequate social support (aOR, 1.66; 1.16–2.37), cognitive impairment (aOR, 1.76; 1.24–2.49), polypharmacy defined as five or more non-antidepressant drugs (aOR, 1.65; 1.14–2.38), multimorbidity ($aOR_{\text{additional CIRS-G point}}$, 1.08; 1.04–1.12), and cancer-related pain (aOR, 1.76; 1.26–2.46).**

***Conclusion*: In older patients with as-yet untreated cancer at various sites and stages, clinical depression was highly prevalent. Clinical depression was independently associated with several geriatric assessment findings (impaired mobility and function, inadequate social support, cognitive impairment, polypharmacy, and multimorbidity) independently from gender, tumor site, and metastatic status.**

Background

Depression is commonly associated with cancer, either as a preexisting condition or as a consequence of the illness and its treatment [1]. Depression is associated with delayed cancer diagnosis and with adverse outcomes such as poor treatment compliance, short survival, long hospital stays, early functional decline, impaired quality of life, and increased healthcare costs [2–10].

Although depressive symptoms are highly prevalent in older adults [11,12], clinical depression often goes underdiagnosed and undertreated [13,14]. The importance

of identifying clinical depression among older patients with physical comorbidities warrants routine geriatric assessments (GAs), in particular to avoid mistakenly attributing depressive symptoms to physical diseases such as cancer. Such misattribution may result in failure to diagnose clinical depression, thus depriving patients from appropriate care. Clinical practice guidelines for geriatric oncology recommend integrating multidimensional GAs into everyday oncological practice [15]. The GA is an extensive and multidimensional assessment of general health status based on validated geriatric scales and tests, semi-structured interviews, and a physical examination. It produces an inventory of health problems, which can then serve to develop an individualized geriatric intervention plan [16]. Assessing depression, anxiety, or general mood is among the main components of GAs. Although various types of assessment tools can help to assess depressive mood, the reference standard for diagnosing clinical depression is an individual clinical interview [14] to evaluate International Classification of Diseases, 10th edition (ICD-10) or Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) criteria [17,18].

Several studies assessed the prevalence and risk factors of depression in middle-aged patients with cancer, but very few focused on older patients. The main factors associated with depression were type of cancer, treatment phase, advanced tumor stage, poor performance status, pain, older age, lack of social support, and higher number of comorbidities [1,5,19–21]. To our knowledge, only two studies specifically assessed geriatric factors associated with depression in older patients with cancer. A prospective study from the USA in 245 older patients with solid cancer or lymphoma found that poor physical function was independently associated with high self-reported distress [22]. In a cross-sectional study of 92 patients with advanced cancer, cognitive impairment and a high mean score for cancer-related symptoms independently predicted depressive symptoms as assessed using the MD Anderson Symptoms Instrument [23]. However, the first study did not involve diagnosing clinical depression, and the second included a small number of patients, all of whom had advanced cancer, suggesting limited external validity of the findings.

Here, our goals were to assess the prevalence of clinical depression in older patients with cancer at various sites and stages and to identify patient-related and tumor-related factors independently associated with clinical depression. We hypothesized that several patient-related factors identified by a GA would be associated with clinical depression in older patients with cancer, independently from tumor-related factors.

Methods

Study design and population

Elderly cancer patient (ELCAPA) is a prospective open cohort of consecutive inpatients and outpatients ≥70 years of age with histologically documented cancer who were referred to the geriatric oncology clinics of two university hospitals in the Paris urban area, France, before treatment decisions were made.

For the present cross-sectional analysis (ELCAPA-10), we used baseline data from all patients included between January 2007 and December 2012. Informed consent was obtained from all patients prior to inclusion. The protocol was approved by the appropriate ethics committee (CPP Ile-de-France I, Paris, France).

Data collection and explanatory variables

Data were collected prospectively. At baseline, we recorded age, gender, tumor site (13 groups: colorectal, pancreas, esophagus or bile tract, stomach, breast, prostate, kidney or bladder or urinary tract, lung, hematological, unknown primary, skin, endometrial or ovarian, and others), and metastatic status. Planned treatment strategies were classified into three groups: curative, palliative, and supportive only [24]. At baseline, all patients underwent a GA, as previously detailed [24]. The GA involved a semi-structured interview and physical examination based on validated tests and scores to assess functional status (activities of daily living [ADL] and Eastern Cooperative Oncology Group Performance Status [ECOG-PS]), mobility (fall history, get-up-and-go test score, timed get-up-and-go test, and one-leg standing test), nutrition (weight loss and body mass index [BMI]), cognitive status (Mini-Mental State Examination [MMSE], history of dementia and/or cognitive dysfunction), social support (primary caregiver, support at home, or circle of family and friends), comorbidities (Cumulative Illness Rating Scale for Geriatrics [CIRS-G], number of grade 3 and 4 conditions, and number of predefined chronic conditions [Table 1]), and polypharmacy (defined as taking five or more oral medications each day). Cancer-related pain (yes/no) was collected. We also recorded the following serum parameters: hemoglobin concentration, C-reactive protein [CRP], and creatinine. Severe renal failure was defined as Cockcroft-and-Gault creatinine clearance <30 mL/min.

