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► **To cite this version:**

Anne-Laure Couderc, Pascale Tomasini, Emilie Nouguerède, Dominique Rey, Florian Correard, et al.. Older Patients Treated for Lung and Thoracic Cancers: Unplanned Hospitalizations and Overall Survival. *Clinical Lung Cancer*, 2021, 22 (3), pp.e405-e414. 10.1016/j.clcc.2020.06.004 . hal-03585200

**HAL Id: hal-03585200**

**<https://hal.science/hal-03585200>**

Submitted on 13 Jun 2023

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## **Older patients treated for lung and thoracic cancers: unplanned hospitalizations and overall survival**

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## **Abstract**

*Background:* Lung cancer affects older adults and is the leading solid tumor in terms of death. Comprehensive Geriatric Assessment (CGA) is recommended before cancer treatment to guide therapy management.

*Methods:* This study was conducted between September 2015 and January 2019. During this period of time, all consecutive older outpatients referred for a CGA before initiation of lung or thoracic tumor treatment were included. The objectives were to describe the impact of geriatric factors on unplanned hospitalizations and overall survival (OS). The study was approved by a local ethics committee.

*Findings:* Overall, 228 patients were recruited. The median age was  $78.7 \pm 5$  years. The majority of patients were diagnosed with non-small-cell lung cancer (82%) and the most common treatment was systemic therapy (40.4%). In multivariate analysis, factors associated with unplanned hospitalizations within the first 3 months were male gender (aOR 3.3; 95% CI [1.5-7.2]), systemic therapy (aOR 2.6; 95% CI [1.1-6.2]), and fall history (aOR 3.6; 95% CI [1.6-8.2]). Factors associated with a decrease in OS in the multivariate Cox model analysis were male gender (HR 3.9; 95% CI [2.1-7.3]), stage IV (HR 1.6; 95% CI [1.0-2.6]), G8  $\leq$  14 (HR 3.5; 95% CI [1.1-11.4]), systemic therapy (HR 2.6; 95% CI [1.2-5.5]), ECOG-PS $\geq$ 2 (HR 2.0; 95% CI [1.2-3.4]), impaired handgrip strength (HR 1.6; 95% CI [1.0-2.5]).

*Interpretation:* G8 score and handgrip strength are important to predict overall survival in older adults treated for thoracic tumor. In the GCA, fall history was associated with unplanned hospitalization.

**Keywords:** older lung cancer patients; comprehensive geriatric assessment; G8; unplanned hospitalizations; overall survival.

## **Introduction:**

Cancer, especially lung cancer, affects older adults: half of patients with lung cancer are aged 70 years or older at diagnosis<sup>[1,2]</sup>. Lung cancer is the leading solid tumor in terms of mortality, in particular in the United States and in Europe<sup>[3]</sup>. The most common histological type of lung cancer analyzed in the geriatric oncological literature is non-small-cell lung cancer (NSCLC). Initial symptoms at diagnosis bear no significant differences between older and younger patients<sup>[4]</sup> but the association between age and mortality is different in the chemotherapy and surgical literature<sup>[1,5,6]</sup>. Management of lung cancer in older patients vary according to the stage. In advanced lung cancer, the new therapeutics as targeted therapy<sup>[7,8]</sup> or immune checkpoint inhibitors<sup>[9,10]</sup> are used as a first- or second-line treatment.

Although older patients are the most affected by cancer, they are still under-represented in clinical trials, especially in an oncological setting<sup>[11]</sup>. Aging is a heterogeneous process: it may be associated with functional, mobility or cognitive impairment, comorbidities and polypharmacy, nutritional disorders or inadequate social support. The development of Geriatric Oncology has greatly improved the management of older patients with Comprehensive Geriatric Assessments (CGA) being conducted before and during cancer treatment<sup>[12,13]</sup>. A CGA is defined “as a multidisciplinary evaluation in which the multiple frailties of older adults are uncovered, described, and explained, if possible, and in which the resources and strengths of the person are cataloged, the need for services assessed and a coordinated care plan developed”<sup>[14]</sup>. The use of CGA is now recognized as essential to guide treatment decisions in older cancer patients<sup>[13]</sup>. The impact of CGA parameters on treatment have become important and the Chemotherapy Risk Assessment Scale for High-Age patients (CRASH) score<sup>[15]</sup> and the Cancer and Aging Research Group (CARG) score<sup>[16]</sup> using CGA factors have been created to evaluate grade 3-4 chemotherapy toxicity in older cancer patients. CGA is now commonly used in lung cancer management, particularly in chemotherapy management<sup>[5,17-26]</sup>. The study by Corre *et al* was the first randomized study to use CGA to guide therapy for older adults with advanced lung cancer<sup>[22]</sup>.

We designed this study to describe the potential impact of geriatric factors on unplanned hospitalizations within 3 months after treatment initiation and overall survival (OS) in older adults treated for lung cancer and thoracic tumor with surgery, systemic therapy, chemo-radiotherapy, or best supportive care (BSC)).

## Methods

### *Study Design and Participants*

This study was conducted between September 2015 and January 2019 at the Marseille University Hospital (AP-HM). During this period, all older patients were screened by thoracic oncologists/surgeons using the G8 score. All patients with an impaired G8 (score of 14 out of 17 or less) were referred to a geriatrician for a GGA according to the French Recommendations<sup>[27]</sup>. Oncologists also referred for CGA patients with a normal G8 score but with suspected frailties undetected by the G8 scale (i.e. depression, postural instability or autonomy loss) The CGA was performed by a geriatrician at AP-HM Geriatric Day care hospital. In this study, all the cancer patients were in an outpatient setting and all types of lung cancer, thoracic tumor and all stages were included. Lung cancer and thoracic tumor treatment could be thoracic surgery, radiotherapy, chemo-radiotherapy, systemic therapy (chemotherapy, targeted therapy, immune checkpoint inhibitor therapy) or best supportive care (BSC).

