Geriatric assessment may help decision-making in elderly patients with inoperable, locally advanced non-small-cell lung cancer

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Background: Although concurrent chemoradiotherapy (cCRT) increases survival in patients with inoperable, locally advanced non-small-cell lung cancer (NSCLC), there is no consensus on the treatment of elderly patients. The aim of this study was to determine the prognostic value of the comprehensive geriatric assessment (CGA) and its ability to predict toxicity in this setting.

Methods: We enrolled 85 consecutive elderly (≥75 years) participants, who underwent CGA and the Vulnerable Elders Survey (VES-13). Those classified as fit and medium-fit by CGA were deemed candidates for cCRT (platinum-based chemotherapy concurrent with thoracic radiation therapy), while unfit patients received best supportive care.

Results: Fit (37%) and medium-fit (48%) patients had significantly longer median overall survival (mOS) (23.9 and 16.9 months, respectively) than unfit patients (15%) (9.3 months, log-rank P = 0.01). In multivariate analysis, CGA groups and VES-13 were independent prognostic factors. Fit and medium-fit patients receiving cCRT (n = 54) had mOS of 21.1 months (95% confidence interval: 16.2, 26.0). In those patients, higher VES-13 (≥3) was associated with shorter mOS (16.33 vs 24.3 months, P = 0.027) and higher risk of G3-4 toxicity (65 vs 32%, P = 0.028).

Conclusions: Comprehensive geriatric assessment and VES-13 showed independent prognostic value. Comprehensive geriatric assessment may help to identify elderly patients fit enough to be treated with cCRT.

As a result of population ageing and increasing incidence of lung cancer in the elderly, oncologists commonly face the challenge of effectively managing older adults with lung cancer (Wingo et al, 2003). Non-small-cell lung cancer (NSCLC) accounts for more than 80% of all lung cancers, and 25–30% of NSCLC patients are diagnosed with locally advanced disease (Walters et al, 2013).

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Concurrent chemoradiotherapy (cCRT) is the standard treatment for good performance status patients with inoperable locally advanced NSCLC (Furuse et al., 1995; Auperin et al., 2010; O’Rourke et al., 2010; Ramnath et al., 2013; Bjerak et al., 2015; Eberhardt et al., 2015). Chemoradiotherapy is considered a reasonable standard of care for fit elderly patients (Pallis et al., 2014; Dawe et al., 2016). However, as a result of misperceptions about poorer survival and higher risk of toxicity, oncologists are often reluctant to treat older patients using conventional therapy at standard doses (Schild et al., 2007; Cardenal et al., 2015). In addition, it remains unclear whether cCRT is suitable for unselected elderly patients due to the limited data available from clinical trials (Werner-Wasik et al., 2000; Rocha Lima et al., 2002; Firat et al., 2006; Schild et al., 2007; Davidoff et al., 2011; Pang et al., 2016). Consequently, undertreatment and overtreatment bias in older adults with inoperable locally advanced NSCLC is a concern.

Ageing is characterised by great heterogeneity, so advanced age alone should not prevent people from accessing the most appropriate treatment (Hung and Mullins, 2013). In all patients, treating physicians have to balance the risk of death due to lung cancer against the potential survival benefit of treatment, but in the elderly they should pay particular attention to the risk of treatment-related adverse events and the patient’s life expectancy irrespective of cancer (Pallis et al., 2014; Antonio et al., 2017). Comprehensive geriatric assessment (CGA) is considered the gold standard for characterising elderly patients according to their frailty profile (Balducci and Beghe, 2000a; Solomon et al., 2003; Extermann et al., 2005; Handforth et al., 2014). Comprehensive geriatric assessment is a multidimensional tool based on several scales that estimates physiological reserves and helps predict poor treatment outcomes, including toxicity, morbidity, and mortality (Extermann and Hurria, 2007). Comprehensive geriatric assessment includes assessment with standardised tools, an intervention plan and follow-through. Because CGA is time consuming and requires expertise to interpret the results and implement the appropriate interventions, screening tools like the Vulnerable Elders Survey (VES-13) are used to preselect the fittest patients from the rest of the elderly population for whom a full CGA might be indicated (Decoster et al., 2015).

