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## Octogenarians treated for thoracic and lung cancers:

### Impact of Comprehensive Geriatric Assessment

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### Abstract

**Background:** Lung cancer affects older and older old adults and is the leading cause of death by cancer. Comprehensive Geriatric Assessment (CGA) is recommended before and during cancer treatment to guide therapy management in this population.

**Methods:** This study was conducted between September 2015 and January 2019 at Marseille University Hospital (AP-HM). During this period, all consecutive outpatients 70 years or older referred for a CGA before initiation of lung cancer treatment were enrolled. The objective of this study was to compare lung and thoracic cancer management of octogenarians ( $\geq 80$  years) and their geriatric profile versus patients aged 70 to 79 years ( $< 80$  years).

*Findings:* In our study, 228 patients were recruited. The median age was  $78.7 \pm 5$  years. There were 94 octogenarians (41.2%), 36.2% of them were diagnosed with stage IV neoplasm and the most common treatment was chemotherapy (43.6%). The logistic regression analysis highlights that handgrip strength was the most commonly impaired domain (OR 2.3; 95% CI [1.3-4.3]) in octogenarians and that they are more likely than their younger counterparts to be treated by targeted therapy (OR 9.8; 95% CI [1.0-92.9]). Overall survival (OS) was similar in both age groups (log rank=0,95).

*Interpretation:* In our study, octogenarians and patients <80 years had equivalent survival, across the different thoracic cancer treatments and tumor stages. Measure of muscle strength in CGA could be very useful in a clinical setting to help improve the management of older old patients treated for lung or thoracic cancer.

**Keywords:** octogenarians; older adults; thoracic and lung cancers; comprehensive geriatric assessment; oncological treatment.

## **Introduction:**

Cancer, especially lung cancer, affects older adults. Half of all patients with lung cancer are aged 70 years or older at diagnosis<sup>[1,2]</sup> and approximately 15% of cases are diagnosed in patients over 80 years<sup>[1]</sup>. Lung cancer is the leading cause of death by cancer, in particular in the United States and Europe<sup>[3]</sup>. Initial symptoms at diagnosis are not significantly different between older and younger patients<sup>[4]</sup>. The association between age and mortality is variable in the literature<sup>[1,5–9]</sup> but the majority of studies show no differences between age groups, in particular when analyses were stratified by treatment.

Although older adults are the most affected by cancer, they are still under-represented in clinical trials, especially in an oncological setting<sup>[10]</sup>. The Society for Geriatric Oncology (SIOG) and the European Organisation for Research and Treatment of Cancer (EORTC)<sup>[11]</sup> both propose guidelines of treatment in older adults; but for octogenarians, more data are needed to develop specific treatment recommendations. The development of Geriatric Oncology has greatly improved the management of older and older old adults with Comprehensive Geriatric Assessments (CGA) being conducted before and during cancer treatment<sup>[12,13]</sup>. The use of a CGA is essential to guide treatment decisions in older patients with cancer<sup>[13]</sup> and is now commonly used in lung and thoracic cancer management<sup>[5,7,14–23]</sup>. Schulkes *et al* showed that propositions of oncological treatment were more often based on the number of geriatric impairments than on the chronological age of the patients<sup>[24]</sup>.

We designed this study to compare geriatric characteristics, treatment decisions, unplanned hospitalizations, and overall survival (OS) between patients under 79 years (<80 years) and patients 80 years or more (≥80 years) treated for lung and thoracic cancers.

## **Methods**

### *Study Design and Participants*

This study was conducted between September 2015 and January 2019 at Marseille University Hospital (AP-HM) and was the result of a close collaboration between the geriatric unit and the thoracic surgery and oncological units of AP-HM. During this period, all consecutive older patients referred to the geriatric unit by the thoracic units for a CGA before initiation of thoracic and lung cancer treatment were included. Potentially frail patients were screened for a CGA by thoracic oncologists/surgeons using the G8 score according to French recommendations<sup>[25]</sup>. Oncologists also referred for a CGA all patients with an impaired G8 (G8 score of 14 or less out of 17) and all 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 Hospital. In this study, all the cancer patients were in an outpatient setting and all types of thoracic cancers and stages were included. Cancer treatment could be thoracic surgery, radiotherapy, chemo-radiotherapy, chemotherapy, targeted systemic therapy, immune checkpoint inhibitor therapy, or exclusive supportive care.

The study was approved by a local ethics committee. All the patients were registered at baseline in compliance 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>[25]</sup>, vulnerability score (ECOG-PS) (impaired  $\geq 2$ )<sup>[26]</sup>, Activities of Daily Living (ADL) (impaired  $< 6/6$ )<sup>[27]</sup>, and Instrumental Activities of Daily Living (IADL) scales (impaired  $< 4/4$ )<sup>[28]</sup>. Nutritional status was assessed using the Body Mass Index (BMI), albumin levels, and the Mini Nutritional Assessment scale (MNA)<sup>[29]</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>[30]</sup>, and depression risk with the Geriatric Depression Scale (impaired GDS  $\leq 1/4$ )<sup>[31]</sup>. Physical performance and mobility were assessed using gait speed (impaired  $\leq 0.8$  m/s)<sup>[32]</sup>, the Timed Up and Go Test (TUG) (impaired TUG  $> 20$  s)<sup>[33]</sup>, the One Leg Balance test (OLBT) (impaired OLBT  $< 5$  s)<sup>[34]</sup>, and the history of falls in the three months prior to the CGA. Handgrip strength was measured three times for each hand using the Jamar Hydraulic Dynamometer according to the American Society of Hand Therapists recommendations<sup>[35]</sup>, and the cutoff values were those of the European Guidelines on Sarcopenia (EGSOP2) (impaired  $< 27$  kg for men;  $< 16$  kg for women)<sup>[36]</sup>. Participants 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>[37]</sup> and polypharmacy ( $\geq 5$  drugs per day) was assessed.

