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Safety and feasibility of radiotherapy treatment in elderly non-small-cell lung cancer (NSCLC) patients

F. Fiorica [a,*], F. Cartei [a], S. Ursino [a], A. Stefanelli [a], Y. Zagatti [a], S. Berretta [b], S. Figura [b], D. Maugeri [c], E. Zanet [b,c,d], D. Spartà [b], C. La Morella [b], U. Tirelli [d], M. Berretta [d]

[a] Division of Radiotherapy, Arcispedale S. Anna Universitary Hospital, Corso Giovecca 203, I-44100 Ferrara, Italy
[b] Department of Surgery, S. Luigi Hospital, University of Catania, V.le Fleming 210, I-95100 Catania, Italy
[c] Department of Aging, Urological and Neurological Sciences, University of Catania, Cannizzaro Hospital, Via Messina 829, I-95126 Catania, Italy
[d] Department of Medical Oncology, National Cancer Institute, Via Franco Gallini 2, I-33081 Aviano (PN), Italy

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ABSTRACT

The purpose of this study was to evaluate the feasibility and activity of radiotherapy (RT) treatment in elderly patients with locally advanced lung cancer. From January 2002 to December 2007, 51 consecutive patients (43 men and 8 women) aged ≥65 received RT for locally advanced lung cancer, 22 with radical intent and 16 in adjuvant setting. Thirty-six patients received chemotherapy. Variables considered were age, co-morbidities, evaluated according to the adult co-morbidity evaluation index (ACE-27), surgery vs. no surgery, radiation dose and chemotherapy. The median age was 74.7 years (range 65–91). Of the patients, 15.7% had no co-morbidity, 41.2% mild, 25.5% moderate, and 17.6% had severe co-morbidities. Sixteen subjects (31.4%) underwent surgery. All patients completed the planned radiation schedule, while chemotherapy was reduced in 16 patients. At a median follow-up of 22 months, the 2- and 3-year overall survival rates were 46.5% and 35.4%, respectively. Patients with no or mild co-morbidities ($p < 0.0001$) and a good performance status ($p < 0.0001$) had a better survival. The actuarial progression-free survival at 2 and 3 years was 41.4% and 38.2%, respectively. Acute lung toxicity rates were different between patients with different ACE-27 indexes, whereas late toxicity was not influenced. In conclusion, in elderly patients, the compliance with RT is good and the rate of toxicity is acceptable. Patients with no or mild co-morbidities have a significantly better survival. The increasing severity of co-morbidities may sufficiently shorten the remaining life expectancy, cancel the gains obtained by RT and increase the acute lung toxicity. Further prospective trials are needed to confirm these results.

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1. Introduction

Lung cancer is the leading cause of cancer deaths in the United States and worldwide (Jemal et al., 2008) and it is a typical cancer of elderly patients. Incidence data from the National Cancer Institute's (NCI) surveillance epidemiology and results (SEER) have shown that older persons have a 10 times greater risk of developing lung cancer than those with an age of less than 65 years.

As the survival of elderly population increases in developed countries worldwide, it is expected that oncologists will be increasingly confronted with the therapeutic challenge of an elderly patient presenting with NSCLC. Unfortunately, at diagnosis most of these patients are judged to have an unresectable disease or an inoperable disease because of age and associated medical conditions. In literature, RT with or without chemotherapy is considered the cornerstone of treatment in unresectable NSCLC (Okawara et al., 2006) and an adjuvant treatment with or without chemotherapy in operable NSCLC for positive margin and stage N2 (PORT, 1998).

Furthermore, two recent randomized trials (West and Albain, 2005; Van Meerbeeck et al., 2007) comparing surgery to RT after induction chemotherapy in patients with stage IIIA-N2 NSCLC, concluded that surgical resection does not improve overall survival or progression-free survival compared with RT. So, RT should be considered the preferred local-regional treatment for locally advanced NSCLC. However, a general consensus on how to treat elderly patients with locally advanced or inoperable NSCLC is still far from being achieved. The elderly are under-represented in clinical trials, account for only 25% of patient enrollment (Talarico et al., 2004). The older (age ranged 75–84) and the oldest (Carreca et al., 2005) patients (>85) are the most under-represented, and

* Corresponding author. Tel.: +39 0532 236 096; fax: +39 0532 237 532.
E-mail address: francesco.fiorica@unife.it (F. Fiorica).