The main objective of this prospective pilot study is to examine the prognostic value of CGA and its ability to predict toxicity in elderly patients with inoperable, locally advanced NSCLC. A secondary objective was to explore the clinical value of the VES-13 in this clinical setting.

Materials and Methods

Study design and participants. This prospective study was conducted at the Institut Català d’Oncologia in L’Hospitalet de Llobregat, Barcelona. Since 2008 all newly diagnosed lung cancer patients aged 75 years or older who are deemed candidates for chemotherapy (with or without radiotherapy) have been systematically referred to the Geriatric Oncology Unit to undergo CGA. Eligible patients for this study were aged 75 years or older, had histological or cytological confirmation of locally advanced NSCLC based on clinical assessments (cardiopulmonary function, contrast thoracic computed tomography (CT) and positron-emitted tomography-CT (PET-CT) scan, and selective mediastinal staging with endobronchial ultrasonography and/or oesophageal ultrasoundography), and were considered candidates for nonsurgical cancer treatment by the Multidisciplinary Thoracic Oncology Tumour Board. We prospectively collected the following data: age, sex, smoking history, Eastern Cooperative Oncology Group (ECOG) performance status, histology, and clinical stage according to the 7th edition of TNM, regimen of chemotherapy and radiotherapy, treatment-related toxicity, CGA variables, and VES-13 scores.

All data related to patients, tumor characteristics, and CGA results were recorded anonymously by the study investigators at the Geriatric Oncology Unit. As the study was based on current clinical practice, all patients signed the standard informed consent form for receiving cCRT. The Institutional Review Board approved the study.

Geriatric assessment. A team including a geriatrician and a geriatric oncologist assessed all patients by means of a CGA that incorporated validated instruments to explore eight domains: functional status, nutritional status, cognitive status, psychological status, comorbidities, medication, social support, and geriatric syndromes (Supplementary Table S1). Functional status was measured using two instruments: (a) the Barthel Activities of Daily Living (ADL) (Mahoney and Barthel, 1965), which uses a 0–100 scale to assess 10 basic self-care abilities (e.g., transfer, bathing, toileting, dressing, feeding); and (b) the Lawton Index of Instrumental Activities of Daily Living (IADL) (Lawton and Brody, 1969), an instrument assessing individuals’ ability to independently interact with the external environment in eight complex daily activities: shopping, cooking, using the telephone, handling finances, housekeeping, laundry, self-managing medication, and using transportation; the summary score ranges from 0 (low function, dependent) to 8 (high function, independent). To assess nutritional status, participants were asked if they had unintentionally lost over 5% of their body weight in the previous 3 months. The team assessed cognitive status using the Short Portable Mental Status Questionnaire (Pfeiffer’s test), which assigns a score from 0 to 10 based on the number of incorrect answers (Pfeiffer, 1975); mood was examined using the four-item Mini-Geriatric Depression Scale (D’Ath et al., 1994); and comorbidity using the Cumulative Illness Rating Scale for Geriatrics, with relevant comorbid conditions defined as those scoring three or more (Linn et al., 1968). We collected data on current medication according to self-report and the participants’ medical charts, defining polypharmacy as taking five or more oral medications each day. We considered that participants had a good social environment if they had a primary caregiver, support at home, or a strong circle of friends and family capable of meeting the patient’s needs. We determined the presence of a geriatric syndrome by self-reported number of falls in the previous 6 months, cognitive impairment, delirium, and urinary and/or faecal incontinence. If Pfeiffer’s test indicated cognitive impairment, we referred the participant to a neuropsychologist for further assessment, classifying significant cognitive impairment as a geriatric syndrome rather than a comorbid condition to avoid overlap between comorbidity and geriatric syndrome domains. We considered only incontinence other than stress incontinence to be a geriatric syndrome.