The main medical information was obtained from the medical records: type of thoracic and lung cancer, cancer stage, detailed treatment before and after a CGA, and biological data (plasma and serum chemistry). Albumin levels  $< 35$  g/l were considered abnormal,

lymphopenia was defined as a lymphocytes number  $< 1.26 \text{ G/l}$ , vitamin B12 levels  $< 145$  or  $> 569 \text{ pmol/l}$  were considered abnormal, C-reactive protein (CRP) levels  $> 5 \text{ mg/l}$  were considered abnormal, and patients with a BCI index  $> 40\,000$ , which is the product of multiplying the CRP level with the vitamin B12 level ( $\text{B12} \times \text{CRP}$ )<sup>[38]</sup>, were considered impaired.

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

Data on cancer progression and treatment were obtained from the medical records. Information about unplanned hospitalizations and the causes, as well as vital status (and causes of death) were 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 describe the main demographic, oncologic, 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 minimum and maximum values for continuous data. A comparative analysis was performed between patients under 79 years ( $<80$  years group) and patients 80 years and older ( $\geq 80$  years group); the Pearson Chi-squared test or Fischer exact test were used to analyze discrete data whereas Student's t-test was used to analyze continuous variables. To determine the differences between both populations, we performed a logistic regression analysis. Variables with a p-value  $\leq 0.1$  in the comparative analysis were added to the model, which was also adjusted by gender and tumor stage. Survival analysis was performed using a cumulative incidence curve with the Kaplan – Meier method. Survival was presented according to age groups ( $\geq 80$  years vs  $<80$  years) and cancer stages (stage IV vs other stages). A p-value  $\leq 0.05$  was considered statistically significant.

A comparative analysis was performed between octogenarians who underwent unplanned hospitalizations within three months after treatment initiation and those who did not; the same comparative analysis was performed among patients under 80 years old. The Chi-squared test was used to analyze discrete data. Survival analysis in the two age groups of patients ( $\geq 80$  years and  $<80$  years) was performed using a Cox regression analysis. For the patients in the  $\geq 80$  years group, we chose not to add albumin and the G8 into the model as they are

strongly correlated to malnutrition. All other variables with a  $p$ -value  $\leq 0.1$  in the univariate analysis were added to a stepwise model, which was adjusted on gender, and tumor stage. The same procedure was used for the survival model of the patients in the  $<80$  years group. All the statistical analyses were performed using SPSS software (version 17.0).

## Results

A total of 228 participants were recruited. The median age was  $78.0 \pm 5$  years (range 67 to 95 years) and 94 patients were 80 years or older. In this  $\geq 80$  years group, the majority of the patients were men (78.7%), adenocarcinoma was the most common histological type (42.6%), stage IV was diagnosed in 34 patients (36.2%) and the most common treatment was chemotherapy (43.6%). In the  $\geq 80$  years group, 32.3% of participants presented with an ECOG-PS score  $\geq 2$  and 94.6% had a G8 screening score  $\leq 14/17$ . In our work, 21.3% of  $\geq 80$  years patients had their initial treatment proposal modified after the CGA; the geriatrician suggested less intensive treatment in almost all these patients.

In the  $<80$  years group, 70.9% of the patients were men, adenocarcinoma was the most common histological type (43.3%), stage IV was diagnosed in 52.2% of patients, the most common treatment was chemotherapy (70.9%), 26.3% patients presented with an ECOG-PS score  $\geq 2$  and 90.2% had a G8 screening score  $\leq 14/17$ . Finally, only 11.5 % of the  $<80$  years patients had their initial treatment modified after the CGA.

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

### *Comparison of the patients according to their age group*

#### *Univariate and logistic regression analysis*

Comparative univariate analysis (Table 1) showed that the  $\geq 80$  years group presented with less metastatic stage cancer ( $p=0.02$ ), were more often treated by targeted therapy ( $p=0.009$ ) or exclusive supportive care treatment ( $p=0.002$ ), and less often by chemotherapy treatment ( $p<0.0001$ ) compared to patients younger than 80. The initial treatment proposal was more frequently modified in the  $\geq 80$  years group ( $p=0.04$ ); the geriatrician suggested less intensive treatment in almost all patients of the  $\geq 80$  years group ( $n=18/20$  patients, 90 %). Concerning the CGA,  $\geq 80$  years patients were more likely to present with impairment in ADL ( $p=0.03$ ), and/or in muscle strength ( $p=0.005$ ) and to display sensory disorders (vision disorders  $p=0.005$ ; hearing disorders  $p=0.03$ ).

The logistic regression analysis comparing  $\geq 80$  years group and  $< 80$  years group is presented in Table 2. The logistic regression comparing  $\geq 80$  years and  $< 80$  years patients highlighted that  $< 80$  years group was more likely to present with stage IV (Odd Ratio (OR) 0.4; 95% CI; [0.2-0.8];  $p = 0.005$ ) and undergo chemotherapy treatment (OR 0.4; 95% CI [0.2-0.9];  $p = 0.01$ ), compared to patients older than 80 who were more likely to be treated by targeted therapy (OR 9.8; 95% CI [1.0-92.9];  $p = 0.04$ ) and more often presented with handgrip strength impairment (OR 2.3; 95% CI [1.3-4.3];  $p = 0.008$ ).