Depression assessment

The main endpoint for the present analysis was a diagnosis of clinical depression based on a semi-structured interview by senior geriatricians specialized in geriatric oncology (P. C. and M. L.). The interview was designed to identify eight of the nine DSM-IV criteria for a major depressive episode, which are also among the ICD-10 criteria for a depressive episode: depressed mood, decreased interest or pleasure, significant weight or appetite change, sleep disorders, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness, and suicidal ideation. For the symptoms potentially related to cancer instead of depression (e.g., fatigue, weight loss,

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Table 1. Univariate analysis of factors associated with clinical depression—the ELCAPA-10 Study

	Total (*n*, %) *n* = 1092	Depression (*n*, %) *n* = 310	No depression (*n*, %) *n* = 782	*p*[a] value
Age (mean, SD)	80.4 (5.7)	81.0 (5.2)	80.2 (5.8)	0.035
Female gender	533 (48.8)	163 (52.6)	370 (47.3)	0.12
Inpatient status	439 (40.2)	169 (54.5)	270 (34.5)	<0.001
Metastasis (*n* = 992)				<0.001
No	439 (44.2)	97 (34.3)	342 (48.2)	
Yes	462 (46.6)	156 (55.1)	306 (43.2)	
Hematological malignancy	91 (9.2)	30 (10.6)	61 (8.6)	
Inadequate social support[b] (*n* = 1087)	243 (22.4)	96 (31.4)	147 (18.8)	<0.001
Living alone (*n* = 1087)	406 (37.4)	117 (38)	289 (37.1)	0.785
ADL (median, [Q1–Q3], *n* = 1083)	6 [4.5–6]	5 [3.5–6]	6 [5–6]	<0.001
Impaired mobility[b] (*n* = 1091)	718 (65.8)	258 (83.5)	460 (58.8)	<0.001
ECOG-PS (≥2, *n* = 1090)	560 (51.4)	230 (74.7)	330 (42.2)	<0.001
Cancer-related pain (*n* = 1086)	368 (33.9)	134 (43.8)	234 (30.0)	<0.001
Malnutrition[b] (*n* = 926)	543 (58.6)	171 (68.9)	372 (54.9)	<0.001
Cognitive impairment[b] (*n* = 1045)	309 (29.6)	126 (43.3)	183 (24.3)	<0.001
Comorbidities				
CIRS-G index, (median, [Q1–Q3], *n* = 841)	12 [9–17]	15 [12–19]	11 [8–16]	<0.001
Number of CIRS-G grade 3 and/or 4 conditions (median, [Q1–Q3], *n* = 709)	0 [0–1]	1 [0–3]	0 [0–1]	<0.001
Cardiovascular diseases[c] (*n* = 1086)	508 (46.8)	160 (50.6)	348 (44.5)	0.03
Arterial hypertension (≥140/90 mmHg, *n* = 1082)	729 (67.4)	206 (67.5)	523 (67.3)	0.94
Diabetes mellitus (*n* = 1079)	251 (23.3)	63 (20.7)	188 (24.3)	0.216
Chronic obstructive pulmonary disease (*n* = 1083)	75 (6.9)	30 (9.8)	45 (5.8)	0.019
Severe renal insufficiency[d] (*n* = 946)	91 (9.6)	33 (12.5)	58 (8.5)	0.069
Anemia[d] (*n* = 992)	629 (63.4)	191 (65.6)	438 (62.5)	0.35
C-reactive protein (mg/L) (median, [Q1–Q3], *n* = 739)	13 [4–48]	22 [5–69]	11 [3–38]	<0.001
Number of non-antidepressant drugs (median, [Q1–Q3], *n* = 1031)	6 [4–8]	7 [5–8]	5 [3–8]	<0.001
Polypharmacy (*n* = 1031)[b]	695 (67.4)	230 (78.5)	465 (63.0)	<0.001

ELCAPA, elderly cancer patient; ADL, activities of daily living; Q1–Q3, interquartile range (25th–75th percentiles); ECOG-PS, Eastern Cooperative Oncology Group Performance Status; BMI, body mass index; CIRS-G, Cumulative Illness Rating Scale for Geriatrics; SD, standard deviation.

[a]Pearson chi-square or Student's *t* test or Wilcoxon's test.