Using the modification of the CGA proposed by Balducci and Beghe (2000b), we classified participants as ‘fit’, ‘medium-fit’, and ‘unfit’ (Supplementary Table S2). We defined ‘fit’ as being able to independently perform all ADLs and IADLs, having no more than one clinically significant comorbid condition, and not having any geriatric syndromes. Medium-fit participants could have up to two clinically significant comorbid conditions and up to three IADL impairments, but no ADL disabilities or geriatric syndromes. Unfit participants were those with any ADL disability, more than three IADL impairments, more than two clinically significant comorbidities, or any geriatric syndrome.

In addition to CGA, we incorporated the Vulnerable Elders Survey (VES-13), a vulnerability screening tool consisting of four groups of questions related to age, self-perceived health, difficulties to perform six specific activities, and difficulties to perform daily living tasks (Saliba et al., 2001). Vulnerability was defined as a VES-13 score of 3 or more on a 0–9 scale.

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Treatment and follow-up. Treatment plan was based on CGA classification, and patients considered fit or medium-fit based on CGA were deemed candidates for cCRT. Radiotherapy was administered concurrently from the first day of chemotherapy up to a total dose of 60–66 Gy in daily fractions of 2 Gy over 6 weeks using a 3D technique. A specific CT scan of the thorax was performed using intravenous contrast. A PET–CT scan was used to contour the gross tumour volume (GTV). Only lymph node areas with suspicious uptake, pathological CT findings, or pathological confirmation of malignancy were included in the GTV (selective nodal irradiation) following international recommendations (De Ruyscher et al, 2010; Ramnath et al, 2013). No prophylactic nodal irradiation was performed. Organs at risk, such as the lungs, trachea, spinal cord, and oesophagus were contoured as per international guidelines (Kong et al, 2011). The following dose constraints were applied: for the lungs, $V_{20}$ (volume of the healthy lung receiving $<20$ Gy) lower than 35%; for the oesophagus, mean dose of $<34$ Gy; and for the spinal cord, mean dose of $<45$ Gy. None of the patients received intensity-modulated radiation therapy. The mean GTV for patients treated with thoracic radiotherapy was $149.23 \text{ cm}^3$.

The treating physician used distinct platinum-based chemotherapy regimens (Supplementary Table S3), none of which included consolidation chemotherapy. Fit and medium-fit patients not undergoing cCRT for any reason were followed up. None of the participants classified as unfit received any active therapy and were assigned to best supportive care and followed up.

Statistical analysis. We expressed patient characteristics and geriatric variables as percentages for qualitative variables and as mean and standard deviation (s.d.) for quantitative variables. Toxicity was scored according to the National Cancer Institute-Common Toxicity Criteria for Adverse Events version 4.0 before each cycle. We recorded data on treatment adherence and cause of discontinuation for any reason. Overall survival (OS) was defined as the time from pathological diagnosis until the date of death due to any cause or the last date the patient was known to be alive. Survival curves were plotted using the Kaplan–Meier method, and differences were assessed using the log-rank test. We constructed univariate and multivariate Cox proportional hazards models and analysed data using SPSS Statistics for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Participant characteristics and geriatric assessment. From July 2008 to September 2016, 85 elderly patients with inoperable, locally advanced NSCLC were enrolled in the study. Mean follow-up was 24 months. Most patients (89%) were men and had a history of smoking (91%). Median age was 79.5 years (range 75–87), and a significant subset of participants (51%) was 80 years or older. The most common histological subtype was squamous cell carcinoma (55%), followed by adenocarcinoma (24%); a further 21% had an unspecified subtype (21%). Most patients ($n = 66, 78\%$) had good ECOG performance status ($<2$) at study entry.

Based on CGA, 31 (37%) participants were classified as fit, 41 (48%) as medium-fit, and 13 (15%) as unfit. A flowchart is presented in Figure 1. There were no statistically significant differences between these groups with regard to age, sex, smoking history, histology, or tumour stage (Table 1). Performance status was significantly correlated with CGA groups ($P < 0.001$), with poorer scores ($\geq 2$) more common in medium-fit (19.5%) and unfit patients (77%) compared with fit patients (3%). We also observed a significant correlation between CGA groups and VES-13 scale ($P < 0.001$). Interestingly, the VES-13 scale classified 23% of fit and 68% of medium-fit patients as vulnerable ($\geq 3$ score).