#### *Overall survival*

Median OS was  $14.8 \pm 2.6$  months (95 % CI [9.7-19.8]) in  $\geq 80$  years patients and  $15.3 \pm 2.0$  (95 % CI [11.5-19.2]) in  $< 80$  years patients. Survival did not vary according to age groups (log rank=0.95) but was significantly reduced in patients with a stage IV disease (log rank  $< 0.0001$ ) (Figure 1).

#### *Factors associated with unplanned hospitalizations and associated with worse OS in the $\geq 80$ years group*

##### *Overall survival in the $\geq 80$ years group*

In univariate analysis, the following factors were associated with worse OS in  $\geq 80$  years group: male gender (HR 3.3; 95% CI [1.3-8.3]), stage IV disease (HR 2.1; 95% CI [1.1-3.7]), malnutrition (HR 2.0; 95% CI [1.1-3.6]), impairment in handgrip strength (HR 2.2; 95% CI [1.2-4.3]), abnormal BCI (HR 2.9; 95% CI [1.1-7.5]), surgery (HR 0.1; 95% CI [0.0-0.5]), chemotherapy (HR 1.9; 95% CI [1.0-3.4]), exclusive supportive care (HR 2.2; 95% CI [1.0-4.5]) and mesothelioma (HR 3.1; 95% CI [1.3-4.8]) (Table 3). In the Cox multivariate model, two characteristics remained significantly associated with the outcome: male gender and impaired handgrip strength (Table 4a).

##### *Unplanned hospitalization in the $\geq 80$ years group*

Factors associated with unplanned hospitalizations in univariate analysis are presented in Table 5. The only factors associated with unplanned hospitalizations within 3 months of treatment initiation in  $\geq 80$  years group were ADL impairment (OR 2.7; 95% CI [1.1-6.5]) and GDS impairment (OR 2.9; 95% CI [1.2-7.1]).

#### *Factors associated with unplanned hospitalizations and associated with worse OS in the $< 80$ years group*

##### *Overall survival in the $< 80$ years group*



In univariate analysis, the following factors were associated with worse OS in <80 years group: male gender (HR 1.8; 95% CI [1.0-3.2]), living alone (HR 1.8; 95% CI [1.0-3.0]), IADL impairment (HR 2.3; 95% CI [1.4-3.9]), albumin < 35g/l (HR 2.7; 95% CI [1.6-4.8]), abnormal TUG (HR 2.9; 95% CI [1.7-4.7]), abnormal OLBT (HR 1.9; 95% CI [1.1-3.2]), lymphopenia (HR 2.2; 95% CI [1.2-4.2]), epidermoid type (HR 2.0; 95% CI [1.2-3.6]) small cells (HR 4.4; 95% CI [1.9-10.1]), stage IV cancer (HR 2.3; 95% CI [1.4-3.9]), exclusive supportive care (HR 5.8; 95% CI [1.8-19.0]) and ECOG PS score  $\geq 2$  (HR 2.6; 95% CI [1.6-4.4]) (Table 3). In the Cox multivariate model, five characteristics remained significantly associated with the outcome: male gender, impaired IADL, stage IV cancer, lymphopenia and ECOG PS score  $\geq 2$  (Table 4b).

#### *Unplanned hospitalization in the <80 years group*

Factors associated with unplanned hospitalizations in univariate analysis are presented in Table 5. The factors associated with unplanned hospitalizations within 3 months of treatment initiation in <80 years group were living alone (OR 2.8; 95% CI [1.2-6.6]), malnutrition (OR 2.5; 95% CI [0.2-5.2]), and ECOG PS score  $\geq 2$  (OR 3.0; 95% CI [1.4-6.7]).

## **Discussion**

This study shows no difference in OS between patients with lung or thoracic cancers whether they belong to  $\geq 80$  years or <80 years age group. This lack of association between age and mortality has already been reported in a few previous studies<sup>[16,18]</sup>. In Quoix *et al*'s study<sup>[7]</sup>, comparison of doublet chemotherapy and monotherapy in older patients with non-small cell lung cancer, showed similar outcomes between  $\geq 80$  years and <80 years patients. This suggests that despite the absence of specific recommendations for this older old population, selected octogenarians can be treated as younger when taking health and geriatric status into account.

The  $\geq 80$  years patients are usually considered *de facto* as frail in oncology, even without objective frailty criteria. That is the reason why we chose to split our sample at the age of 80 years, as it corresponds to clinical reality. This may explain why, in our study, <80 years patients presented more often with metastatic disease at diagnosis compared to  $\geq 80$  years patients: many  $\geq 80$  years patients with metastatic thoracic cancer may have not been considered suitable for oncological treatment and therefore were not referred to oncologists or to a geriatrician for a CGA. This difference in the observed rates of cancer stage in the two age groups may partly explain the differences in treatment options; the <80 years patients

were mostly managed with chemotherapy, while the  $\geq 80$  years participants were more often treated with targeted therapy and exclusive supportive care. Even if older old patients are still underrepresented in clinical trials, a limited number of studies have shown that octogenarians treated with targeted therapies had clinical outcomes and a toxicity profile comparable to younger patients<sup>[39]</sup>.