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consequently, the data related to treatment-tolerance and results in this subset of patients are scarce. This is true for all tumor types but it is of particular relevance in lung cancer where the median age at diagnosis is 71 years (Ries et al., 2008).

As regards co-morbidities, elderly patients are an extremely heterogeneous population. Subjects can vary from very fit to not being able to live independently due to co-morbidities. It is not so clear whether the toxicity of treatment is justified by the gain in life prolongation or whether co-morbidities can influence the acute and late toxicities due to RT. Nevertheless, patients who have reached their 80th year of life still have a mean life expectancy of 7 years for men and 9 years for women (Lichtman, 2005). In order to clarify this issue, we decided to analyze retrospectively, whether elderly cancer patients could benefit from a RT regimen routinely used in younger patients as NSCLC treatment.

2. Patients and methods

2.1. Patients characteristics

Data were collected between January 2002 and December 2007 from 51 patients aged over 65 years, who received RT for NSCLC in our RT department staged to be American Joint Committee on Cancer (AJCC) Stage IIIA or IIIB. In all patients, the clinical workup included a detailed medical history, physical examination, blood tests, electrocardiogram, bronchoscopy, pulmonary function test, thoracic and upper abdomen computed tomography (CT) scan. A CT or a magnetic resonance imaging (MRI) of the head and bone scan were done in 98.0% (50 patients). A positron emission tomography (PET) was used in 20 patients (39.2%) for staging. NSCLC diagnosis was obtained by fine-needle aspiration biopsy, endobronchial biopsy, bronchoscopic brushing or washing and/or by direct surgery.

The patients characteristics are summarized in Table 1. The analyzed patients had a performance status $\geq$60 and a life expectancy of more than 3 months. The ACE-27 was retrospectively used to take into account co-morbidities (Piccirillo et al., 2004). Co-morbidity scores were assigned without having any information regarding the outcome of the patient. In the presence of more than one co-morbidity related to an organ system, the one with the highest severity was counted. Patients were divided into four subgroups, having "no", "mild", "moderate" and "severe" co-morbidities. Furthermore, patients were divided into three age groups: 65–74, 75–84, and>85 years of age.

Sixteen patients (31.4%) underwent a surgical treatment and received radiation therapy for mediastinal nodes involvement (N2) and/or for positive resection margins.

Table 1
Characteristics of the patients studied.

Parameters	No. of patients (%)
Age (years)	
Range	65–91
Mean	74.84
Age-groups	
65–75	19 (37.3)
76–85	28 (54.9)
>85 years	4 (7.8)
Gender	
Males	43 (84.3)
Females	8 (15.7)
ACE-27	
Overall co-morbidity score	
Grade 0	8 (15.7)
Grade 1	21 (41.2)
Grade 2	13 (25.5)
Grade 3	9 (15.7)
Performance status	
90–100	7 (13.7)
70–80	28 (54.9)
60	9 (31.4)
Stages	
IIIA	28 (54.9)
IIIB	23 (45.1)
Nodes	
No	1 (2)
N1	7 (13.7)
N2	41 (80.4)
N3	3 (3.9)
Chemotherapy	
1–3	19 (37.3)
>3	17 (33.3)
No	15 (29.4)
RT	
Postoperative	16 (31.4)
Exclusive	22 (43.1)
Palliative	13 (25.5)
Biological RT dose	
>60 Gy_{10}	28 (56.9)
50–60	13 (25.5)
<50	10 (19.6)
Surgery	
Yes	16 (31.4)
No	35 (68.6)