Univariate and multivariate analysis of OS. At the data cutoff point for this survival analysis, 65 out of 85 patients had died. At mean follow-up of 24 months, median OS was 17.7 months (95% confidence interval (CI): 14.9, 20.6). Regardless of the treatment received, the CGA categories were significantly associated with OS.

![Figure 1. Study flowchart. CGA=comprehensive geriatric assessment; NSCLC=non-small-cell lung cancer.](Image)
**Table 1. Clinicopathological characteristics and geriatric features according to the CGA risk groups**

| Characteristic                        | Fit, n = 31 | Medium-fit, n = 41 | Unfit, n = 13 | All, n = 85 | P-value |
|---------------------------------------|-------------|--------------------|---------------|-------------|---------|
| **Age (years)**                       |             |                    |               |             |         |
| Median                                | 79.7        | 79.0               | 80.5          | 79.5        | 0.290*  |
| ≥80, n (%)                            | 17 (55)     | 18 (45)            | 8 (61.5)      | 43 (51)     | 0.454*  |
| **Sex, n (%)**                        |             |                    |               |             |         |
| Men                                   | 26 (84)     | 39 (95)            | 11 (85)       | 76 (89)     | 0.253*  |
| Women                                 | 5 (16)      | 2 (5)              | 2 (15)        | 9 (11)      |         |
| **Smoking history, n (%)**            |             |                    |               |             |         |
| Current                               | 4 (13)      | 9 (22)             | 3 (23)        | 16 (19)     |         |
| Former                                | 22 (71)     | 30 (73)            | 9 (69)        | 61 (72)     |         |
| Never                                 | 5 (16)      | 2 (5)              | 1 (8)         | 8 (9)       | 0.499*  |
| **Histology, n (%)**                  |             |                    |               |             |         |
| Squamous cell                         | 11 (35.5)   | 26 (63.5)          | 10 (77)       | 47 (55)     |         |
| Adenocarcinoma                        | 11 (35.5)   | 7 (17)             | 2 (15)        | 20 (24)     |         |
| Unspecified                           | 9 (29)      | 8 (19.5)           | 1 (8)         | 18 (21)     |         |
| **Stage, n (%)**                      |             |                    |               |             |         |
| IIA                                   | 1 (3)       | 2 (5)              | 0 (0)         | 3 (4)       |         |
| IIB                                   | 3 (10)      | 4 (10)             | 1 (8)         | 8 (9)       |         |
| IIIA                                  | 20 (64)     | 23 (56)            | 6 (46)        | 48 (58)     |         |
| IIIB                                  | 7 (23)      | 12 (29)            | 6 (46)        | 25 (29)     | 0.806b  |
| **ECOG-PS, n (%)**                    |             |                    |               |             |         |
| 0–1                                   | 30 (97)     | 33 (80.5)          | 3 (23)        | 66 (78)     | <0.001b |
| ≥2                                    | 1 (3)       | 8 (19.5)           | 10 (27)       | 19 (22)     |         |
| **Geriatric assessment variables**    |             |                    |               |             |         |
| **Physical function, n (%)**          |             |                    |               |             |         |
| ADL – Barthel                         |             |                    |               |             |         |
| ≥ 90                                  | 31 (100)    | 41 (100)           | 4 (31)        | 76 (89)     | <0.001b |
| < 90                                  | 0 (0)       | 0 (0)              | 9 (69)        | 11 (9)      |         |
| IADL – Lawton                         |             |                    |               |             |         |
| ≥ 5                                  | 31 (100)    | 0 (0)              | 3 (23)        | 34 (40)     | <0.001b |
| < 5                                  | 0 (0)       | 41 (100)           | 10 (77)       | 51 (60)     |         |
| **Cognitive function, n (%)**         |             |                    |               |             |         |
| Pfeiffer                              |             |                    |               |             |         |
| ≥ 2                                  | 31 (100)    | 41 (100)           | 10 (77)       | 82 (96.5)   | <0.001b |
| ≥ 2                                  | 0 (0)       | 0 (0)              | 3 (23)        | 3 (3.5)     |         |
| **Mood assessment, n (%)**            |             |                    |               |             |         |
| Yesavage                              |             |                    |               |             |         |
| < 1                                  | 30 (97)     | 38 (93)            | 12 (92)       | 80 (94)     | 0.732b  |
| ≥ 1                                  | 1 (3)       | 3 (7)              | 1 (8)         | 5 (6)       |         |
| **Comorbidity, n (%)**                |             |                    |               |             |         |
| CIRS-G                                |             |                    |               |             |         |
| Total score (median)                  | 4           | 6                  | 11            | 6           | <0.001a |
| Severity score (median)               | 1.5         | 1.6                | 2.2           | 1.7         | <0.001a |
| **Polypharmacy, n (%)**               |             |                    |               |             |         |
| ≤ 5                                  | 19 (61)     | 9 (22)             | 0 (0)         | 28 (33)     | <0.001b |
| > 5                                  | 12 (39)     | 32 (78)            | 13 (100)      | 57 (67)     |         |
| **Geriatric syndromes, n (%)**        |             |                    |               |             |         |
| 0                                    | 31 (100)    | 41 (100)           | 9 (69)        | 81 (95)     | <0.001b |
| ≥ 1                                  | 0 (0)       | 0 (0)              | 4 (31)        | 4 (5)       |         |
| **Social support, n (%)**             |             |                    |               |             |         |
| Yes                                  | 31 (100)    | 36 (88)            | 11 (85)       | 78 (92)     | 0.105b  |
| No                                   | 0 (0)       | 5 (12)             | 2 (15)        | 7 (8)       |         |
| **Weight loss, n (%)**                |             |                    |               |             |         |
| < 5%                                 | 26 (84)     | 29 (71)            | 9 (69)        | 64 (75)     | 0.379b  |
| > 5%                                 | 5 (16)      | 12 (29)            | 4 (31)        | 21 (25)     |         |
| **VES-13 scale, n (%)**               |             |                    |               |             |         |
| < 3                                  | 24 (77)     | 13 (32)            | 0 (0)         | 37 (43.5)   | <0.001b |
| ≥ 3                                  | 7 (23)      | 28 (68)            | 13 (100)      | 48 (56.5)   |         |