In current guidelines<sup>[11]</sup>, there are no specific recommendations for octogenarians, and in the literature, older patients are often treated less aggressively than younger patients, with treatments of lower toxicity risk and/or better survival potential<sup>[40,41]</sup>. However, Kale *et al* showed recently that octogenarians were as likely as patients aged 70-79 years to tolerate chemotherapy and radiotherapy for advanced non-small cell lung cancers<sup>[42]</sup>. Moreover, in thoracic surgery which is the gold standard of the treatment of early-stage disease, new studies showed older adults had good tolerance, in particular in infra-lobar thoracic surgery, even among octogenarians adults<sup>[43,44]</sup>. In our survey, the initial proposal of treatment was more often modified in octogenarians than in younger patients after taking into account the results of the geriatric assessment. However, these adaptations of treatment only occurred in one in five octogenarians. This highlights the importance of CGA before treatment initiation and confirms that age itself should not be a limitation to access to standard treatment.

In our study, handgrip strength was more often impaired among the octogenarians than in the younger group. Measurement of handgrip strength is usually used to assess sarcopenia<sup>[36]</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 as a risk factor of early death, falls, and mobility impairment in older populations<sup>[36]</sup>. Diagnosis is based on a combination of measurements of muscle mass and muscle strength including one-leg balance test, gait speed, and handgrip strength<sup>[36]</sup>. Measurements of physical performance are used to appreciate the severity of the disease. Patients with thoracic cancer are more likely to be malnourished<sup>[45]</sup> and to develop sarcopenia, in particular patients with small cell lung cancer<sup>[46]</sup> and/or older old patients. Sarcopenia is associated with complications in surgery and chemotherapy, and is associated with worse OS during chemotherapy<sup>[46]</sup>.

In our survey, we only had information on handgrip strength impairment, which is not sufficient to suspect sarcopenia but has been shown to be a predictor of mortality in older adults<sup>[47]</sup>. We did not find any relation between mortality risk and handgrip strength in the  $<80$  years group. But, interestingly, a decrease in handgrip strength was, with male gender, the only factors significantly associated with mortality risk in octogenarians. Among older old

patients, geriatric deficits have more negative impacts on survival than the severity of cancer and type of treatments, contrary to what we found in <80 years group, and more generally to what has been observed among patients 70 years and older<sup>[48]</sup>. This result highlights the importance of measuring muscle strength and assessing physical performance on a systematic basis, in older old patients with lung or thoracic cancer.

Concerning geriatric deficits, we only found a significant association between IADL impairment and mortality risk in <80 years group, which may be related to the high frequency of cognitive disorders (26.7%) in this population. Cognitive disorders are known to negatively impact functional status, causing loss of instrumental autonomy<sup>[49]</sup>. Finally, ECOG-PS which is also associated with mortality risk in the <80 years group is a performance scale not specific for older old patients<sup>[50]</sup>.

In the  $\geq 80$  years group, dysfunction in ADLs: the other part of functional status impairments, was a statistically significant risk factor for unplanned hospitalization within 3 months. Loss of functional capacity can increase the risk of treatment-related complications and the risk of poor outcomes in older patients with cancer<sup>[50]</sup>. Functional deficits assessed as part of the CGA include mobility disorders, cognitive impairment, depression, and sensorial disorders. ADL score has been associated with OS in other studies with older patients with lung cancer<sup>[7]</sup> but not with unplanned hospitalizations. This result is innovative in this octogenarian population especially since depression ( $GDS \geq 1$ ) is also a risk factor of unplanned hospitalizations. In the literature, depression has only been associated with OS in mixed cancer sites<sup>[51]</sup>.

This study has some limitations. It was a monocentric survey that included a population of older and older old patients suffering from thoracic and lung cancer of various histological types, different clinical stages, and all types of treatment. Logistic regression was performed to compare patients according to their age group, but the small sample of octogenarians did not allow us to perform multivariate models for unplanned hospitalizations in the octogenarian population.

Conversely, our study has strengths. First, this work includes a rather large sample of older old outpatients with thoracic cancer ( $n=94$ ) and a large set of data for each of them, which is rare in the oncologic literature. Moreover, our total sample size of older outpatients with thoracic cancer was also large ( $n=228$  patients 70 years or older), and, as G8 screening is conducted routinely by the thoracic oncologists at our center, we were able to perform a CGA for all the patients with an impaired G8 in accordance with the international

recommendations<sup>[13]</sup>. 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 patients to benefit from standard treatments. This is the case in our university hospital where a multidisciplinary team including an oncologist, a geriatrician, a physical therapist, and a pharmacist has been set up since September 2013. More studies including large samples of older old patients are needed to determine the geriatric profile of older patients able to benefit from standard treatment with limited side effects. Moreover, improvements in patient follow-up are still needed. The role of the geriatrician should not be limited to the detection of geriatric impairments and the implementation of strategies to improve health status (i.e. physical activities with a therapist and dietary advice in case of muscle strength impairment). It should also include a follow-up with regular reassessments of geriatric frailties during oncologic treatment to allow oncologists to adapt treatment on a more personalized basis.

## **Conclusion**

Management of thoracic and lung cancer in octogenarian patients is challenging due to the heterogeneity of this population, the absence of specific recommendations, the large number of histological forms and treatments, and the under-representation of octogenarians in clinical trials. In our study, octogenarians were more often treated with targeted therapy and less often with chemotherapy. Consequently, it is of major importance to detect frailties, through geriatric screening and/or a CGA and allow personalized treatment adapted to patient specific profiles. In geriatric domains, muscle strength (handgrip strength), functional status (ADL) and mood evaluation (GDS) may be used in a clinical setting to help improve the management of octogenarians with thoracic and lung cancer by offering them more personalized care.