2.2. Radical or adjuvant treatment

All patients had conformational RT with 6–15 MV photon beams using CT-assisted three-dimensional treatment planning (Pinnacle®). Sixteen patients (31.4%) received adjuvant RT, 9 with sequential chemotherapy. In this setting the clinical target volume (CTV) included the residual macroscopic tumor (12 patients) or tumor bed (microscopic positive resection margins) in 4 patients and all clinically or radiologically involved lymphnodes; all detected by transverse CT sections (thickness 3 mm). A radical RT program was scheduled in 22 patients (43.1%) sequentially to chemotherapy in all patients but 3. In this setting, CTV included the primary tumor and the radiologically involved nodes with a short axis diameter of $\geq$1 cm or positive PET. The remaining 13 patients received palliative treatment, 8 patients received combined chemotherapy and RT. Total radiation dose and fractionation were in function of the treatment intent. In order to improve the comparability of the different therapeutic regimens and to assess the relationship between radiation dose, survival benefit and toxicity, the biologically effective dose (BED) was estimated. A fractionation of 2 Gy/die or 2.5 Gy/die was employed in all patients, except for palliative treatment. As adjuvant approach, an equivalent dose >60 Gy was administered to 12 patients and a dose between 50 and 60 Gy in 4 of them. In the radical approach, 15 patients received a biological dose >60 Gy and 7 a dose between 50 and 60 Gy. In 16 patients a total dose of 70 Gy in conventional fractionation was delivered, in 12 patients a dose of 65 Gy with a fractionation of 2.5 Gy/die in 26 days. All the 13 patients treated, palliatively received a biological dose inferior to 50 Gy. Globally, 41 patients in this study received sequential chemotherapy, the chosen chemotherapy regimen was decided by treating physicians. During treatment, patients were monitored for hematological and non-hematological toxicity; physical examinations as well as

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blood cell counts and blood chemistry were performed every week. A chest X-ray was obtained according to clinical necessity.

2.3. Follow-up and restaging

In accordance with an internal protocol, NSCL cancer patients have to be re-evaluated at 3 months intervals for 2 years and every 6 months thereafter. All analyzed patients received at least two follow-up visits. Evaluation consisted of pertinent medical history, physical examination, complete blood counts and blood chemistry exams, including carcino-embryonic antigen (Cea) at every follow-up visit. Thoracic and upper abdomen CT scan were performed at 3 and 6 months and then at regular intervals. Acute morbidities were classified according to WHO criteria (Miller et al., 1981), and weekly recorded during radiation therapy. Following lung cancer treatments, the most expected acute side effects were thrombocytopenia, leukocytopenia, esophagitis and dyspnea. Furthermore, during follow-up examinations, late effects were recorded according to NCI-EORTC criteria (Pavy et al., 1995), especially chest X-rays changes and damage to spinal cord and heart.

2.4. Statistical analysis

The primary endpoint of the study was to evaluate the overall survival. The secondary end-points were: (a) acute and late toxicity rate, (b) progression-free survival and (c) time to local progression and time to distant metastases during follow-up. The Kaplan–Meier method (Kaplan and Meier, 1958) was used to estimate survival, late toxicity rate, time to local recurrence and time to metastases. Differences in survival and late toxicity rate were assessed by the log-rank test. The observed survival time was the interval between diagnosis and death or the final follow-up. For overall progression, the disease-free time was the interval between the end of the last treatment and the progression/relapse of tumor. In this analysis, patients dying without recurrence were censored at the time of death and were classified as progression-free. An actuarial method was employed to estimate the occurrence of late side effects in relation to time; the late side effect free time was the interval of time without evidence of late effects starting from three months after the RT. The Cox model (Cox, 1972) was used to identify the risk factors for overall survival, cancer-free survival, and occurrence of late complications.

The following variables at baseline were considered for survival univariate analysis: age, sex, stage, co-morbidity, performance status, surgery (yes or no), RT (radical vs. adjuvant vs. palliative), chemotherapy (yes or no). Furthermore, we considered the rate of acute side effects while analyzing late effects. All analyses were conducted with SPSS vers.13.0 (SPSS for Windows, Rel. 13.0 2004. Chicago: SPSS Inc.).

3. Results

3.1. Features of patients at baseline

Fifty-one consecutive patients were included in the study: 43 males (84.3%) and 8 females (15.7%). Four subjects out of 51 (7.8%) were over 85 years of age, 28 (54.9%) ranged between 76 and 84 years and 19 (37.3%) between 65 and 80 years. Patients characteristics and treatment data are shown in Table 1. In this cohort, a stage III A was observed in 54.9% and stage III B in 45.1%. Forty-one (84.3%) patients had at least one co-morbidity (Table 2). The classification of patients co-morbidities by the ACE-27 index was 0 in 8 patients (15.7 %), 1 in 21 patients (41.2%), 2 in 13 patients (25.5%) and 3 in 9 patients (17.6%). The Karnofsky index value was: 60 in 16 patients (31.4%), 70–80 in 28 patients (54.9%), and $\geq$90 in 7 patients (13.7%). All patients received a specific treatment. Sixteen patients (31.4%) underwent surgery. Surgery consisted in lobectomy with nodes sampling in all patients. All patients received adjuvant RT for residual macroscopic or microscopic disease and for mediastinal nodes. Instead, RT was delivered as radical and palliative treatment in 22 (43.1%) and 13 (25.5%) patients, respectively.