The study was approved by a local ethics committee. All the patients were registered at baseline in accordance with the French database and Privacy law (Commission Nationale de l'Informatique et Liberté CNIL registration number: 2017-33).

### *Data collection and baseline measurements*

The different components of the CGA were collected by a geriatrician. Geriatric frailties and functional status were detected using the G8 screening tool (impaired  $\leq 14/17$ )<sup>[27]</sup>, vulnerability score (ECOG-PS) (impaired  $\geq 2$ )<sup>[28]</sup>, Activities of Daily Living (ADL) (impaired  $<6$ )<sup>[29]</sup>, and Instrumental Activities of Daily Living (IADL) scales (impaired  $<4$ )<sup>[30]</sup>. Nutritional status was assessed using the Body Mass Index (BMI), albumin levels, and the Mini Nutritional Assessment scale (MNA)<sup>[31]</sup>. The definition of malnutrition was taken from the recommendations issued by the French Department of Health (BMI  $< 21$  and/or albumin levels  $< 35$  g/l and/or MNA  $< 17$ ). Cognitive disorders were assessed using the Mini Mental State Examination (MMSE) (impaired MMSE  $< 24$ )<sup>[32]</sup>, and depression risk with the Geriatric Depression Scale (impaired GDS  $\leq 1$ )<sup>[33]</sup>. Physical performance and mobility were assessed using gait speed (impaired  $\leq 0.8$  m/s)<sup>[34]</sup>, the Timed Up and Go Test (impaired TUG  $> 20$  s)<sup>[35]</sup>, the One Leg Balance test (OLBT) (impaired OLBT  $< 5$  s)<sup>[36]</sup>, and the history of falls in the three months prior to the CGA. Handgrip strength was determined, and the cutoff values were those of the European Guidelines on Sarcopenia (EGSOP2) (impaired  $< 27$  kg for men;  $< 16$  kg for women)<sup>[37]</sup>. Patients were asked about their demographic characteristics and

lifestyle (age, living place, and presence of a caregiver). Severe comorbidities were identified using the geriatric Cumulative Illness Rating Scale (CIRS-G)<sup>[38]</sup> and polypharmacy ( $\geq 5$  drugs per day) was assessed.

The main medical information was obtained from the medical records: type of lung or thoracic cancer, cancer stage, detailed treatment before and after CGA, and biological data (plasma and serum chemistry). Anemia was defined as hemoglobin levels  $\leq 11.5$  g/dl, lymphopenia was defined as lymphocyte levels  $< 1.26$  G/l. Albumin levels  $< 35$  g/l were abnormal, vitamin B12 levels  $< 145$  or  $> 569$  pmol/l were abnormal, C-reactive protein (CRP) levels  $> 5$  mg/l were abnormal, and patients with a BCI index  $> 40\ 000$ , which is the product of multiplying the CRP level with the vitamin B12 level (B12 X CRP)<sup>[39]</sup>, were impaired. For analysis purpose we pooled together chemotherapy, targeted therapy and immunotherapy under the term “systemic therapy”.

#### *Follow-up data and measurements*

Data on treatments and outcomes were obtained from the medical records. Information about unplanned hospitalizations and their causes, as well as vital status (and causes of death) was collected in July 2019. Overall survival (OS) was defined as the time between the date of the CGA and the date of death or last known follow-up.

The oncological treatment proposed initially, and the final oncological treatment chosen following the CGA were recorded.

#### *Statistical analysis*

A descriptive analysis was performed to detail the main demographic, oncological, geriatric, and treatment characteristics of our population using headcounts and percentages for discrete data, as well as mean values plus or minus the standard error and the interval between the minimum and maximum values for continuous data. A comparative analysis was performed between patients who underwent unplanned hospitalizations within three months after treatment initiation and patients who did not; the Chi-squared test was used to analyze discrete data whereas Student’s t-test was used to analyze continuous variables. To determine the factors associated with unplanned hospitalizations, we performed a logistic regression analysis. Variables with a p-value  $\leq 0.1$  in the comparative analysis were added to a stepwise model, adjusted on age, gender, and tumor stage. Survival analysis was performed using a Cox regression analysis. Variables with a p-value  $\leq 0.1$  in the univariate analysis were added to a stepwise model, which was adjusted on age, gender, and tumor stage. Two models were

developed, with and without unplanned hospitalization. BCI index, although significantly associated to OS in the univariate analysis, was not computed in the multivariate model due to high number of missing data. A p-value  $\leq 0.05$  was considered statistically significant. All the statistical analyses were performed using SPSS software (version 17.0) for windows.

## **Results**

Overall, 228 patients were recruited. The median age was 78.7 years (range 67 to 95 years) and 74.1 % were male. The majority of the patients were diagnosed with NSCLC (82%) and adenocarcinoma was the most common histological type (43%). Stage IV was diagnosed in 104 patients (45.6%). The most common treatment was systemic therapy alone (40.4%): chemotherapy (n=76; 33.4% ), targeted therapy (n=8; 3.5%), and immunotherapy (n=8; 3.5%). Moreover, 22.4 % of patients had thoracic surgery and 20.6% had radio-chemotherapy. First-line oncological treatment involved 86% of patients. In our work, 15.6% of patients had their initial treatment proposal modified after the CGA; the geriatrician suggested less intensive treatment in almost all these patients (n=33/35 patients). The ECOG PS score was  $\geq 2$  in 28.8% of patients and the G8 screening score was  $\leq 14$  in 92% of older patients.

Patient demographics, as well as the oncological and geriatric characteristics, are presented in Table 1.

Biological data were available for 221 patients, of whom 92 (41.6%) had anemia, 17 (7.7%) had thrombopenia, and 47 (21.3%) had lymphopenia. An abnormal BCI (B12 X CRP)  $> 40000$  was observed in 15 patients (8.1%) (data were missing for 42 patients).

### *Unplanned hospitalization*

The univariate and multivariate analyses of unplanned hospitalizations are presented, respectively, in Table 2 and Figure 1.