Abbreviations: ADL = Barthel Activities of Daily Living; ANOVA = analysis of variance; CGA = comprehensive geriatric assessment; CIRS-G = Cumulative Illness Ratio Scale for Geriatrics; ECOG-PS = Eastern Cooperative Oncology Group performance status; IADL = Lawton Index of Instrumental Activities of Daily Living; VES-13 = Vulnerable Elders Survey. Values in bold are statistically significant.

*ANOVA P-value

**P-value.
Median OS was significantly shorter for unfit and medium-fit patients (9.3 and 16.9 months, respectively) compared with fit patients (23.9 months, log-rank P = 0.01; Figure 2A). The respective 2- and 5-year OS rates were 47% and 15% in fit, 23% and 8% in medium-fit, and 10% and 0% in unfit participants.

Participants with a VES-13 score indicating vulnerability (≥3) also had significantly shorter median OS (11.6 months, 95% CI: 4.3, 18.9) than non-vulnerable patients (22.9 months, 95% CI: 16.1, 29.6; log-rank P = 0.007; Figure 2B).

In the univariate Cox regression analysis, performance status, geriatric classification, and VES-13 were prognostic factors for OS (Supplementary Table S4). In the multivariate Cox regression analysis adjusted for age, sex, histology, tumour stage, and weight loss, and compared to fit participants, OS was worse for medium-fit (hazard ratio (HR) 1.98, 95% CI: 1.06, 3.71) and unfit groups (HR = 3.81, 95% CI: 1.53, 9.45; Table 2). In the multivariate Cox regression adjusted for the same covariates, vulnerability was also significantly associated with worse OS (HR = 2.30, 95% CI: 1.28, 4.15, P = 0.005, Table 2).