Table 2
Distribution of type and severity of co-morbidities.

Co-morbidity	%	ACE-27 grades		
		1	2	3
Total number = 51				
Alcohol abuse	0	–	–	–
Hypertension	56.8	23	4	2
Respiratory disease	68.6	27	6	2
Congestive heart failure	17.6	6	2	1
Diabetes mellitus	29.4	10	4	1
Arrhythmia	11.7	5	1	0
Myocardial infarction	13.7	5	2	0
Coronary artery disease/angina	15.7	6	2	0
Stroke	5.9	3	0	0
Peripheral arterial disease	25.5	10	2	1
Renal insufficiency	29.4	10	4	1
Gastrointestinal disease	27.5	12	2	0
Dementia	3.9	1	0	0
Psychiatric	3.9	1	0	0
Liver disease	9.8	5	0	0
Paralysis	7.8	3	1	0
Neuromuscular disease	1.9	1	0	0
Other solid tumor	9.8	4	1	0
Obesity	3.9	2	0	0
Venous disease	3.9	2	0	0
Pancreatic disease	3.9	1	0	0
Rheumatological	0	–	–	–
Inmunological disease/AIDS	0	–	–	–
Leukemia/myeloma	0	–	–	–
Lymphoma	3.9	1	0	0
Drug users	0	–	–	–

Chemotherapy was associated to RT in 36 patients (70.6%) sequentially. In 17 patients a carboplatin and gemcitabine regimen was used, in 13 a cisplatin and gemcitabine or vinorelbine and in 8 a mono-chemotherapy with gemcitabine or vinorelbine. Seventeen subjects (33.3%) received 1–3 cycles of chemotherapy, 19 (37.3%) more than three cycles.

All patients completed the planned RT treatment; instead chemotherapy was reduced to 75% or 50% in 16 subjects.

3.2. Follow-up

The mean length of follow-up after RT was 22.0 ± 11 months (median 18 months, range 6–39 months) for all the patients. None was lost at follow-up visits. During follow-up, a total of 35 deaths occurred. Death due to cancer occurred in 26 patients (50.9%). The actuarial overall survival rates at 24 and 36 months were 46.5% and 35.4%, respectively (Fig. 1a). Survival was longer among patients with no or mild co-morbidities (74.8% and 45.7% at 24 and 36 months, respectively) than among patients with moderate or severe co-morbidities (9% at 24 months with a median survival of 11 months) ($p < 0.0001$ by log-rank test) (Fig. 1b). A better result was reached for subjects treated with surgery and adjuvant treatment (median survival of 36 months, all patients in stage IIIA) than in subjects treated with chemo-RT as radical approach (median survival 29 months, 8 patients with III A stage and 14 with III B stage), ($p < 0.001$ log-rank test) (Fig. 1c). The results of the univariate analysis are displayed in Table 3. The multivariable Cox model included gender, age, ACE-27 index, stage, Karnofsky index and treatment type for all models. For overall survival, the final multivariable Cox model maintained an ACE-27 index value equal or higher than 2 (HR = 5.897; 95% CI = 3.334–10.431, $p < 0.001$).