[b]Inadequate social support was defined as no primary caregiver or inadequate support at home or no strong circle of family and friends able to meet the needs of the patient; mobility impairment as a history of fall, get-up-and-go score ≥3/4 and/or timed get-up-and-go >20 s, or single-leg standing test <5 s on one or both sides; malnutrition as BMI < 21 kg/m^2 or at least 10% weight loss in 6 months or 5% in 3 months; cognitive impairment as previous history of dementia or diagnosis of cognitive dysfunction; and polypharmacy as ≥5 oral non-antidepressant drugs/day.

[c]Cardiovascular disease included heart failure, coronary artery disease, and arrhythmia.

[d]Anemia was defined as hemoglobin <12 g/dL in women or <13 g/dL in men and severe renal insufficiency as Cockcroft–Gault creatinine clearance <30 mL/min.

and loss of appetite), the geriatricians made clinically based judgments for each patient instead of routinely applying DSM-IV organic exclusion criteria [25,26]. History of previous depressive episodes and antidepressant drug use at the time of the GA was recorded.

Data analysis

Categorical variables were described as *n* (%) and quantitative variables as median (25th–75th percentiles) or mean (standard deviation) according to their distributions. The prevalence of clinical depression was expressed as a percentage with the 95% confidence interval (95% CI). To compare features in the groups with and without clinical depression, we chose Pearson's chi-square test for categorical variables and Student's *t*-test or Wilcoxon's test for quantitative variables, as appropriate.

To avoid introducing strongly correlated variables into multivariate models, we assessed correlations using Cramer's *V* for categorical variables and the nonparametric Spearman's rank correlation coefficient (rho) for quantitative variables; values ≥0.40 were taken to indicate strong correlations. Variables associated with clinical depression with $p < 0.20$ were included in multivariate logistic models. Pairwise analyses were performed to assess confounding factors. Given the known association between gender and depression, we routinely adjusted for gender [27]. Adjusted odds ratios (aORs) and their 95% CIs were estimated.

We conducted a sensitivity analysis by defining cognitive impairment as an MMSE score <24 instead of as a previous history of dementia or a diagnosis of cognitive dysfunction. Similarly, we built three models in which functional status was assessed using the ECOG-PS, ADL score, and mobility, respectively.

All tests were two sided, and *p* values <0.05 were considered significant. Analyses were performed with STATA software version 12.0 (StataCorp, College Station, TX, USA). We performed neither multiple imputation for missing data nor adjustment for multiple testing.

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Results

Of the 1121 patients enrolled in the ELCAPA cohort during the study period, 1092 were included in the present study. Data on depression were missing for 29 patients. Mean age was 80.4 years (5.7); 48.8% of patients were women, 59% were outpatients, and 91.7% had solid cancers including 51.3% with metastases. The overall prevalence of clinical depression was 28.4% (95% CI, 25.7–31.2%); 14.2% of patients had a previous history of depression, and 15.7% were currently taking antidepressant medications. As expected, patients with depression more often had a previous history of depression (24.4% vs. 10.1%, $p < 0.001$) and current antidepressant pharmacotherapy (33.9% vs. 8.5%, $p < 0.001$). The prevalence of depression varied from 21.0% in men with prostate cancer to about 40–50% in men as in women with lung or pancreatic cancer and women with ovarian and endometrial cancer. These differences were not strictly significant ($p = 0.064$). Figure 1 displays prevalence of depression across tumor sites and gender.

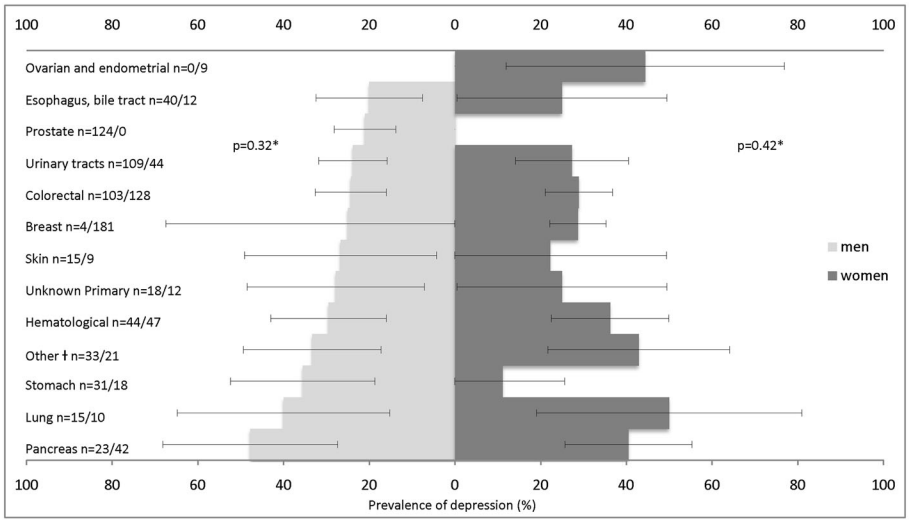
By univariate analysis, factors significantly associated with depression (Table 1) were older age, inpatient status, metastatic disease, inadequate social support, functional impairment (decreased ADL, ECOG-PS < 2), presence of cancer-related pain, impaired mobility, malnutrition, cognitive impairment, higher CIRS-G index, higher number of grade 3 or 4 comorbidities (CIRS-G), cardiovascular disease, chronic obstructive pulmonary disease, severe renal insufficiency, higher CRP level, ≥5 non-antidepressant drugs per day, and palliative or supportive care. A trend for association was observed for female gender ($p = 0.12$). Neither living alone nor being widowed (even combined) was associated with clinical depression.