**Conflict of interest:** None of the authors have conflict of interest to declare.

**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, F. Correard, F. Barlesi, P. Thomas, P. Villani, L. Greillier.

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**Table 1:** Demographic, geriatric and oncologic characteristics comparative analysis according age in  $\geq 80$  and  $< 80$  years groups

Characteristics	Total population (n=228)		<80 years group (n=134)		$\geq 80$ years group (n=94)		P value
	n or Mean $\pm$ ET	(%) or [min-max]	n or Mean $\pm$ ET	(%) or [min-max]	n or Mean $\pm$ ET	(%) or [min-max]	
<b>Gender</b> Men	169	(74.1)	95	(70.9)	74	(78.7)	0.19
<b>Age</b>	78.7 $\pm$ 5.0	[67-95]	75.3 $\pm$ 2.8	[67-79]	83.7 $\pm$ 3.0	[80-95]	NA
<b>Caregiver</b> <sup>a</sup>	156	(68.7)	86	(64.7)	70	(74.5)	0.12
<b>Housing</b> care facility (vs. home) <sup>o</sup>	19	(8.3)	11	(8.2)	8	(8.5)	0.94
<b>Living alone</b>	39	(17.1)	28	(20.9)	11	(28.2)	0.07
<b>Fall History</b> (in the past 3 months)	42	(18.4)	24	(17.9)	18	(19.1)	0.81
<b>Autonomy</b> (ADL $<6$ ) <sup>a</sup>	73	(32.2)	35	(26.3)	38	(40.4)	<b>0.03</b>
<b>Instrumental autonomy</b> (IALD $<4$ )	124	(54.4)	71	(53.0)	53	(56.4)	0.61
<b>Cognitive disorders</b> (MMSE $<24$ ) <sup>b</sup>	57	(25.6)	35	(26.7)	22	(23.9)	0.64
<b>Suspicion of depression</b> (GDS $\geq 1$ ) <sup>c</sup>	107	(47.3)	69	(51.9)	38	(40.9)	0.10
<b>Impaired handgrip strength</b> (men $<27$ kg, women $<16$ kg) <sup>d</sup>	102	(45.9)	49	(38.0)	53	(57.0)	<b>0.005</b>
<b>Nutritional status</b> BMI	24.0 $\pm$ 4.4	[15.5-38.0]	23.7 $\pm$ 4.3	[15.9-38.0]	24.3 $\pm$ 4.5	[15.5-38.0]	0.35
Albumin	38.3 $\pm$ 5.2	[22-49]	38.4 $\pm$ 5.3	[23-49]	38.0 $\pm$ 4.9	[22-47]	0.61
Malnutrition	102	(44.7)	64	(47.8)	38	(40.4)	0.27
<b>Mobility</b> Timed up and go Test ( $>20$ s)	88	(38.6)	49	(36.6)	39	(41.5)	0.45
One-leg balance test ( $< 5$ s)	139	(61.0)	78	(58.2)	61	(64.9)	0.31
Gait speed ( $\leq 0.8$ m/s)	111	(48.7)	58	(43.3)	53	(56.4)	0.05
<b>Vision disorders</b>	101	(44.3)	49	(36.6)	52	(55.3)	<b>0.005</b>
<b>Hearing disorders</b>	85	(37.3)	42	(31.3)	43	(45.7)	<b>0.03</b>
<b>Number of comorbidities</b>	4.1 $\pm$ 2.3	[0-13]	4.0 $\pm$ 2.3	[0-11]	4.2 $\pm$ 2.4	[0-13]	0.55
<b>Severe comorbidities present</b>	0.7 $\pm$ 0.8	[0-4]	0.7 $\pm$ 0.8	[0-4]	0.7 $\pm$ 0.8	[0-4]	0.98
<b>Polypharmacy</b> ( $\geq 5$ drugs)	161	(70.6)	99	(61.5)	62	(66.0)	0.19
<b>Type of cancer</b> Adenocarcinoma	98	(43.0)	58	(43.3)	40	(42.6)	0.91
Epidermoid	89	(39.0)	54	(40.3)	35	(37.2)	0.64
Mesothelioma <sup>o</sup>	18	(7.9)	9	(6.7)	9	(9.6)	0.46
Small cells <sup>o</sup>	15	(6.6)	9	(6.7)	6	(6.4)	0.57
Other <sup>o</sup>	8	(3.5)	4	(1.8)	4	(4.3)	0.72
<b>Stage IV</b> (vs stage $<IV$ )	104	(45.6)	70	(52.2)	34	(36.2)	<b>0.02</b>
<b>Treatments</b> Surgery	51	(22.4)	30	(22.4)	21	(22.3)	0.99
Chemotherapy	136	(59.6)	95	(70.9)	41	(43.6)	<b>&lt;0.0001</b>
Radiotherapy	69	(30.3)	41	(30.6)	28	(29.8)	0.89
Targeted therapy <sup>o</sup>	8	(3.5)	1	(0.7)	7	(7.4)	<b>0.009</b>
Immunotherapy <sup>o</sup>	10	(4.4)	8	(6.0)	2	(2.1)	0.20
Exclusive supportive care <sup>o</sup>	20	(8.8)	5	(3.7)	15	(6.6)	<b>0.002</b>
<b>Final treatment modified from initial proposal</b>	35	(15.6)	15	(11.5)	20	(21.5)	<b>0.04</b>
<b>Unplanned hospitalization</b>	82	(36.0)	50	(37.3)	32	(34.0)	0.61

<b>G8 Score ≤14 (vs. &gt;14)<sup>c</sup></b>	208	(92.0)	102	(90.2)	88	(94.6)	0.23
<b>ECOG 2-4 (vs. 0-1)<sup>c</sup></b>	65	(28.8)	35	(26.3)	30	(32.3)	0.33
<b>Treatment line 1 (vs. 2<sup>d</sup> line and over)</b>	196	(86.0)	118	(88.1)	78	(83.0)	0.28