In our study, 82 patients (36 %) had at least one unplanned hospitalization within 3 months. The most common reason for unplanned hospitalizations was disease progression (n=44 patients, 53.7%) followed by treatment toxicity (n=25 patients, 30.5%) and other causes (n=13 patients, 15,9%).

Variables significant at the 10 % level in the univariate analysis were included in the multivariate model (stepwise procedure). The model was also adjusted on age. The factors that remained independently associated with unplanned hospitalizations within 3 months of

treatment initiation were male gender (aOR 3.3; 95% CI [1.5-7.2]), systemic therapy (aOR 2.6; 95% CI [1.1-6.2]), and fall history in the 3 months before treatment initiation (aOR 3.6; 95% CI [1.6-8.2]).

### *Overall survival (OS)*

Overall survival in the univariate analysis and both the multivariate cox models are presented in Tables 3, Figures 2 and 3, respectively

In our study, 66 patients (28.9%) died at six months. The leading cause of death at six months was disease progression or treatment toxicity in 63 patients (95.4%) and other causes in 3 patients. To evaluate OS, the median survival time was 18.7 months (from 1 to 60.6 months) and the death rate was 48% (n=110).

Variables significant at the 10 % level in the univariate analysis were included in the multivariate model. BCI was not included in the multivariate model due to missing data, and as the G8 screening tool contains questions on nutrition, malnutrition and albumin level were dropped from the multivariate model for strong correlation with G8. Moreover, age was forced in the model (Figure 2). The following factors remained independently associated with decrease of OS: male gender (HR 2.7; 95% CI [1.4-5.1]), stage IV cancer (HR 2.0; 95% CI [1.2-3.5]), unplanned hospitalization (HR 4.3; 95% CI [2.7-7.0]), G8  $\leq$  14 (HR 4.0; 95% CI [1.2-13.7]), systemic therapy (HR 2.5; 95% CI [1.1-5.6]), supportive care (HR 4.6; 95% CI [1.7-12.5]), mesothelioma (HR 3.3; 95% CI [1.3-8.8]), and small cell lung cancer (HR 2.8; 95% CI [1.3-6.0]).

The second model was adjusted on age, but we removed from the statistical model the unplanned hospitalizations within 3 months (Figure 3). The following factors remained independently associated with OS decrease: male gender (HR 3.9; 95% CI [2.1-7.3]), stage IV cancer (HR 1.6; 95% CI [1.0-2.6]), systemic therapy (HR 2.6; 95% CI [1.2-5.5]), ECOG PS  $\geq$  2 (HR 2.0; 95% CI [1.2-3.4]), G8  $\leq$  14 (HR 3.5; 95% CI [1.1-11.4]), and impaired handgrip strength (HR 1.6; 95% CI [0.9-2.5]).

### **Discussion**

This study highlights the importance of a CGA to assess the risks of unplanned hospitalizations and poor survival in older outpatients with lung cancer and thoracic tumor. In our survey, the CGA detected geriatric impairments in a majority of patients. Mobility, instrumental autonomy, emotional health, and nutritional status were the most frequently impaired. These results are consistent with the prevalence of geriatric impairments reported in



the literature in older patients with lung cancer<sup>[5]</sup>. For 15.6% of patients, the CGA resulted in an adaptation of the oncological treatment. This is noteworthy that less aggressive treatment was more often advised and implemented without a negative impacts on unplanned hospitalizations and on patient's overall survival. These results concur with the study by Corre *et al.*<sup>[22]</sup>, showing that adaptation of treatment according to CGA did not show any difference in overall survival.

One-third of the patients had an unplanned hospitalization in the three months after initiation of treatment. This proportion is higher than those found in other studies (19% reported by Ruiz, 2019)<sup>[24]</sup> and may be related to the large proportion of advanced cancers (nearly 50% stage IV) in our study sample. We found an association between the risk of unplanned hospitalizations and male gender, systemic therapy, and history of falls in the 3 months prior to the oncological treatment initiation. The relation between systemic therapy and unplanned hospitalizations has already been highlighted and is often related to systemic therapy toxicity. In older patients, functional impairment<sup>[40]</sup> and comorbid conditions may increase the risk of treatment-related complications including surgery complications<sup>[41]</sup>. Recent studies have also shown that major drug-drug interactions are highly prevalent in older adults on chemotherapy (in particular with comorbid conditions) and are a risk factor for early unplanned hospitalizations<sup>[42,43]</sup>. CGA interventions are associated with improved chemotherapy tolerance in older cancer patients<sup>[44]</sup>. Conversely, without a CGA before initiation of treatment, geriatric factors are often the primary cause of chemotherapy discontinuation or mortality, irrespective of the type of tumor<sup>[45-47]</sup>. The study by Corre *et al.* (2016)<sup>[22]</sup> was the first randomized study to show that treatment allocation chosen on the basis of the CGA could reduce treatment toxicity in older patients with advanced lung cancer.

Previous studies have shown an association between chemotherapy toxicity and frailty factors (FFI) or impaired autonomy<sup>[24,26]</sup>. Fall history is a prognostic factor of the CARG score that is used to assess the risk of chemotherapy toxicity<sup>[16]</sup> but, to our knowledge, the relation we found between the history of falls and unplanned hospitalizations in older patients with lung or thoracic cancer has not yet been shown. In older lung or thoracic cancer outpatient care, identifying factors associated with a higher risk of unplanned hospitalization is essential to define the risk profile of each patient and optimize treatment selection.

This is all the more important that, according to our results, unplanned hospitalization is itself a factor with a very negative impact on survival ( $p < 0.001$ ). This new factor in the

management of older adults with lung or thoracic cancer has been studied little in the literature and should be included in the mortality risk scores.