Given the strong correlations linking ADL, ECOG-PS, and mobility (Cramers's $V > 0.40$), these three variables were introduced separately in the multivariate analysis. CIRS-G and CRP were not introduced in the main model because of missing data. Table 2 reports the results from the final multivariate model. Factors independently associated with clinical depression were inpatient status, inadequate social support, impaired mobility, cognitive

Table 2. Multivariate analysis of factors independently associated with clinical depression—the ELCAPA-10 Study ($n = 892$ patients)

	aOR (95% CI)	p value[a]
Female gender	1.23 (0.90–1.70)	0.19
Inpatient status	1.68 (1.20–2.37)	0.008
Metastasis		0.30
No	1.00 (reference)	
Yes	1.25 (0.88–1.79)	
Hematological malignancy	0.88 (0.49–1.60)	
Inadequate social support[b]	1.66 (1.16–2.37)	0.006
Impaired mobility[b]	2.35 (1.59–3.46)	<0.001
Cognitive impairment[b]	1.76 (1.24–2.49)	0.001
Polypharmacy[b]	1.65 (1.14–2.38)	0.008
Cancer-related pain	1.76 (1.26–2.46)	0.001

ELCAPA, elderly cancer patient; aOR, adjusted odds ratio; 95% CI, 95% confidence interval.
[a]By Wald test.
[b]Inadequate social support was defined as no primary caregiver or inadequate support at home or no strong circle of family and friends able to meet the needs of the patient; mobility impairment as a history of fall, get-up-and-go score ≥3/4 and/or timed get-up-and-go >20 s, or single-leg standing test <5 s on one or both sides; malnutrition as BMI < 21 kg/m^2 or at least 10% weight loss in 6 months or 5% in 3 months; cognitive impairment as previous history of dementia or diagnosis of cognitive dysfunction; and polypharmacy as ≥5 oral non-antidepressant drugs/day.



*p-value from Chi² test stratified for sex
ǂ includes patients with sarcoma (n=14), head-and-neck cancer (n=9), two tumor sites (n=8), hepatocellular carcinoma (n=7), central nervous system cancer (n=6), small intestine cancer (n=5), gastrointestinal stromal tumor (n=2), desmoplastic carcinoma (n=1), duodenum cancer (n=1), and parotid gland cancer (n=1)

Figure 1. Prevalence of clinical depression with 95% confidence intervals by gender and tumor site—the ELCAPA-10 Study

impairment, polypharmacy, and cancer-related pain. The association between metastasis and depression remains significant after adjustment for inpatient status, inadequate social support, impaired mobility, cognitive impairment, and polypharmacy (aOR = 1.42; 95% CI: 1.01 to 2.01) but disappeared after supplemental adjustment for cancer-related pain (Table 2). Tumor site was not associated with clinical depression after adjustment for impaired mobility and metastatic disease. Adjusting for impaired mobility abolished the association between age and clinical depression. The type of cancer-treatment strategy was not significantly associated with clinical depression after full adjustment (data not shown).

Sensitivity analyses

Results were unchanged when ADL or ECOG-PS was used instead of impaired mobility (ADL < 6: aOR, 2.43 [1.73–3.41]; and ECOG-PS ≥ 2: aOR, 2.39 [1.66–3.43]). Similarly, using an abnormal MMSE (available for 1018 patients) instead of cognitive impairment did not change the results (aOR, 1.70 [1.19–2.41]).

Secondary analysis

In the 841 patients with available CIRS-G data, a higher CIRS-G value and presence of grade 3 or 4 comorbidities were independently associated with depression after adjustment for inpatient status, malnutrition, impaired mobility, and cancer-related pain ($aOR_{1\ \text{additional CIRS-G point}}$, 1.08 [1.04–1.12], and aOR, 1.20 [1.05–1.38], respectively). In the 739 patients with available CRP values, the significant association of CRP elevation with clinical depression persisted after individual adjustments for each confounder but not after simultaneous adjustment for impaired mobility and metastatic disease.

Among patients given a diagnosis of clinical depression during the GA, the treatment prescribed by the geriatrician was referral to a psychologist and/or psychiatrist in 23.3%, a new or modified antidepressant regimen in 28.8%, and both in 33.9% (no recommendation for 14%).