<sup>°</sup>Fischer exact test for small population

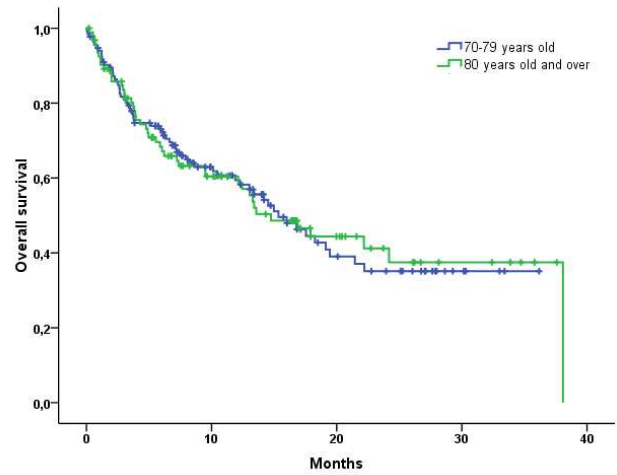
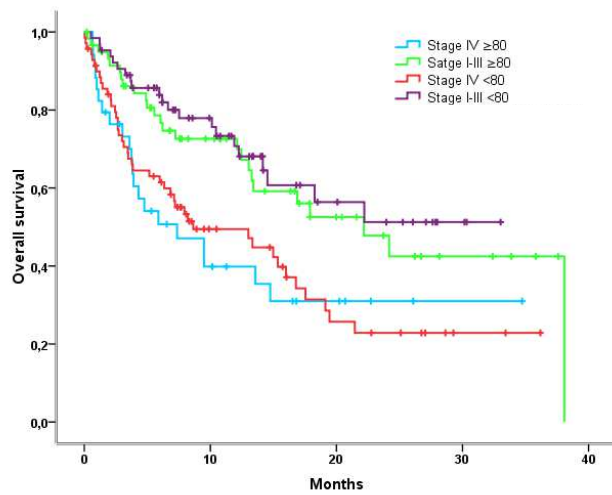
<sup>a</sup> Missing data n= 1; <sup>b</sup> Missing Data n=5; <sup>c</sup> Missing Data n=2; <sup>d</sup> Missing data n=6

*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*

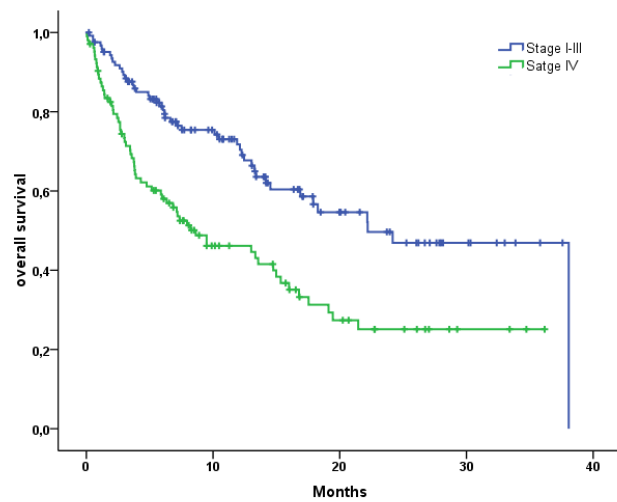
**Table 2:** Logistic regression multivariable analysis of geriatric and oncological factors for <80 years patients compared to  $\geq 80$  years patients, adjusted on gender and presence or not of metastasis (included in the stepwise descending elimination analysis: Social isolation (n=228); chemotherapy (n=228), targeted therapy (n=228) or palliative care treatments (n=228), ADL score (n=227), handgrip strength and gait speed (n=224), final treatment modified from initial proposal (n=222) due to cumulative missing data, the analysis was done on 217 patients)

Characteristics	N=217	aOR	IC 95%	P value
Men	162	1.8	[0.9-3.8]	0.11
Stage IV	96	0.4	[0.2-0.8]	<b>0.005</b>
Chemotherapy	132	0.4	[0.2-0.9]	<b>0.02</b>
Targeted therapy	7	9.8	[1.0-92.9]	<b>0.04</b>
Exclusive supportive care	14	4.7	[0.9-24.4]	0.06
Abnormal handgrip strength	120	2.3	[1.3-4.3]	<b>0.008</b>

aOR : adjusted odds ratio



**Figure 1:** Overall survival according to age and stage group, panel A shows Kaplan-Meier analysis according to stage and age group, panel B shows Kaplan-Meier analysis comparing  $\geq 80$  versus  $< 80$  group, panel, C shows Kaplan-Meier analysis for patients with stage IV tumor versus patients with stage I to III tumors.