Several studies carried out on older adults with lung cancer have taken into account geriatric factors in the choice of cancer treatment or in the analysis of chemotherapy toxicity or treatment completion<sup>[17,19–24,26,48–50]</sup>. However, few of them have focused on the impact of geriatric characteristics on patient survival<sup>[19,23,48–51]</sup>. In our work, abnormal handgrip strength is strongly associated with poor survival. Handgrip strength is used to assess sarcopenia<sup>[37]</sup>, a muscle disorder characterized by loss of muscle strength and muscle mass with or without an increase in fat mass. In addition to aging, many factors may contribute to sarcopenia such as malnutrition, inactivity, or cancer. Sarcopenia is known to be a risk factor of early death, falls, and mobility impairment in older populations<sup>[37]</sup>. Patients with lung cancer are more likely to be malnourished and develop sarcopenia, in particular with small cell lung cancer<sup>[52]</sup>. In the literature, sarcopenia is associated with complications in surgery<sup>[53]</sup> and chemotherapy and negatively associated with OS during chemotherapy<sup>[52]</sup>. Measurements of muscle strength and physical performance are important in the outcome in older patients treated for lung cancer.

CGA has become a cornerstone of the routine care of older patients with cancer<sup>[13]</sup> and the G8 screening tool is used in nearly all oncological centers. Our work, as well as research in the literature, has proven that a G8 score under 14 out of 17 is an unfavorable prognostic factor<sup>[49,50]</sup>. The G8 nutrition items show impairment in the nutritional domain that has been demonstrated to be associated with poor survival<sup>[19,48]</sup>. The G8 screening tool also allows assessment of mobility or cognitive impairment, making it more suitable for the risk assessment of older cancer patients than the ECOG PS. In the second multivariate model for OS (without unplanned hospitalization), an ECOG PS  $\geq 2$  was associated with poor OS in accordance with the literature<sup>[19,25,48–50,54,55]</sup>. The ECOG PS describes frailty but poorly reflects functional and nutritional impairment in older cancer patients<sup>[28,56]</sup>, unlike the G8 screening tool.

Thoracic tumor type and stage were also important in OS: mesothelioma and SCLC were associated with poor outcomes in this study. Mesothelioma is a type of thoracic tumor with a poor outcome in the older population even though treatment has evolved in recent years with pemetrexed plus platinum, prophylactic irradiation of intervention tracts, and bevacizumab (if patients < 75 years)<sup>[57]</sup>. The outcome of SCLC is also poor in the literature, in particular in older adults<sup>[58,59]</sup>. According to the literature, stage IV disease is a prognostic factor associated with a low survival rate<sup>[49]</sup>.

This study does, however, have some limitations. First, it was a monocentric survey that included a population of older patients suffering from lung cancer and thoracic tumor of various histological types, different clinical stages, and all types of treatment (surgery, systemic therapy, chemo-radiotherapy, radiotherapy, and best supportive care). Second, targeted geriatric adjustments implemented on the basis of CGA findings may have modified the outcomes but their impact were not measurable. Third, we took into account unplanned hospitalizations occurring within 3 months of the geriatric assessment. As such, some patients may have been hospitalized before initiation of oncological treatment.

The strengths of the study include data collection on unplanned hospitalizations in older patients treated for lung cancer and thoracic tumor, which is rare in the oncologic literature. Moreover, our sample size of older outpatients with thoracic cancer was large (n=228), and, as G8 screening is conducted routinely by the thoracic oncologists at our center, we were able to perform a CGA on all the patients with an impaired G8 according to the recommendations of the Society for Geriatric Oncology (SIOG) and the European Organization for Research and Treatment of Cancer (EORTC)<sup>[7]</sup>. This work highlights the importance of the geriatric screening (G8) for older patients treated for lung and thoracic tumors. Older population is heterogeneous with numerous comorbidities and frailties which can compromise the implementation of a cancer treatment, especially of a systemic therapy with potential toxicities. The role of the geriatrician, upstream of the therapeutic decision, is essential. Screening of frailties and management of deficits that can be improved, can allow frail patient to benefit of standard treatment. This is the case in our university hospital where a multidisciplinary team including oncologist, geriatrician, physical therapist and pharmacist has been set up since September 2013. However, G8 explore a limited number of geriatric factors, and, as shown in our study, some patients with a normal G8 score were referred for CGA as they were felt by the oncologist to be frail. Improvements of patient's management are still needed as our survey showed the deleterious impact of fall history and muscle strength impairment on unplanned hospitalizations and survival in older patient with lung or thoracic cancers. Muscular conditions should be consolidated before or during oncologic treatment and falls could be avoid by specific prevention strategies (i.e removing home hazards or stopping some medications).

## **Conclusions**

Management of lung and thoracic cancers in older patients is challenging due to the heterogeneity of the older population, the large number of histological forms and treatments, and the under-representation of older patients with lung cancer in clinical trials. Consequently, it is of major importance to detect, through geriatric screening (G8), the geriatric frailties that may be responsible for poor outcomes, and address them before initiation of cancer treatment. Moreover history of falls and handgrip strength that are part of the CGA may also be responsible for unplanned hospitalizations and poor survival respectively. The value of geriatric oncology care, which involves a multidisciplinary team including oncologist, geriatrician, physical therapist and pharmacist, should be better recognized in the management of older patients with lung cancer, as this new organization seems superior to the routine organization in terms of mortality and hospitalizations rate reduction.

**Conflict of interest:** None of the authors have conflict of interest to declare in this submitted work.

**Author contributions:** *Study concepts and design:* AL. Couderc. *Study material or patients:* AL. Couderc, P. Tomasini, L. Greillier. *Quality control of data and algorithms:* AL. Couderc, D. Rey, E. Nouguerede. *Data analysis and interpretation:* AL. Couderc, D. Rey, E. Nouguerede, P. Tomasini, L. Greillier. *Statistical analysis:* AL. Couderc, D. Rey, E. Nouguerede, L. Greillier. *Manuscript preparation:* AL. Couderc, D. Rey. *Manuscript editing:* AL. Couderc and L. Greillier. *Manuscript review:* AL. Couderc, P. Tomasini, D. Rey, E. Nouguerede, Correard F, C. Montegut, PA. Thomas, P. Villani, F. Barlesi, L. Greillier.