Conclusion

In this large cohort of consecutive older patients with as-yet untreated cancer at various sites and stages, 28.4% had clinical depression diagnosed using a semi-structured interview based on DSM-IV criteria and performed by senior geriatricians specialized in geriatric oncology. Clinical depression was twice as common in the subgroups of patients with pancreatic or lung cancer compared with that of the other subgroups. By routinely obtaining a GA before cancer treatment, we were able to explore relationships between clinical depression and several geriatric variables. Inpatient status, an inadequate social environment, impaired mobility, poor functional status, impaired cognition, and multimorbidity or polypharmacy were associated with clinical depression independently from metastatic disease and gender. Cancer-related pain was also independently associated with clinical depression.

The 28.4% prevalence of clinical depression is slightly higher than the pooled prevalences reported in two recent meta-analyses. In a meta-analysis of 70 studies in oncological and hematological settings, there was a 20.7% (95% CI, 12.9–29.8%) pooled prevalence of any type of depression diagnosed using psychiatric interviews to assess DSM-IV or ICD-10 criteria [28]. In the other meta-analysis, the pooled mean prevalence of depression in cancer patients ranged from 8% to 24% and differed with the diagnostic method (interviews vs. self-report questionnaire), type of cancer, and treatment phase [1]. However, few studies focused on older patients. In our study, the high prevalence of clinical depression might be ascribable to selection bias owing to preferential geriatrician referral of patients with comorbidities for a GA. However, there is evidence that depression is underdiagnosed among older patients with cancer [13,14], perhaps especially those with physical comorbidities [14]. Compared with previous assessments, the GA performed in the present study may have greater accuracy for diagnosing depression. There is considerable debate about the appropriate criteria for depression in patients with physical diseases [26]. Many depression scales exclude the somatic symptoms of depression from the diagnostic algorithm in patients with severe comorbidities. According to the DSM-IV, depression cannot be diagnosed when the symptoms are the direct psychological result of a medical condition. This approach may lead to underdiagnosis of depression, as the direction of causality may be difficult to determine. Moreover, a recent study demonstrated low sensitivity of commonly used screening tools for geriatric depression (Geriatric Depression Scale Short Form, Hospital Anxiety and Depression Scale, and Center for Epidemiologic Studies Depression Scale) [29]. A more sensitive approach, often referred to as inclusive, consists in taking into account all known symptoms of depression regardless of whether they may be secondary to a physical illness. Age-related variations in the clinical picture of depression may complicate the diagnosis in older patients. Although older adults with depression tend to report lower levels of self-criticism, guilt, and suicidality than their younger counterparts, they report higher levels of somatic complaints [30]. To achieve a reasonable balance between sensitivity and specificity, the geriatricians in our study assessed whether somatic symptoms were ascribable to clinical depression on a case-by-case basis.

The prevalence of depression varied across cancer types, being highest in patients with pancreatic and lung cancer, in keeping with earlier data [31]. However, the small size of the cancer-type subgroups limits the validity

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of this finding. Moreover, tumor site was not significant after adjustment for metastatic status and impaired mobility. This association may be reciprocal. On the one hand, the higher rate of depression observed in patients with pancreatic and lung cancer (and women with ovarian cancer) may partially result from greater lethality of advanced cancer and thus more challenging emotion regulation demands. On the other hand, depression has been associated with higher risk of delayed cancer diagnosis, thus leading to higher stage at time of diagnosis [10].

The prevalence of clinical depression was not associated with older age or female gender, in accordance with data from a recent meta-analysis [28]. Although depression is typically twice as common in women as in men, there is epidemiological evidence that the excess risk for major depression in women is confined to individuals with low stress exposure [32]. Gender differences in depression rate are thus expected to be lower in the context of cancer, which arguably constitutes high stress exposure.

Several factors identified by the GA were associated with depression. There was some overlap between these factors and those identified previously in older patients without cancer, that is, mobility and functional impairment [26,33], cognitive impairment [34,35], inadequate social support [27,36], and polypharmacy and comorbidities [36,37]. Thus, some factors associated with clinical depression in older patients with cancer may be related to a high-risk geriatric profile rather than to the malignancy [38,39].

Outside the context of cancer, prospective epidemiological studies suggest that functional impairment may precipitate major depression [40]. However, few data on the relationship between depression and functional impairment are available for older patients with cancer to date. Among younger adults, depression has been identified as one of the most disabling conditions worldwide [41] and may even increase functional impairment associated with other chronic diseases [42]. Depressed older people are thus more likely to experience functional limitations when facing cancer. Longitudinal studies are needed to determine whether the causality sequence is cancer, depression, and functional impairment, or cancer, functional impairment, and depression.