**Survival results in patients treated with cCRT.** All patients classified as unfit (n = 13) received best supportive care, which included palliative thoracic radiotherapy in four cases. Out of 72 fit and medium-fit patients initially considered candidates for cCRT, only 54 patients (75%) were actually treated (Figure 1). The reasons for not administering cCRT were: non-suitable for medium-fit (hazard ratio (HR) 1.98, 95% CI: 1.06, 3.71) and unfit groups (HR = 3.81, 95% CI: 1.53, 9.45, Table 2). In the multivariate Cox regression adjusted for the same covariates, vulnerability was also significantly associated with worse OS (HR = 2.30, 95% CI: 1.28, 4.15, P = 0.005, Table 2).

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**Table 2. Multivariate Cox regression analysis of OS for all patients (n = 85) based on CGA and VES-13 categories**

| Variable                  | HR (95% CI) | P-value |
|---------------------------|-------------|---------|
| Age, continuous           | 0.94 (0.86, 1.02) | 0.128   |
| Sex (men vs women)        | 1.72 (0.60, 4.92) | 0.308   |
| Histology (SCC vs non-SCC)| 1.55 (0.87, 2.75) | 0.135   |
| Stage (III vs II)         | 1.14 (0.47, 2.72) | 0.777   |
| Weight loss (≥5 vs <5%)   | 1.25 (0.63, 2.46) | 0.525   |
| CGA group (fit vs medium-fit) | 1.98 (1.06, 3.71) | 0.033   |
| CGA group (fit vs unfit)  | 3.81 (1.53, 9.45) | 0.004   |

**Notes:**
- For dichotomous variables, HR indicates the risk for the first variable.
- Abbreviations: CGA = comprehensive geriatric assessment; CI = confidence interval; HR = hazard ratio; OS = overall survival; SCC = squamous cell carcinoma; VES-13 = Vulnerable Elders Survey.
- Values in bold are statistically significant.
completed the planned treatment, and there were no differences in compliance between CGA groups. The reasons for not completing the planned cCRT were treatment-related toxicity (n = 3), cancer progression (n = 1), patient’s decision (n = 1), or aggravation of comorbidities (n = 1).

The chemotherapy schedules used most often were carboplatin 2.5 AUCs (area under the plasma drug concentration–time curve) plus vinorelbine 15 mg m⁻² on days 1, 8, 22, and 29 and weekly carboplatin 2 AUCs plus paclitaxel 45 mg m⁻² (Supplementary Table S3).

Analysis did not show any statistically significant differences in median OS between fit and medium-fit patients treated with cCRT (24.3 and 19.1 months, respectively, log-rank P = 0.096; Figure 2C). Non-vulnerable patients (according to VES-13) receiving cCRT had significantly longer median OS (24.3 months, 95% CI: 16.6, 32.1) than vulnerable patients (16.3 months, 95% CI: 4.7, 27.9, log-rank P = 0.027; Figure 2D). Interestingly, in the multivariate Cox regression adjusted for age, sex, histology, tumour stage, and weight loss, vulnerable patients (VES-13 score ≥3) had significantly shorter median OS (HR 2.90, 95% CI: 1.30, 6.45, P = 0.009).

Association between CGA and toxicity. Among the 54 patients receiving cCRT, medium-fit patients experienced a higher rate of grade 3–4 adverse events (59%) than fit patients (37%), but these differences were not statistically significant (P = 0.173). Vulnerable patients as defined by VES-13 had a significantly higher rate of grade 3–4 adverse events (65%) than non-vulnerable patients (32%, P = 0.028). We did not observe differences in grade 3–4 haematologic toxicity between fit and medium-fit patients or between vulnerable and non-vulnerable patients. Four (3.8%) fit and no medium-fit patients experienced grade 3–4 haematologic toxicity (P = 0.31), while eight (24%) fit and three (10%) medium-fit patients experienced grade 3–4 non-haematologic toxicity (P = 0.09).