**Acknowledgments:** This work has no funding.

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**Table 1:** Demographic, oncologic and geriatric characteristics of older patients with lung and thoracic cancers - descriptive analysis (n=228)

Characteristics	Total (n=228)		Characteristics	Total (n=228)	
	n or Mean+ET	(%) or [min-max]		n or Mean+ET	(%) or [min-max]
<b>Gender</b>			<b>Treatments</b>		
Men	169	(74.1)	Surgery	51	(22.4)
<b>Age</b>	78.7±5.0	[67-95]	Systemic therapy alone°	92	(40.4)
70-74	45	(19.7)	Radio-chemotherapy	47	(20.6)
75-79	89	(39.0)	Radiotherapy	18	(7.9)
80-84	62	(27.2)	Supportive care	20	(8.8)
85 and more	32	(14.0)			
<b>Caregiver</b>	156	(68.4)	<b>G8</b>	10.6±2.8	[3-17]
Housing care facility (vs. home)	19	(8.3)	Score ≤14 (vs. >14)	208	(92.0)
<b>Fall History</b>	42	(18.4)	<b>ECOG-PS 2-4 (vs. 0-1)</b>	65	(28.8)
<b>ADL&lt;6</b>	73	(32.0)	<b>Type of thoracic tumor</b>		
<b>IADL &lt;4</b>	124	(54.4)	Adenocarcinoma	98	(43.0)
<b>Cognitive disorders (MMSE&lt;24)</b>	57	(25.6)	Epidermoid	89	(39.0)
<b>Suspicion of depression (GDS ≥1)</b>	107	(47.3)	Mesothelioma	18	(7.9)
<b>Abnormal handgrip strength*</b>	102	(45.9)	SCLC	15	(6.6)
<b>Polymedication</b>	161	(70.6)	Other	8	(3.5)
<b>Nutritional status</b>			<b>Stage IV</b>	104	(45.6)
BMI	24.0±4.4	[15.5-38.0]	<b>Final treatment modified from initial proposal</b>	35	(15.6)
Albumin	38.3±5.2	[22-49]	<b>Treatment line</b>		
Malnutrition	102	(44.7)	First line	196	(86.0)
<b>Mobility</b>			Second line	24	(10.5)
Timed up and go Test (>20s)	88	(38.6)	Third line	7	(3.1)
One-leg balance test (< 5s)	139	(61.0)	Sixth line	1	(0.4)
Gait speed (≤0.8m/s)	111	(48.7)	<b>Number of comorbidities</b>	6.7±3.8	[0-13]
<b>Abnormal BCI**</b>	15	(8.1)	<b>Severe comorbidities</b>	119	(52.2)
<b>Lymphopenia</b>	47	(21.3)			

\*Abnormal handgrip strength is <27kg for men and <16kg for women; \*\*N=186 for BCI, missing data for other variables <5%;

°Systemic therapy comprehend: Chemotherapy (n=76 ; 82.6 %) , Targeted therapy (n=8 ;8.7 %) and immunotherapy (n=8; 8.7%)

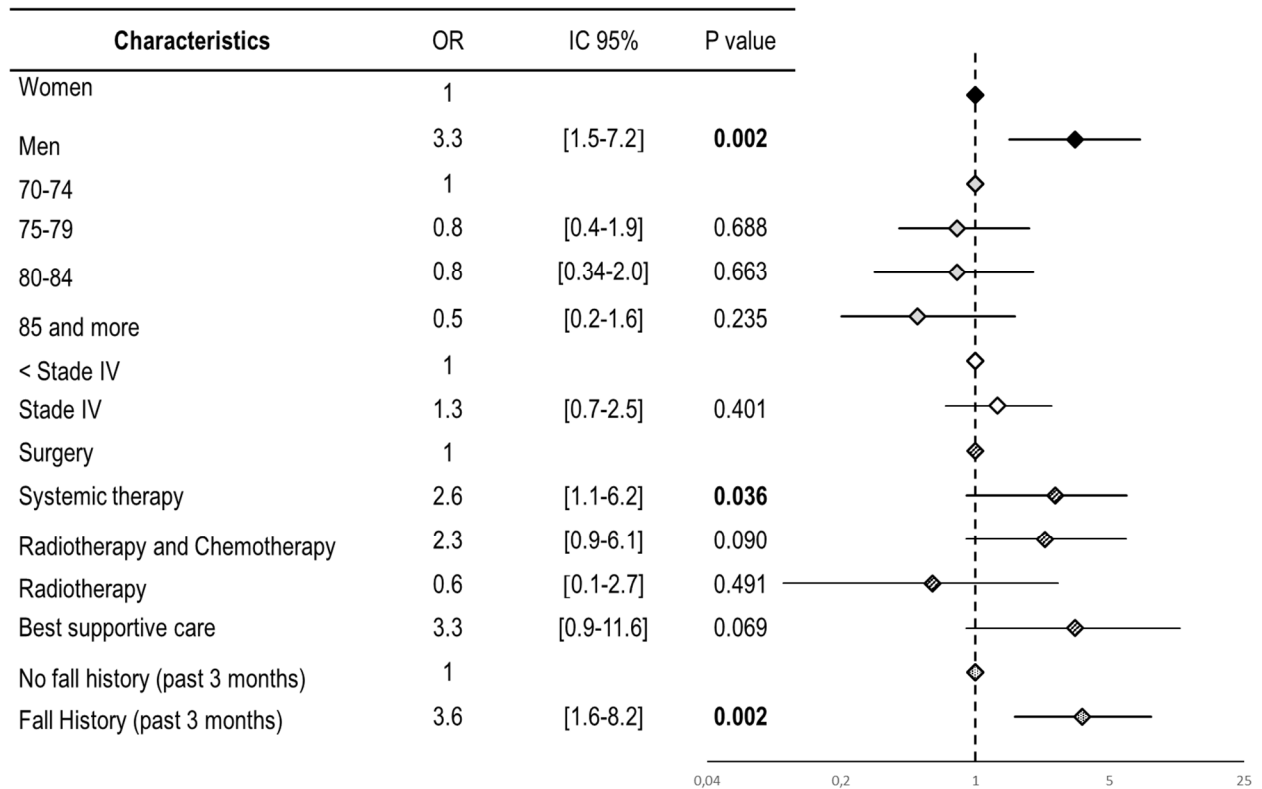
ADL: activities of daily living; BCI: B12 X C reactive protein index; BMI: body mass index; ECOG-PS: eastern cooperative oncology group- performance status; G8: Oncodage; GDS: geriatric depression scale; IADL: instrumental activities of daily living; MMSE: mini mental state examination; SCLC: small cells lung cancer