In line with our findings, community-based studies in normally aging populations suggest that depression may be associated with cognitive decline [43]. Whether depression diagnosed before dementia represents a risk factor for dementia or a prodromal feature of dementia is unclear [44]. Inadequate social support was independently associated with depression in our cohort, in keeping with a study of older patients with colorectal cancer, who more often had depression if they had fewer sources of social contact [36].

Several studies support our finding that medical comorbidities are associated with an increased prevalence of depression [37,45], most probably because of higher psychological burden.

We found that the association between metastasis and depression disappeared after supplemental adjustment for cancer-related pain. It may indicate that cancer-related pain is an independent associated factor with depression [46] and that it explained, at least partially, the pathway between metastasis and depression. It is in accordance with findings of results from a large meta-analysis that found no strong association between metastasis and depression [28].

Several limitations of our study should be acknowledged. First, we studied older patients referred to the geriatric oncology clinics of two teaching hospitals in the Paris urban area. Therefore, our findings may not be applicable to all older adults with cancer. Second, we did not assess depression severity. Third, the cross-sectional design precludes an assessment of possible causal links. The time from initial cancer diagnosis to disclosure of the diagnosis to the patients was not recorded. Depressive symptoms may be particularly common among patients having recently learned they had cancer. Finally, difficulty concentrating, one of the DSM-IV and ICD-10 items, was not assessed, but we did have an objective assessment of cognitive impairment.

Despite these limitations, our study has important strengths. Few studies have specifically measured clinical depression and its geriatric and oncological associated factors, jointly, in older adults with cancer. Moreover, these studies used short screening tools or self-reported questionnaires of limited accuracy for diagnosing clinical depression [22,23]. We used individual semi-structured interviews performed by senior geriatricians specialized in geriatric oncology and based on DSM-IV/ICD-10 criteria. Moreover, the routine use of a GA allowed us to assess a wide range of parameters potentially associated with depression in older adults with cancer, including specific geriatric factors. The GA also helped to determine whether somatic symptoms were related to depression. Finally, most previous studies focused on a single tumor site, limiting the external validity of their findings and the ability to compare tumor sites.

Implications

Although depression rates are typically lower in older individuals than in their younger counterparts in the general population [47], it might not be true among patients with cancer. From a clinical perspective, recent guidelines advocate for repeatedly screening patients with cancer for depression and to identify risk factors [48]. Our results suggest that several geriatric features, that is, impaired mobility and function, inadequate social support,

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cognitive impairment, and multimorbidity, are risk factors of depression among older patients with cancer independently from oncological factors. Thus, these features warrant special attention when screening for depression. This might be especially critical for cognitive impairment as such impairment may impede the recommended, questionnaire-based screening procedure. Longitudinal studies are needed to assess the temporal link of our findings and interventional ones to assess strategies for reducing clinical depression in older patients with cancer [49].

To conclude, our results suggest that, among older patients with as-yet untreated cancer at various sites and stages who are referred for a GA, over one-fourth may have clinical depression. Clinical depression was independently associated with several GA findings (impaired mobility and function, inadequate social support, cognitive impairment, polypharmacy, and multimorbidity) independently from gender, tumor site, and metastatic status. Cancer-related pain was also independently associated with clinical depression.

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Conflict of interest

No authors had conflict of interest.