The most common grade 3–4 adverse events were neutropenia (20%), febrile neutropenia (7.5%), asthenia/fatigue (11%), respiratory infection (13%), and radiation pneumonitis (13%). All treatment-related deaths occurred in the medium-fit group: two due to radiation pneumonitis and two due to respiratory infection. Toxicity according to geriatric group is summarised in Table 3.

Logistic regression was performed to assess the ability of distinct variables to predict grade 3–4 toxicity. While CGA-defined groups were not predictive of this outcome, vulnerable patients as defined by VES-13 were at significantly higher risk of grade 3–4 toxicity (odds ratio (OR) 3.99, 95% CI: 1.28, 12.37, P = 0.017; Table 4).

DISCUSSION

This prospective study, carried out in the clinical practice setting, included a cohort of 85 consecutive participants aged 75 years or older with inoperable, locally advanced NSCLC who were evaluated by CGA. To our knowledge, this is the first prospective study assessing the value of CGA for selecting patients for cCRT therapy in this specific elderly population, for whom treatment decisions are particularly challenging. Indeed, a significant proportion of participants were octogenarians.

At present, treatment decisions are based on clinical assessment, age, and performance status. Patients of advanced age, with poor performance status, weight loss, or comorbidities are considered ‘poor-risk’ patients and have generally been excluded from clinical trials evaluating cCRT (Cardenal et al, 2015). However, CGA detects geriatric impairments even in patients with good performance status (Jolly et al, 2015). A recent systematic review on CGA for lung cancer patients found that CGA could detect multiple geriatric impairments that are generally missed by other measures such as ECOG performance status (Schulkes et al, 2016), and some of these can be reversed through subsequent geriatric-based interventions (Kalsi et al, 2015). In our study, 3% of fit and 19.5% of medium-fit patients had a performance status score of 2 or more and would be considered as ‘poor-risk’ and excluded from cCRT.

Most previous studies addressing the relevance of CGA in lung cancer were conducted in patients with advanced disease or with distinct tumour stages (Maione et al, 2005; Corre et al, 2016; Gajra et al, 2016; Karampeazis et al, 2017). Recently, the Elderly Selection on Geriatric Index Assessment study compared a standard strategy of treatment allocation (carboplatin-based doublet or single agent on the basis of performance status and age) vs an experimental CGA-based allocation to the same chemotherapies or best supportive care in elderly patients with advanced NSCLC (Corre et al, 2016). Although that study failed to show an improvement in failure-free survival and OS in patients in the CGA-guided arm, these patients showed better tolerance to chemotherapy and lower

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**Table 3. Moderate and severe toxicity in patients treated with concurrent chemoradiotherapy according to the CGA groups (n = 54)**

| Toxicity          | Fit (n = 27) | Medium-fit | Total (n = 54) |
|-------------------|-------------|------------|---------------|
|                   | G3–4, n (%) | G5, n (%)  | G3–4, n (%)   |
| Neutropenia       | 7 (26)      | 0 (0)      | 4 (15)        |
| Febrile           | 2 (7.5)     | 0 (0)      | 2 (7.5)       |
| Anaemia           | 0 (0)       | 0 (0)      | 2 (7.5)       |
| Thrombocytopenia  | 1 (4)       | 0 (0)      | 2 (7.5)       |
| Fatigue           | 2 (7.5)     | 0 (0)      | 4 (15)        |
| Diarrhoea         | 1 (4)       | 0 (0)      | 2 (7.5)       |
| Oesophagitis      | 0 (0)       | 1 (2)      | 0 (0)         |
| Respiratory       | 2 (7.5)     | 0 (0)      | 7 (26)        |
| Radiation pneumonitis | 2 (7.5) | 0 (0)  | 5 (18.5) |

Abbreviation: CGA = comprehensive geriatric assessment.