**Table 3:** Factors negatively associated with OS in old patients with thoracic cancers, according to age groups (univariate cox analysis)

Characteristics	<80 years group (n=134)				≥80 years group (n=94)			
	n	HR	IC 95%	P value	n	HR	IC 95%	P value
<b>Gender Men</b>	95	1.8	[1.0-3.2]	<b>0.04</b>	74	3.3	[1.3-8.3]	<b>0.01</b>
<b>Caregiver</b>	86	0.9	[0.5-1.5]	0.75	70	0.8	[0.4-1.5]	0.49
<b>Living alone</b>	28	1.8	[1.0-3.0]	<b>0.04</b>	11	1.0	[0.3-2.7]	0.93
<b>Autonomy (ADL&lt;6)</b>	35	1.1	[0.7-2.0]	0.66	38	1.3	[0.7-2.3]	0.46
<b>Instrumental Activities of Daily Living (IADL &lt;4)</b>	71	2.3	[1.4-3.9]	<b>0.002</b>	53	1.5	[0.8-2.7]	0.19
<b>Cognitive disorders (MMSE&lt;24)</b>	35	1.6	[1.0-2.8]	0.07	22	1.3	[0.7-2.7]	0.40
<b>Suspicion of depression (GDS ≥1)</b>	89	1.1	[0.7-1.9]	0.65	38	1.1	[0.6-2.0]	0.71
<b>Handgrip Strength (&lt;27kg for men, &lt;16kg for women)</b>	49	1.4	[1.0-2.7]	0.06	53	2.2	[1.2-4.3]	<b>0.02</b>
<b>Nutritional status</b>								
BMI (<21)	99	1.0	[0.6-1.8]	0.91	23	1.1	[0.5-2.2]	0.85
Albumin (<35g/L)	87	2.7	[1.6-4.8]	<b>&lt;0.0001</b>	18	1.8	[0.9-3.5]	0.09
Malnutrition	64	1.6	[1.0-2.7]	0.05	38	2.0	[1.1-3.6]	<b>0.02</b>
<b>Mobility</b>								
Timed up and go Test (>20s)	49	2.9	[1.7-4.7]	<b>&lt;0.0001</b>	39	1.4	[0.8-2.5]	0.29
One-leg balance test (< 5s)	78	1.9	[1.1-3.2]	<b>0.02</b>	61	1.7	[0.9-3.3]	0.11
Gait speed (<0.8m/s)	58	1.5	[0.9-2.5]	0.10	53	1.1	[0.6-2.0]	0.79
<b>Number of comorbidities</b>	134	0.9	[0.8-1.0]	0.05	92	1.1	[1.0-1.2]	0.11
<b>Severe comorbidities present</b>	68	1.0	[0.6-1.6]	0.90	51	0.8	[0.5-1.5]	0.52
<b>Polypharmacy (≥5 drugs)</b>	99	0.8	[0.4-1.3]	0.33	62	1.5	[0.8-2.9]	0.23
<b>Abnormal BCI</b>	10	2.1	[0.9-5.0]	0.09	5	2.9	[1.1-7.5]	<b>0.03</b>
<b>Lymphopenia</b>	24	2.2	[1.2-4.2]	<b>0.01</b>	23	1.3	[0.7-2.7]	0.43
<b>Type of cancer</b>								
Adenocarcinoma (ref)	58	1		-	40	1		
Epidermoid	54	2.0	[1.2-3.6]	<b>0.01</b>	35	0.9	[0.4-1.8]	0.73
Mesothelioma	9	1.1	[0.3-3.6]	0.92	9	3.1	[1.3-4.8]	<b>0.01</b>
Small cells	9	4.4	[1.9-10.1]	<b>0.001</b>	6	1.6	[0.5-4.8]	0.39
Other	4	2.7	[0.6-11.6]	0.19	4	0.4	[0.0-2.7]	0.32
<b>Stage IV (vs stage &lt;IV)</b>	70	2.3	[1.4-3.9]	<b>0.002</b>	34	2.1	[1.1-3.7]	<b>0.02</b>
<b>Treatments</b>								
Surgery	30	0.4	[0.2-0.9]	<b>0.02</b>	21	0.1	[0.0-0.5]	<b>0.001</b>
Chemotherapy	95	1.1	[0.6-2.0]	0.64	41	1.9	[1.0-3.4]	<b>0.04</b>
Radiotherapy	41	0.9	[0.5-1.5]	0.61	28	0.5	[0.3-1.1]	0.10
Targeted therapy	1	3.4	[0.4-24.8]	0.23	7	0.8	[0.2-2.5]	0.67
Immunotherapy	8	1.1	[0.4-3.2]	0.80	2	1.0	[0.1-7.3]	0.99
Exclusive supportive care	4	5.8	[1.8-19.0]	<b>0.003</b>	12	2.2	[1.0-4.5]	<b>0.04</b>
Simple surveillance	1	0.05	[0.0-289.6]	0.49	3	1.9	[0.3-13.7]	0.54
<b>G8 Score ≤14 (vs. &gt;14)</b>	120	2.0	[0.7-5.6]	0.17	88	23.4	[0.2-2298.0]	0.18
<b>ECOG 2-4 (vs. 0-1)</b>	35	2.6	[1.6-4.4]	<b>&lt;0.0001</b>	30	2.1	[1.2-3.9]	<b>0.02</b>
<b>Treatment line 2 and over (vs. 1<sup>st</sup> line)</b>	16	0.7	[0.3-1.6]	0.47	16	1.3	[0.6-2.8]	0.43
<b>Unplanned hospitalization</b>	50	4.6	[2.8-7.7]	<b>&lt;0.0001</b>	32	2.9	[1.6-5.3]	<b>&lt;0.0001</b>

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; HR: Hazard Ratio

**Table 4a:** Factors negatively associated with OS among patients with thoracic cancers aged 80 years and older, adjusted on gender and presence or not of metastasis (multivariate cox model)

Characteristics	N=80	aHR	IC 95%	P value
Men	65	3.0	[1.4-11.4]	<b>0.012</b>
Stage IV	28	1.8	[0.9-3.6]	<b>0.078</b>
Abnormal handgrip strength	33	3.7	[1.7-7.8]	<b>0.001</b>