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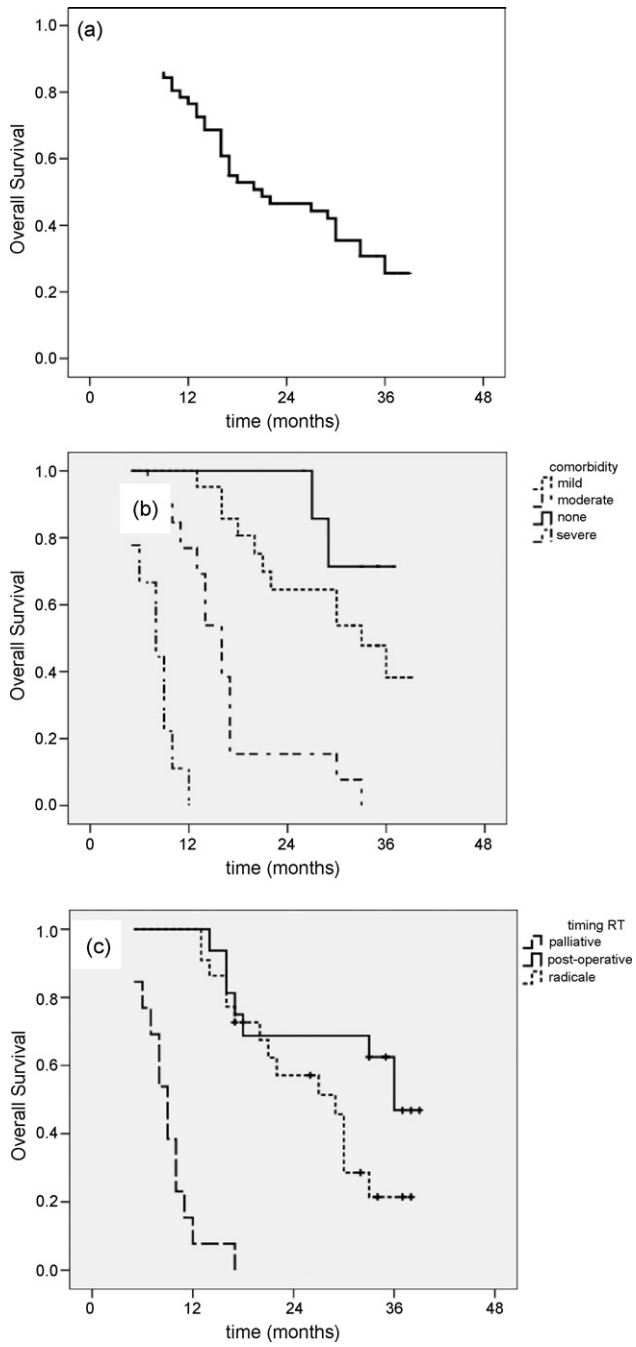


Fig. 1. Overall survival curve for all 51 patients evaluated (a), in figure (b) overall survival distribution by ACE-27 value and in figure (c) overall survival distribution by timing of radiotherapy.

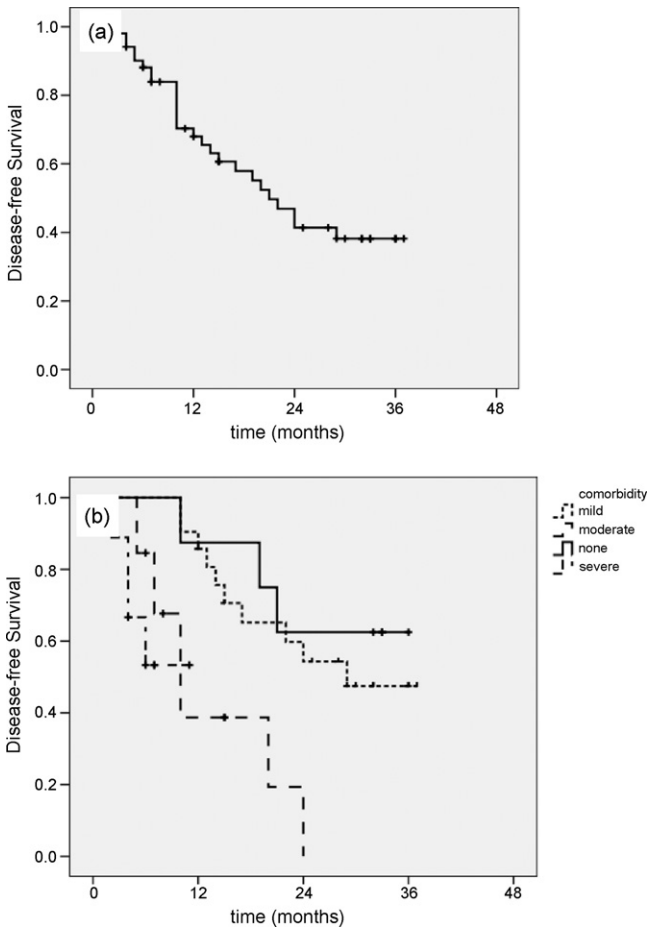


Fig. 2. Disease-free survival, in (a) overall, and in (b) distribution by ACE-27 value.

Twenty-five patients (49.1%) experienced tumor progression: 11 patients (21.6%) experienced only local tumor progression, 11 (21.6%) only distant metastases and 3 (5.9%) both local and distant progression. The mean time to progression was 26.1 ± 1.7 months. The actuarial progression-free survival at 24 and 36 months was 41.4% and 38.2%, respectively (Fig. 2a). The actuarial local progression-free survival rate at 2 and 3 years was 55.6% and 51.4%, respectively, while the actuarial metastases rate was 59.1 at 2 and 3 years.