References

1. Krebber AM, Buffart LM, Kleijn G *et al.* Prevalence of depression in cancer patients: a meta-analysis of diagnostic interviews and self-report instruments. *Psycho-Oncology* 2014;**23**:121–130. DOI:10.1002/pon.3409.
2. DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med* 2000;**160**: 2101–2107.
3. Satin JR, Linden W, Phillips MJ. Depression as a predictor of disease progression and mortality in cancer patients: a meta-analysis. *Cancer* 2009;**115**:5349–5361. DOI:10.1002/cncr.24561.
4. Prieto JM, Blanch J, Atala J *et al.* Psychiatric morbidity and impact on hospital length of stay among hematologic cancer patients receiving stem-cell transplantation. *J Clin Oncol* 2002;**20**:1907–1917.
5. Jayadevappa R, Malkowicz SB, Chhatre S *et al.* The burden of depression in prostate cancer. *Psycho-Oncology* 2012;**21**:1338–1345. DOI:10.1002/pon.2032.
6. O'Rourke RW, Diggs BS, Spight DH *et al.* Psychiatric illness delays diagnosis of esophageal cancer. *Dis Esophagus* 2008;**21**:416–421.
7. Kanesvaran R, Li H, Koo KN *et al.* Analysis of prognostic factors of comprehensive geriatric assessment and development of a clinical scoring system in elderly Asian patients with cancer. *J Clin Oncol* 2011;**29**:3620–3627. DOI:10.1200/JCO.2010.32.0796.
8. Chan CM, Wan Ahmad WA, Md Yusof M *et al.* Effects of depression and anxiety on mortality in a mixed cancer group: a longitudinal approach using standardised diagnostic interviews. *Psycho-Oncology* 2015;**24**:718–725. DOI:10.1002/pon.3714.
9. Hoppe S, Rainfray M, Fonck M *et al.* Functional decline in older patients with cancer receiving first-line chemotherapy. *J Clin Oncol* 2013;**31**:3877–3882. DOI:10.1200/JCO.2012.47.7430.
10. Boyd CA, Benarroch-Gampel J, Sheffield KM *et al.* The effect of depression on stage at diagnosis, treatment, and survival in pancreatic adenocarcinoma. *Surgery* 2012;**152**:403–413. DOI:10.1016/j.surg.2012.06.010.
11. Copeland JR, Beekman ATF, Braam AW *et al.* Depression among older people in Europe: the EURODEP studies. *World Psychiatry* 2004;**3**:45–49.
12. Hybels CF, Landerman LR, Blazer DG. Age differences in symptom expression in patients with major depression. *Int J Geriatr Psychiatry* 2012;**27**:601–611. DOI:10.1002/gps.2759.
13. Parpa E, Tsilika E, Gennimata V *et al.* Elderly cancer patients' psychopathology: a systematic review: aging and mental health. *Arch Gerontol Geriatr* 2015;**60**:9–15. DOI:10.1016/j.archger.2014.09.008.
14. Kessler RC, Birnbaum H, Bromet E *et al.* Age differences in major depression: results from the National Comorbidity Survey Replication (NCS-R). *Psychol Med* 2010;**40**:225–237. DOI:10.1017/S0033291709990213.
15. Wildiers H, Heeren P, Puts M *et al.* International society of geriatric oncology consensus on geriatric assessment in older patients with cancer. *J Clin Oncol* 2014;**32**: 2595–2603.
16. Caillet P, Laurent M, Bastuji-Garin S *et al.* Optimal management of elderly cancer patients: usefulness of the comprehensive geriatric assessment. *Clin Interv Aging* 2014;**9**:1645–1660. DOI:10.2147/CIA.S57849.
17. WHO. *The ICD-10 Classification of Mental and Behavioural Disorders*: *Diagnostic Criteria for Research*, World Health Organization: Geneva, 1993.
18. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (4th ed.), American Psychiatric Press: Washington, DC, 1994.
19. Linden W, Vodermaier A, Mackenzie R *et al.* Anxiety and depression after cancer diagnosis: prevalence rates by cancer type, gender, and age. *J Affect Disord* 2012;**141**:343–351. DOI:10.1016/j.jad.2012.03.025.
20. Ciaramella A, Poli P. Assessment of depression among cancer patients: the role of pain, cancer type and treatment. *Psycho-Oncology* 2001;**10**:156–165.
21. Simon AE, Thomson MR, Flashman K *et al.* Disease stage and psychosocial outcomes in colorectal cancer. *Colorectal Dis* 2008; **11**:19–25. DOI:10.1111/j.1463-1318.2008.01501.
22. Hurria A, Li D, Hansen K *et al.* Distress in older patients with cancer. *J Clin Oncol* 2009;**27**:4346–4351. DOI:10.1200/JCO.2008.19.9463.
23. Mystakidou K, Parpa E, Tsilika E *et al.* Geriatric depression in advanced cancer patients: the effect of cognitive and physical functioning. *Geriatr Gerontol Int* 2013;**13**:281–288. DOI:10.1111/j.1447-0594.2012.00891.
24. Caillet P, Canoui-Poitrine F, Vouriot J *et al.* Comprehensive geriatric assessment in the decision-making process in elderly patients with cancer: ELCAPA Study. *J Clin Oncol* 2011;**29**:3636–3642. DOI:10.1200/JCO.2010.31.0664.
25. Weinberger MI, Roth AJ, Nelson CJ. Untangling the complexities of depression diagnosis in older cancer patients. *Oncologist* 2009;**14**:60–66. DOI:10.1634/theoncologist.2008-0147.
26. Mitchell AJ, Lord K, Symonds P. Which symptoms are indicative of DSMIV depression in cancer settings? An analysis of the diagnostic significance of somatic and non-somatic symptoms. *J Affect Disord* 2012;**138**:137–148. DOI:10.1016/j.jad.2011.11.009.