**Table 2:** Factors associated with unplanned hospitalization within 3 months after treatment initiation among older patients with lung and thoracic cancers (univariate analysis, n=228 patients ≥70 years)

Characteristics	Unplanned hospitalization (n=82)		No unplanned hospitalization (n=146)		p
	n or Mean±ET	(%) or [min-max]	n or Mean±ET	(%) or [min-max]	
<b>Male Gender</b>	68	(82.9)	101	(69.2)	<b>&lt;0.05</b>
<b>Age</b>	78.8±5.2	[70-91]	78.5±4.7	[67-95]	
70-74	17	(20.7)	28	(19.2)	0.93
75-79	33	(40.2)	56	(38.9)	
80-84	22	(26.8)	40	(27.8)	
85 and more	10	(12.2)	22	(15.3)	
<b>Caregiver</b>	52	(63.4)	104	(71.2)	0.19
<b>Housing</b> care facility (vs. home)	9	(11.0)	10	(6.8)	0.28
<b>Fall History</b>	23	(28.0)	19	(13.0)	<b>&lt;0.01</b>
<b>Autonomy</b> (ADL<6)	32	(39.0)	41	(28.1)	0.08
<b>Instrumental autonomy</b> (IALD <4)	53	(64.6)	71	(48.6)	<b>&lt;0.05</b>
<b>Cognitive disorders</b> (MMSE<24)	21	(25.6)	36	(24.7)	0.67
<b>Suspicion of depression</b> (GDS ≥1)	44	(53.7)	63	(43.2)	0.09
<b>Impaired handgrip strength *</b>	44	(53.7)	58	(39.7)	<b>&lt;0.05</b>
<b>Nutritional status</b>					
BMI	23.6±4.4	[15.9-38.0]	24.2±4.4	[15.5-38.0]	0.34
Albumin	36.3±5.0	[22-47]	39.4±5.0	[25-49]	<b>&lt;0.001</b>
Malnutrition	44	(53.7)	58	(39.7)	<b>&lt;0.05</b>
<b>Mobility</b>					
Timed up and go Test (>20s)	40	(48.8)	48	(32.9)	<b>&lt;0.05</b>
One-leg balance test (< 5s)	54	(65.9)	85	(58.2)	0.26
Gait speed (≤0.8m/s)	45	(54.9)	66	(45.2)	0.16
<b>Number of comorbidities</b>	3.8±2.2	[0-9]	4.3±2.4	[0-13]	0.55
<b>Severe comorbidities</b>	42	(51.2)	77	(52.7)	0.82
<b>Polymedication</b> (≥5 drugs)	59	(72.0)	102	(69.9)	0.74
<b>Abnormal BCI**</b>	7	(5.9)	8	(11.8)	0.16
<b>Lymphopenia</b>	27	(19.7)	20	(24.7)	0.39
<b>Type of thoracic tumor</b>					
Adenocarcinoma	32	(39.0)	66	(45.2)	0.37
Epidermoid	35	(42.7)	54	(37.0)	0.40
Mesothelioma	6	(7.3)	12	(8.2)	0.81
SCLC	7	(8.5)	8	(5.5)	0.37
Other	2	(2.4)	6	(4.1)	0.51
<b>Stage IV</b> (vs stage <IV)	45	(54.9)	59	(40.4)	<b>&lt;0.05</b>
<b>Treatments</b>					
Surgery	11	(13.4)	40	(28.0)	
Systemic therapy	38	(46.3)	54	(37.8)	
Radiotherapy	3	(3.8)	15	(10.5)	<b>0.02</b>
Radio-chemotherapy	19	(23.2)	28	(19.2)	
Supportive care	11	(13.8)	9	(6.3)	
<b>Treatment modified after CGA***</b>	16	(19.5)	19	(13.0)	0.20
<b>G8</b>	9.8±2.8	[3-16]	11.0±2.7	[4-17]	<b>&lt;0.01</b>
Score ≤14 (vs. >14)	76	(92.7)	132	(90.4)	0.46
<b>ECOG 2-4</b> (vs. 0-1)	32	(39.0)	33	(22.6)	<b>&lt;0.01</b>
<b>Treatment line 2 and over</b> (vs. 1 <sup>st</sup> line)	9	(11.0)	23	(15.8)	0.32

\* Abnormal handgrip strength is <27kg for men and <16kg for women; \*\*N=186 for BCI, other variables are < 5%; \*\*\*N= 35 patients

ADL: activities of daily living; BCI: B12 X C reactive protein index; BMI: body mass index; ECOG-PS: eastern cooperative oncology group- performance status; G8: oncodage; GDS: geriatric depression scale; IADL: instrumental activities of daily living; MMSE: mini mental state examination; SCLC: small cells lung cancer