**Table 4. Univariate logistic regression analysis to predict grade 3–4 toxicity in patients treated with concurrent chemoradiotherapy (n = 54)**

| Variable         | OR (95% CI) | P-value |
|------------------|-------------|---------|
| Age, continuous  | 0.92 (0.76, 1.12) | 0.409   |
| Sex (men vs women)| 4.35 (0.45, 41.8) | 0.203   |
| Histology (SCC vs non-SCC) | 1.08 (0.37, 3.19) | 0.884  |
| Smoking status (smoker vs never smoker) | 4.35 (0.45, 41.8) | 0.203  |
| Stage (I vs II)  | 1.90 (0.41, 8.94) | 0.414   |
| Weight loss (≥5 vs <5%) | 1.33 (0.27, 6.63) | 0.725 |
| ECOG-PS (≥2 vs <2) | 1.04 (0.14, 7.99) | 0.969  |
| VES-13 score (≥3 vs <3) | 3.99 (1.28, 12.37) | 0.017  |
| CGA group (medium-fit vs fit) | 2.72 (0.89, 8.26) | 0.078 |

Note: For dichotomous variables, the OR indicates the risk for the first variable. Abbreviations: CGA = comprehensive geriatric assessment; CI = confidence interval; ECOG-PS = Eastern Cooperative Oncology Group performance status; OR = odds ratio; SCC = squamous cell carcinoma; VES-13 = Vulnerable Elders Survey. Values in bold are statistically significant.
treatment failure due to toxicity, and nearly one-quarter of them were spared chemotherapy without compromising survival for the whole group.

A recent individual patient data meta-analysis of 16 trials (n = 3600) assessing cCRT in unresectable stage III NSCLC included 832 (23%) elderly participants (≥70 years old); elderly patients had a shorter OS than their younger counterparts (17.0 vs 20.7 months, P < 0.01) (Stinchcombe et al., 2017). The JCOG0301 randomised phase III clinical trial, performed specifically in patients aged 70 years or older with stage III NSCLC, showed better outcomes for cCRT vs RT alone in a group of participants who had not undergone geriatric characterisation (Atagi et al., 2012). An ongoing phase II study assessing CGA in the inoperable, locally advanced NSCLC setting (RACCOSSA, GFPC 08-06) is evaluating tolerance to cCRT (cisplatin plus vinorelbine concurrently with thoracic radiotherapy) in participants aged 70 years or older and considered fit by geriatric assessment (Locher et al., 2011).

We observed a significant association between CGA groups and clinical outcome, as fit and medium-fit patients had longer median OS than unfit patients. This survival outcome cannot be entirely attributed to the expected beneficial effect of cCRT; rather, this difference is likely related to the poorer health profile of unfit patients compared with fit and medium-fit patients. Besides, as our study is non-comparative, the interaction between treatment and CGA categories in terms of prognosis cannot be assessed.

On the other hand, the survival results in the selected group of fit and medium-fit patients who did receive cCRT (median OS 21.1 months, 95% CI: 16.2, 26.0) were in the range of those reported for younger patients in clinical trials (Santana-Davila et al., 2015; Steuer et al., 2016). Atagi et al. (2012) reported that cCRT resulted in a median OS slightly higher than ours (22.4 months, 95% CI: 16.5, 33.6), but inclusion was restricted to participants of Asian ethnicity with good performance status (96% of patients had an ECOG score of 0–1). A recent systematic review of sequential or concurrent CRT vs radiotherapy alone in elderly patients with stage III NSCLC concluded that fit patients showed good tolerance to cCRT, which was associated with a 34% reduction in the hazard ratio for death (Dawe et al., 2016).

Toxicity is a special concern in elderly patients because of its greater potential impact on functionality and quality of life compared to the general population. Our safety data provides support for using cCRT in older adults. In our sample, the rate of grade 3–4 toxicities associated with cCRT was consistent with the expected benefit of cCRT; rather, this difference is likely related to the poorer health profile of unfit patients compared with fit and medium-fit patients. Besides, as our study is non-comparative, the interaction between treatment and CGA categories in terms of prognosis cannot be assessed.

The authors declare no conflict of interest.

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