27. Luppa M, Sikorski C, Luck T *et al.* Age- and gender-specific prevalence of depression in latest-life—systematic review and meta-analysis. *J Affect Disord* 2012;**136**:212–221. DOI:10.1016/j.jad.2010.11.033.
28. Mitchell A, Chan M, Bhatti H *et al.* Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. *Lancet Oncol* 2011;**12**:160–174. DOI:10.1016/S1470-2045(11)70002-X.
29. Nelson CJ, Cho C, Berk AR *et al.* Are gold standard depression measures appropriate for use in geriatric cancer patients? A systematic evaluation of self-report depression instruments used with geriatric, cancer, and geriatric cancer samples. *J Clin Oncol* 2010;**28**:348–356. DOI:10.1200/JCO.2009.23.0201.
30. Hegeman JM, Kok RM, van der Mast RC *et al.* Phenomenology of depression in older compared with younger adults: meta-analysis. *Br J Psychiatry* 2012;**200**:275–281. DOI:10.1192/bjp.bp.111.095950.
31. Massie MJ. Prevalence of depression in patients with cancer. *J Natl Cancer Inst Monogr* 2004;**32**:57–71.
32. Kendler KS, Kuhn J, Prescott CA. The interrelationship of neuroticism, sex, and stressful life events in the prediction of episodes of major depression. *Am J Psychiatry* 2004;**161**:631–636.
33. Biddulph JP, Iliffe S, Kharicha K *et al.* Risk factors for depressed mood amongst a community dwelling older age population in England: cross-sectional survey data from the PRO-AGE study. *BMC Geriatr* 2014;**14**:5. DOI:10.1186/1471-2318-14-5.
34. Weyerer S, Eifflaender-Gorfer S, Wiese B *et al.* Incidence and predictors of depression in non-demented primary care attenders aged 75 years and older: results from a 3-year follow-up study. *Age Ageing* 2013;**42**:173–180. DOI:10.1093/ageing/afs184.
35. Cole MG, Dendukuri N. Risk factors for depression among elderly community subjects: a systematic review and meta-analysis. *Am J Psychiatry* 2003;**160**:1147–1156.
36. Kurtz ME, Kurtz JC, Stommel M *et al.* Predictors of depressive symptomatology of geriatric patients with colorectal cancer: a longitudinal view. *Support Care Cancer* 2002;**10**:494–501.
37. Weiss Wiesel TR, Nelson CJ, Tew WP *et al.* On behalf of the Cancer Aging Research Group (CARG). The relationship between age, anxiety, and depression in older adults with cancer. *Psycho-Oncology* 2015;**24**:712–717. DOI: 10.1002/pon.3638.
38. Bardwell WA, Natarajan L, Dimsdale JE *et al.* Objective cancer-related variables are not associated with depressive symptoms in women treated for early-stage breast cancer. *J Clin Oncol* 2006;**24**:2420–2427.
39. Janberidze E, Hjermstad MJ, Brunelli C *et al.* EURO IMPACT. The use of antidepressants in patients with advanced cancer—results from an international multicentre study. *Psycho-Oncology* 2014;**23**:1096–1102. DOI:10.1002/pon.3541.
40. Cole MG, Dendukuri N. Risk factors for depression among elderly community subjects: a systematic review and meta-analysis. *Am J Psychiatry* 2003;**160**:1147–1156.
41. Prince M, Patel V, Saxena S *et al.* No health without mental health. *Lancet* 2007;**370**:859–877.
42. Stein MB, Cox BJ, Afifi TO *et al.* Does comorbid depressive illness magnify the impact of chronic physical illness? A population-based perspective. *Psychol Med* 2006;**36**:587–596.
43. Köhler S, van Boxtel MP, van Os J *et al.* Depressive symptoms and cognitive decline in community-dwelling older adults. *J Am Geriatr Soc* 2010;**58**:873–879. DOI:10.1111/j.1532-5415.2010.02807.x.
44. Panza F, Frisardi V, Capurso C *et al.* Late-life depression, mild cognitive impairment, and dementia: possible continuum? *Am J Geriatr Psychiatry* 2010;**18**:98–116. DOI:10.1097/JGP.0b013e3181b0fa13.
45. Zhang AY, Cooper GS. Recognition of depression and anxiety among elderly colorectal cancer patients. *Nurs Res Pract* 2010;**2010**:693961. DOI:10.1155/2010/693961.
46. Mystakidou K, Parpa E, Tsilika E *et al.* The influence of distressing symptoms to levels of depression in cancer patients. *J BUON* 2013;**18**:751–759.
47. Hoertel N, McMahon K, Olfson M *et al.* A dimensional liability model of age differences in mental disorder prevalence: evidence from a national sample. *J Psychiatr Res* 2015;**64**:107–113. DOI:10.1016/j.jpsychires.2015.03.017.
48. Andersen BL, DeRubeis RJ, Berman BS *et al.* Screening, assessment, and care of anxiety and depressive symptoms in adults with cancer: an American Society of Clinical Oncology guideline adaptation. *J Clin Oncol* 2014;**32**:1605–1619. DOI:10.1200/JCO.2013.52.4611.
49. Kornblith AB, Dowell JM, Herndon JE 2nd *et al.* Telephone monitoring of distress in patients aged 65 years or older with advanced stage cancer: a cancer and leukemia group B study. *Cancer* 2006;**107**:2706–2714.