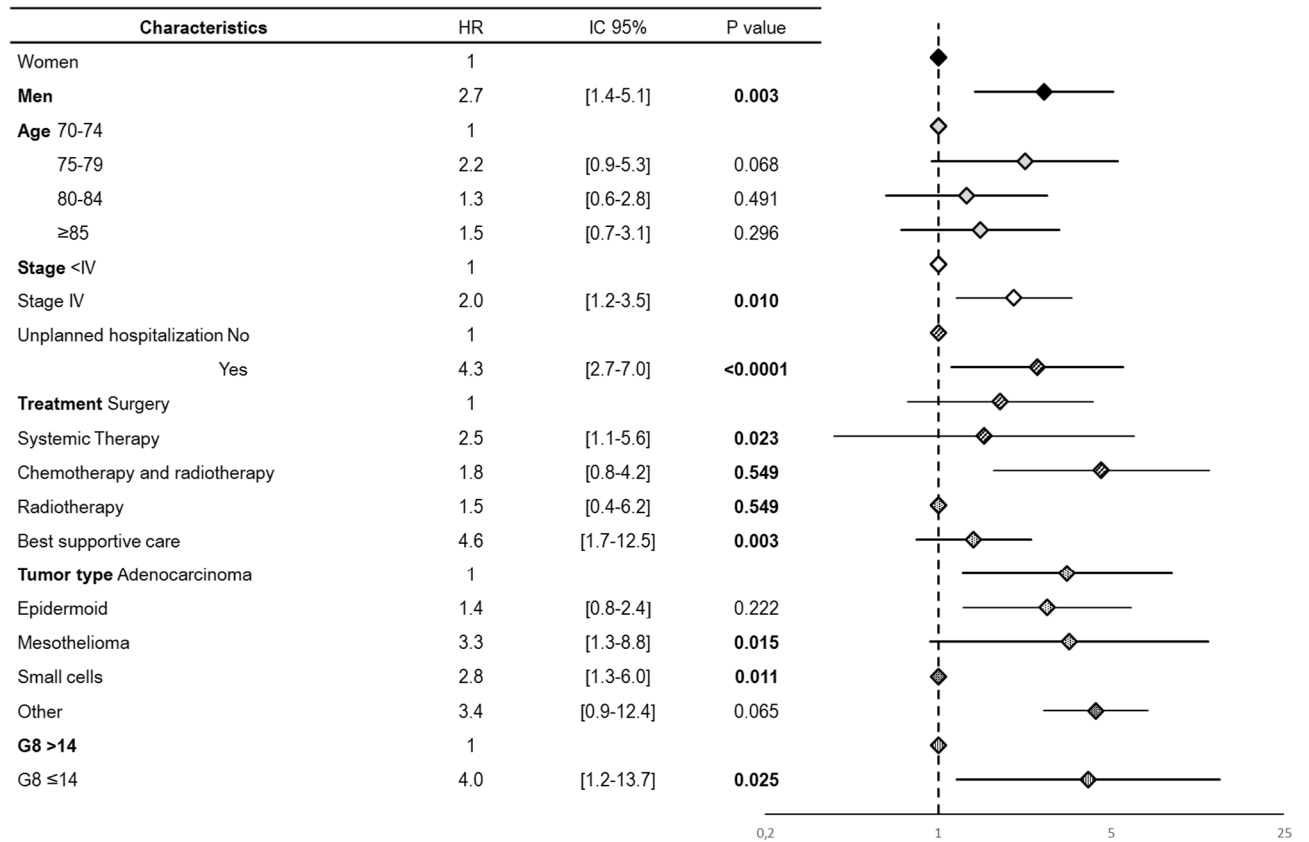
**Figure 1:** Factors associated with unplanned hospitalization within 3 months after treatment initiation in older patients with lung and thoracic cancers (multivariate analysis, n=221 patients  $\geq 70$  years). All variables with a p-value  $\leq 0.1$  in the comparative analysis were added to a stepwise model. Results presented above are only variables significant in the multivariate model. Model was adjusted on gender, age and tumor metastatic stage (stage IV or not).  
aOR : adjusted odds ratio

**Table 3:** Factors associated with mortality among older patients with lung and thoracic cancers (univariate analysis, n=228 patients  $\geq$ 70 years)