**Table 4b :** Factors negatively associated with OS among patients with thoracic cancers aged less than 80 years, adjusted on gender and presence or not of metastasis (multivariate cox model)

Characteristics	N=124	aHR	IC 95%	P value
Men	88	4.0	[2.1-7.8]	<b>&lt;0.001</b>
Stage IV	66	2.8	[1.6-5.1]	<b>&lt;0.001</b>
Impaired IADL (IADL<4)	64	2.2	[1.2-4.2]	<b>0.012</b>
Lymphopenia	24	3.6	[1.8-7.0]	<b>&lt;0.001</b>
ECOG-PS 2-4	33	2.3	[1.3-4.2]	<b>0.007</b>

*IADL: instrumental activities of daily living; ECOG-PS: eastern cooperative oncology group- performance status; aHR: adjusted Hazard Ratio*

**Table 5:** Factors associated with unplanned hospitalizations within 3 months after treatment initiation, in patients with thoracic cancer, according to age group (univariate analysis)

Characteristics	Patient < 80 years group (n=134)			Patients ≥80 years group (n=94)		
	Unplanned Hospitalization			Unplanned Hospitalization		
	OR	IC 95%	P value	OR	IC 95%	P value
<b>Gender Men</b>	2.1	[0.9-4.8]	0.07	2.4	[0.7-8.0]	0.19
<b>Caregiver</b>	0.6	[0.3-1.3]	0.26	0.8	[0.3-2.1]	0.80
<b>Living alone</b>	2.8	[1.2-6.6]	<b>0.03</b>	0.7	[0.2-2.8]	0.74
<b>Autonomy (ADL&lt;6)</b>	1.2	[0.5-2.7]	0.69	2.7	[1.1-6.5]	<b>0.03</b>
<b>Instrumental Activities of Daily Living (IALD &lt;4)</b>	1.8	[0.9-3.7]	0.11	2.2	[0.9-5.4]	0.12
<b>Cognitive disorders (MMSE&lt;24)</b>	0.8	[0.3-1.7]	0.68	2.1	[0.8-5.6]	0.19
<b>Suspicion of depression (GDS ≥1)</b>	1.1	[0.5-2.2]	0.86	2.9	[1.2-7.1]	<b>0.03</b>
<b>Handgrip Strength</b> (<27kg for men, <16kg for women)	0.6	[0.3-1.2]	0.13	0.5	[0.2-1.2]	0.12
<b>Nutritional status</b>						
BMI (<21)	1.2	[0.5-3.4]	0.80	1.2	[0.5-3.4]	0.80
Albumin (<35g/L)	0.4	[0.2-1.3]	0.16	0.4	[0.2-1.3]	0.16
Malnutrition	2.5	[0.2-5.2]	<b>0.01</b>	0.0	[0.4-2.4]	0.58
<b>Mobility</b>						
Timed up and go Test (>20s)	0.5	[0.2-0.9]	0.05	0.6	[0.2-1.4]	0.27
One-leg balance test (< 5s)	0.6	[0.3-1.1]	0.21	1.0	[0.4-2.3]	0.55
Gait speed (<0.8m/s)	0.4	[0.3-1.3]	0.28	0.7	[0.3-1.6]	0.51
<b>Polypharmacy (≥5 drugs)</b>	0.9	[0.4-1.9]	0.70	1.5	[0.6-3.8]	0.49
<b>Abnormal BCI</b>	0.4	[0.1-1.4]	0.17	0.8	[0.1-5.2]	0.59
<b>Lymphopenia</b>	2.1	[0.9-5.3]	0.11	0.8	[0.3-2.2]	0.80
<b>Type of cancer</b>						
Adenocarcinoma	0.8	[0.4-1.6]	0.59	0.7	[0.3-1.7]	0.52
Epidermoid	1.3	[0.66-2.6]	0.59	1.2	[0.5-3.0]	0.66
Mesothelioma	0.5	[0.1-2.3]	0.48	1.6	[0.4-6.5]	0.48
Small cells	1.4	[0.4-5.4]	0.73	2.0	[0.4-10.7]	0.41
Other	1.7	[0.2-12.5]	0.48	0.6	[0.6-0.8]	0.29
<b>Stage IV (vs stage &lt;IV)</b>	1.9	[0.9-3.8]	0.08	1.6	[0.7-3.9]	0.36
<b>Treatments</b>						
Surgery	0.4	[0.2-1.1]	0.09	0.4	[0.1-1.2]	0.12
Chemotherapy	2.1	[0.9-4.8]	0.07	1.5	[0.6-3.5]	0.39
Radiotherapy	0.7	[0.3-1.5]	0.37	0.9	[0.3-2.3]	0.49
Targeted therapy	0.6	[0.5-0.7]	0.44	0.3	[0.04-2.6]	0.42
Immunotherapy	0.2	[0.03-1.9]	0.14	2.0	[0.1-32.5]	0.57
Exclusive supportive care	5.3	[0.5-52.4]	0.29	3.2	[0.9-11.0]	0.09
Simple surveillance	0.6	[0.5-0.7]	0.63	1.0	[0.1-11.1]	0.73
<b>G8 Score ≤14 (vs. &gt;14)</b>	1.0	[0.3-3.1]	0.95	1.5	[1.3-1.8]	0.17
<b>ECOG 2-4 (vs. 0-1)</b>	3.0	[1.4-6.7]	<b>0.005</b>	1.5	[0.6-3.8]	0.36
<b>Treatment line 2 and over (vs. 1<sup>st</sup> line)</b>	1.2	[0.4-3.7]	0.52	1.2	[0.4-3.7]	0.52

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  
OR : adjusted odds ratio