3.3. Treatment safety

3.3.1. Acute toxicity

Acute RT toxicity was weekly recorded by the physician during the chemo-RT. No treatment-related mortality was found. The main RT-related toxicities were esophagitis and pulmonary toxicity: 39 (76.5%) and 29 (56.9%) patients, respectively suffered from these toxicities. No grade toxicity over 2 was observed, 16

Table 3
Univariate analysis of survival data according to various classifications.

Parameters	Groups	β	±SE	p	HR (95% CI)
Gender	0: male, 1: female	−0.193	0.484	0.690	0.824(0.320–2.127)
Age category	0: 65–75, 1: 76–85, 2:>85	0.809	0.311	0.009	2.245(1.221–4.131)
Performance	0:90–100, 1: 70–80, 2:60	1.351	0.321	0.001	3.863 (2.059–7.249)
Staging	0: IIIA, 1: III B	0.859	0.344	0.013	2.360(1.202–4.634)
Co-morbidity	0: none, 1: mild, 2: moderate, 3: severe	1.774	0.291	0.001	5.897(3.334–10.431)
Surgery	0: yes, 1: no	1.230	0.432	0.004	3.421 (1.468–7.974)
Timing of RT	0: preoperative, 1: postoperative, 2: palliative, 3: exclusive	1.779	0.340	0.001	5.927(3.046–11.532)
Chemotherapy	0: yes, 1: no	0.239	0.366	0.514	1.270(0.619–2.604)

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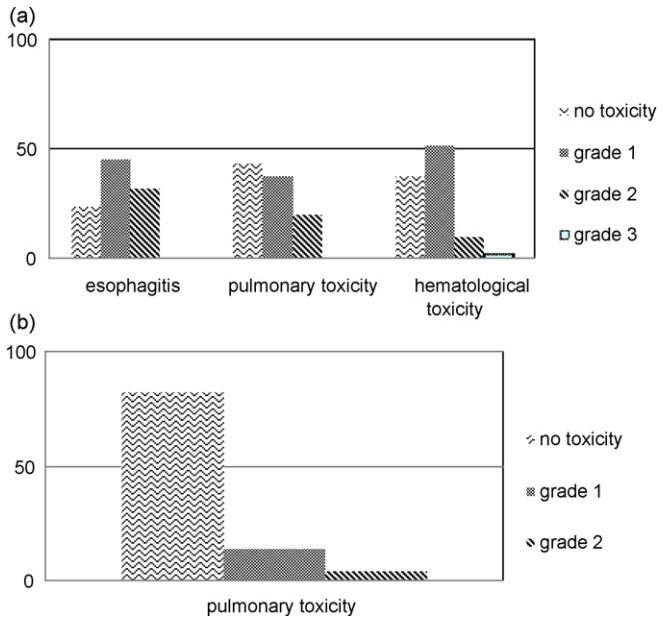


Fig. 3. Distribution of acute toxicities (a) and late complications (b).

(31.4%) and 10 (19.6%) experienced grade 2 esophagitis and pulmonary toxicity, respectively. Hematological toxicity was observed in 32 patients (62.7%). No grade toxicity over 3 was observed, 5 patients (9.8%) had grade 2 toxicity and only one patient (2%) experienced grade 3 toxicity. Fig. 3a shows the toxicity grade of treated patients. None of the baseline variables analyzed were significantly associated with the occurrence of acute toxicity, except co-morbidity detected between ACE-27 classes ($p = 0.013$) and surgery ($p = 0.043$) with lung toxicity.