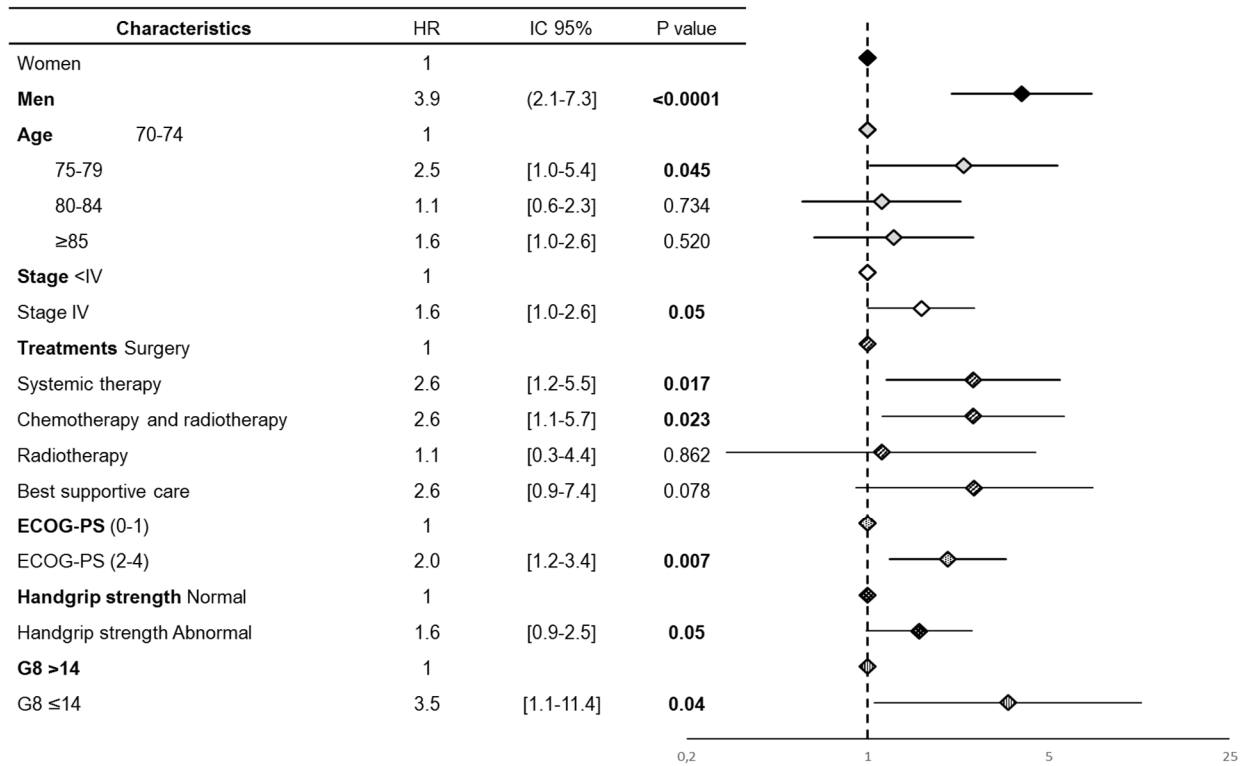
Characteristics	Univariate mortality analysis		
	HR	IC 95%	P value
<b>Male gender</b>	2.1	[1.3-3.4]	<b>&lt;0.01</b>
<b>Age</b>	1.0	[0.9-1.0]	0.74
70-74	1.3	[0.2-9.8]	0.80
75-79	1.3	[0.2-9.3]	0.81
80-84	1.1	[0.2-8.4]	0.90
85 and more	1.5	[0.2-11.5]	0.68
<b>Caregiver</b>	0.9	[0.6-1.3]	0.45
<b>Housing</b> care facility (vs. home)	1.6	[0.9-3.1]	0.10
Fall History	1.4	[0.9-2.3]	0.12
<b>ADL</b> <6	1.2	[0.8-1.7]	0.49
<b>IALD</b> <4	1.9	[1.3-2.9]	<b>0.001</b>
<b>Cognitive disorders</b> (MMSE<24)	1.5	[1.0-2.2]	0.08
<b>Suspicion of depression</b> (GDS $\geq$ 1)	1.1	[0.8-1.6]	0.58
<b>Impaired handgrip strength*</b>	1.8	[1.2-2.6]	<b>&lt;0.01</b>
<b>Nutritional status</b>			
BMI (<21)	1.1	[0.7-1.7]	0.78
Albumin (<35g/L)	2.3	[1.5-3.6]	<b>&lt;0.001</b>
Malnutrition	1.8	[1.2-2.6]	<b>&lt;0.01</b>
<b>Mobility</b>			
Timed up and go Test (>20s)	2.1	[1.4-3.1]	<b>&lt;0.001</b>
One-leg balance test (< 5s)	1.8	[1.2-2.7]	<b>&lt;0.01</b>
Gait speed (<0.8m/s)	1.4	[0.9-2.0]	0.12
<b>Number of comorbidities</b>	1.0	[0.9-1.1]	0.65
<b>Severe comorbidities</b>	0.9	[0.6-1.4]	0.72
<b>Polymedication</b> ( $\geq$ 5 drugs)	1.0	[0.7-1.6]	0.88
<b>Abnormal BCI**</b>	2.5	[1.3-4.7]	<b>&lt;0.01</b>
<b>Lymphopenia</b>	1.8	[1.1-2.9]	<b>0.01</b>
<b>Type of thoracic tumor</b>			
Adenocarcinoma	1		
Epidermoid	1.4	[0.9-2.2]	0.11
Mesothelioma	1.9	[1.0-3.9]	0.06
SCLC	2.8	[1.5-5.4]	<b>&lt;0.01</b>
Other	1.0	[0.3-3.1]	0.94
<b>Stage IV</b> (vs stage <IV)	2.1	[1.4-3.1]	<b>&lt;0.01</b>
<b>Treatments</b>			
Surgery	1		
Systemic therapy	3.7	[1.9-7.1]	<b>&lt;0.01</b>
Radio-chemotherapy	3.2	[1.6-6.6]	<b>&lt;0.01</b>
Radiotherapy	0.9	[0.3-3.4]	0.93
Supportive care	5.5	[2.5-12.4]	<b>&lt;0.01</b>
<b>Treatment modified after CGA***</b>	1.3	[0.8-2.2]	0.32
<b>Unplanned hospitalization</b>	3.8	[2.6-5.5]	<b>&lt;0.001</b>
<b>G8 Score</b> $\leq$ 14 (vs. >14)	3.2	[1.2-8.6]	<b>&lt;0.05</b>
<b>ECOG 2-4</b> (vs. 0-1)	2.3	[1.6-3.5]	<b>&lt;0.001</b>
<b>Treatment line 2 and over</b> (vs. 1 <sup>st</sup> line)	1.0	[0.6-1.7]	0.97

\* Abnormal handgrip strength is <27kg for men and <16kg for women; \*\*N=186 for BCI, other variables are < 5%; \*\*\* N= 35 patients

ADL: activities of daily living; BCL: B12 X C reactive protein index; BMI: body mass index; ECOG-PS: eastern cooperative oncology group- performance status; G8: oncophage; GDS: geriatric depression scale; IADL: instrumental activities of daily living; MMSE: mini mental state examination; HR: Hazard ratio  
SCLC: small cells lung cancer



**Figure 2:** Factors associated with mortality in older patients with lung and thoracic cancers (Cox regression analysis n=190 patients ≥70 years). All variables with a p-value ≤ 0.1 in the comparative analysis were added to a stepwise model. Results presented above are only variables significant in the multivariate model. Model was adjusted on gender, age and tumor metastatic stage (stage IV or not).  
HR: Hazard Ratio



**Figure 3:** Factors associated with mortality in older patients with lung and thoracic cancers (Cox regression analysis n=190 patients ≥70 years). Model without unplanned hospitalization within 3 months after treatment initiation (early risk factors). All variables with a p-value ≤ 0.1 in the comparative analysis were added to a stepwise model. Results presented above are only variables significant in the multivariate model. Model was adjusted on gender, age and tumor metastatic stage (stage IV or not).

HR: Hazard Ratio