3.3.2. Late toxicity

Nine patients (17.6%) experienced a late toxicity. Given the variable risk of developing a late effect, an actuarial method was employed to estimate the occurrence of late side effects in relation to time. In all patients, a pulmonary toxicity was found, moderate in 2 patients (3.9%) (Fig. 3b shows the detected grades of late toxicity). The late side effects-free survivals were 81.5 and 77.0 % at 24 and 36 months, respectively (Fig. 4). No significant differences

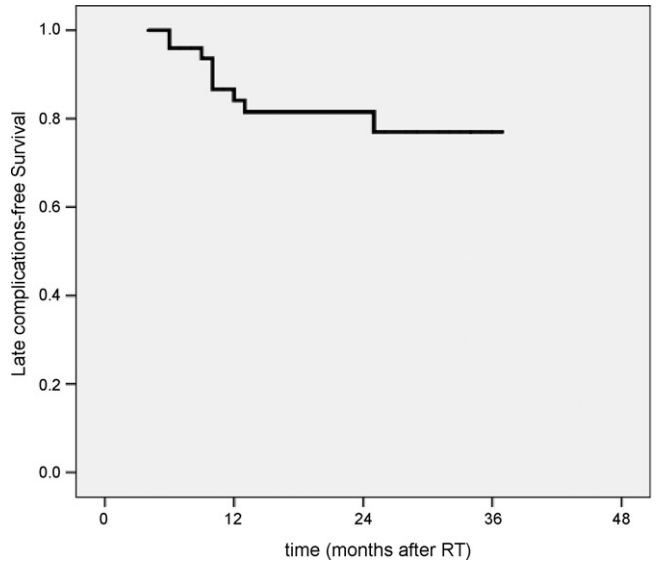


Fig. 4. Late complication-free survival.

were found among the baseline variables analyzed. There was a relationship between the acute pulmonary toxicity rate and the development of late toxicity ($p = 0.025$).

4. Discussion

NSCLC is a predominant disease in elderly patients, with a median age at diagnosis of 71 years, and 20% of lung cancer-related deaths occurs in patients aged ≥80 years (Jemal et al., 2003). For many years, however, elderly patients were thought to be less tolerant to cancer treatment than younger patients and chronological age has often been considered as a risk factor. RT rates, in patients IIIA and IIIB NSCLC, vary widely by age from 85% (age <59 years) to 45% (age >75 years) (De Rijke et al., 2004). Age rather than PS or co-morbidities are reported as the major reason for non-standard management in elderly patients (De Rijke et al., 2004).

The consequences of this approach are that the proper role of RT in the treatment of elderly NSCLC patients remains an unresolved issue in geriatric oncology and information is scarce in the international literature. The published randomized trials on RT in NSCLC include patients aged 70 years or older. However, no clear information is available from these trials on specific features of the elderly patients. In 2000, the Radiation Therapy Oncology Group (RTOG) performed a recursive partitioning analysis of 1999 patients enrolled in various protocols and identified age as a factor in therapeutic outcome in locally advanced NSCLC. (Werner-Wasik et al., 2000). Patients older than 70 years of age with KPS less than 90 had a median survival time between 5.6 months and 6.4 months. Due to poor results and to high incidence of side effects, radiation therapy was not indicated for elderly NSCLC patients.

Two more recent retrospective analyses in patients receiving combined modality therapy showed no negative impact of age on treatment tolerance, response to treatment, or survival (Langer et al., 2002; Rocha Lima et al., 2002). However, a SEER study (Ramsey et al., 2004) clearly demonstrated that only 46% of individuals aged >65 with NSCLC IIIb and IV stage received RT, 24% of them combined with chemotherapy. Furthermore, RT in this setting of patients is principally delivered to those with a more advanced disease within same stage (tumors that pose imminent threats to survival). This fact confirms that a prejudice in treating elderly patients with advanced lung cancer really exists despite elderly patients treated with chemo-RT having a survival rate equivalent to younger individuals (Schild et al., 2003). The same conclusion is recently reported by Firat et al. (2006) where age affects patient selection for combined modality therapy (CMT) independently from co-morbidity and weight loss in patients with stage III NSCLC and good performance status. This nihilistic approach is caused by the fact that a pre-treatment age selection exists, arising from the incorrect opinion that chronological age is a real limit to the application of radical treatments without increased morbidity (Scalliet, 1991). However, Pignon et al. (1998) analyzed the toxicities in 1208 patients enrolled in six different European Organization for Research and Treatment of Cancer (EORTC) trials for thoracic RT, and revealed that the difference in distribution for age was not significant for acute nausea, dyspnea, oesophagitis, weakness and WHO performance status alteration. Forty percent of patients were free of complication at 4 years, showing no significant difference between age groups.

Recently, Semrau et al. (2008), retrospectively examined 66 patients with inoperable NSCLC suffering from substantial co-morbidities or with advanced age (>70 years) treated with chemo-RT, analyzed according to co-morbidity, and concluded that chemo-RT was safely feasible in elderly patients with NSCLC, although elderly patients had a higher prevalence of higher degree hematological toxicity than younger patients.

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The aim of the present study was to analyze our experience in the use of RT regimens combined to chemotherapy routinely applied in elderly NSCLC patients with advanced disease. The overall survival at 2 and 3 years was 46.5% and 35.4%, respectively. These rates are comparable to those of published studies with younger patients (Fietkau, 2004); in our data the age is not a significant prognostic factor for survival. This finding could be explained with the treatment approach applied at our center where age was not a contraindication to radical treatment intent.

The significance of age as a prognostic factor in cancer patients has been widely discussed with authors either supporting or denying its importance. Studies detailing non-small-cell lung cancer have shown that older patients do not have different outcomes when compared with younger patients (Zachariah et al., 1997; Gauden and Tripcony, 2001; Schild et al., 2003; Semrau et al., 2008). Other studies have shown results sustaining the prognostic effect of age, even when adjusting for other prognostic factors (Patterson et al., 1998; Werner-Wasik et al., 2000; Firat et al., 2006).

Consequently, we believe that an evaluation of co-morbidities in the group of older patients could help in elucidating the prognostic effect of each factor. Multiple co-morbidities are common in elderly cancer patients and can affect cancer stage at presentation and survival (Extermann, 2000). Co-morbidities were retrospectively analyzed and classified according to ACE-27 in patients treated with RT for NSCLC. The ACE-27, a validated chart-based co-morbidity index (Piccirillo et al., 2004), was especially created to describe co-morbidities for patients with cancer. In this series of elderly patients we found high frequency of co-morbidities (84.3%), however, the severity of disease as measured by ACE-27 was mild in most cases. The most frequent co-morbidities were: respiratory and cardiovascular diseases (hypertension, congestive heart disease, arrhythmia, myocardial infarction), diabetes mellitus, gastrointestinal disease, and renal insufficiency, which are common in geriatric population.

In our study, no or mild co-morbidities assessed by ACE-27 score emerge as independent predictors for better survival upon multivariate analysis. This finding suggests that if a co-morbidity could be compensated (generally a mild co-morbidity), then the patient would receive the standard treatment offered to a patient without co-morbidities. The increasing severity of co-morbidities may sufficiently shorten the remaining life expectancy, minimizing or negating the benefit of any treatment. As an evidence for this, 9 out of 22 deaths (40.9%) in the moderate/severe subgroup were not cancer specific. Furthermore, the ACE-27 index was not statistically associated with disease-free survival (Fig. 2b) or recurrence in the multivariate analysis.

Our findings suggest the prognostic importance of co-morbidities and the potential value of including co-morbidities in clinical studies in which overall survival are relevant. Globally, the present paper supports the opinion that RT with or without chemotherapy can also be applied in elderly patients with non-small-cell lung cancer due to the well-tolerated toxicities and compliance. The planned treatment was completed by all patients. RT-induced side effects, present in a high rate of patients, were the following: esophagitis, dyspnea and hematologic toxicity. However, these rates were acceptable since patients suffered mainly from grade 1 toxicities, that can be successfully managed. No subjects had grade 4 side effects and, globally, a toxicity level >grade 2 was reported in only one patient (2%). There is no evidence of an increase of acute side effects due to timing of RT, chemotherapy and age; co-morbidities are associated with an increase of lung toxicity. Delivering conformal radiation therapy to involved nodes routinely used in non-small-cell lung cancer patients, confers high doses to tumor targeted volumes in most elderly patients with a good or acceptable tolerance avoiding significant side effects.

An overall actuarial late complication-free survival of 77% at 36 months was found. The present study, as suggested by Pignon et al. (1998), includes all types of late effects graded from 1 to 4. Considering only grade ≥2 late complications, our results show a rate of 3.9% of pulmonary toxicity. Globally, the late tolerance of elderly patients is not different from results in younger age groups. A correlation between late complications and acute pulmonary toxicity was found.

In conclusion, our data show that RT with or without chemotherapy maintains its activity and feasibility also in elderly patients with NSCLC. It is difficult to determine a standard therapy for elderly patients based only on chronological landmarks, as the effects of aging depend on the individual. It is very important to assess co-morbidities with their severity in order to arrange the development of treatment plans. Whenever possible and appropriate, elderly patients, correctly stratified for co-morbidities, should be allowed and encouraged to participate in clinical studies.

Conflict of interest statement

None.

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