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The outcomes of three-dimensional conformal radiotherapy for early-stage non-small-cell lung cancer patients eligible and ineligible for stereotactic body radiotherapy

Wyniki konformalnej radioterapii chorych na niedrobnokomórkowego raka płuca we wczesnym stopniu zaawansowania spełniających kryteria oraz niespełniających kryteriów kwalifikacji do napromieniania stereotaktycznego

Abstract

Introduction: Stereotactic body radiotherapy (SBRT) in early-stage non-small-cell lung cancer (NSCLC) results in promising outcomes, comparable with the outcomes of surgery. However, not all such patients are good candidates for this treatment. We conducted a retrospective evaluation of the outcomes of three-dimensional conformal radiotherapy (3D-CRT) in patients with stage I/II NSCLC with a special focus on the outcomes of patients who were eligible for SBRT but received 3D-CRT due to the unavailability of the former.

Material and methods: We evaluated 132 consecutive patients with stage I/II NSCLC who had received radical 3D-CRT between 1998 and 2009. As various radiotherapy schedules had been used, biologically equivalent doses (BEDs) were calculated for all the patients. A total of 68 patients were eligible for SBRT (peripheral T1-3 N0 tumours < 5 cm in diameter). Overall survival (OS) and local progression free survival (LPFS) were estimated using Kaplan-Meier methodology for the entire study population and for the groups eligible and ineligible for SBRT. Univariate and multivariate analyses were performed for the prognostic factors.

Results: Median BED in the study population was 74 Gy (58–82 Gy). Patients eligible for SBRT had a significantly lower gross tumour volume (GTV) than the other patients ($p < 0.00001$). Three-year OS and LPFS were 37% and 50%, respectively. When we compared patients eligible for SBRT and those ineligible for SBRT the only significant difference was for three-year LPFS (58% v. 35%, $p = 0.04$). Multivariate analysis showed that only GTV, performance status and tumour stage were significantly correlated with local curability.

Conclusions: We showed an improved local control following 3D-CRT in patients eligible for SBRT compared to the other patients. However, also in these cases, local control was inferior compared to the outcomes of SBRT reported in the literature.

Key words: non-small-cell lung cancer, radiotherapy, conformal radiotherapy, SBRT, early-stage disease

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Introduction

Surgery (lobectomy, bilobectomy or pneumonectomy) is the treatment of choice for early-stage (stage I or II) non-small-cell lung cancer (NSCLC) and is associated with a 5-year survival of 50–60% [1]. Brown et al. [2] showed that only 18% of patients below 65 years of age, 12% of patients aged

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66–75 years and 2% of patients over 75 years of age were eligible for surgery at diagnosis. Lung cancer affects the elderly population; more than 50% of patients with NSCLC are over 65 and nearly one third are over 70 years of age [3]. In 2005 in Poland, 42% of patients who had died from lung cancer were at least 70 years of age [4]. Radiotherapy remains the treatment of choice in NSCLC patients ineligible for surgery due to non-oncologic reasons. However, the outcomes of radiotherapy in early-stage NSCLC remain unsatisfactory compared to the outcomes of surgery. Five-year survival and local control following radical radiotherapy alone for early-stage NSCLC are estimated at 30% and 50%, respectively [5].

In recent years, the hopes to improve treatment outcomes in patients with NSCLC ineligible for surgery, especially in patients with peripheral tumours, are associated with the use of stereotactic body radiotherapy (SBRT). A systematic review, 5-year survival in patients undergoing SBRT was estimated at 47% (range: 18–78%) and local control at 80–100% [6]. These outcomes are comparable with treatment outcomes in patients undergoing surgery and are far superior than the outcomes of conventional radiotherapy. Randomised studies to compare SBRT with surgery and with radiotherapy are, however, lacking. In the case of conventional radiotherapy the patients often have larger tumours, often centrally located, in which case the toxicity of SBRT is considerable. Timmerman et al. [7] administered SBRT to 70 patients with central tumours and recorded 14 cases of grade 3–5 toxicity (6 toxic deaths), which suggests a limitation of this method in centrally located lung cancers. Two prospective phase II studies are currently ongoing and their aim is to compare the outcomes of conventionally fractionated three-dimensional conformal radiotherapy (3D-CRT) with the outcomes of SBRT, namely an Australian study (TROG 09.02) comparing 3D-CRT at the dose of 60–66 Gy given in 30–33 fractions versus SBRT at the dose of 54 Gy in 3 fractions, and a Scandinavian study (SPACE, Scandinavian Stereotactic Precision and Conventional Radiotherapy Evaluation) comparing 3D-CRT at the dose of 70 Gy given in 35 fractions versus SBRT at the dose of 45 Gy in 3 fractions.

At our centre, in peripheral tumours, we often use accelerated hypofractionated 3D-CRT, which results in a higher biological dose. SBRT is not available. Given the lack of prospective studies comparing 3D-CRT versus SBRT, a retrospective assessment of 3D-CRT outcomes in patients with NSCLC who would have been potentially eligible for SBRT but received 3D-CRT with dose escalation also provides important information.

The aim of our study was to perform a retrospective assessment of treatment outcomes in patients with early-stage NSCLC who had received 3D-CRT with a particular focus on patients who were potential candidates for SBRT.

Material and methods

We evaluated 132 patients with stage I or II NSCLC according to the UICC TNM classification (5th and 6th editions) [8] who had received radical conformal radiotherapy at the Oncology Centre — Maria Skłodowska-Curie Memorial Institute in Warsaw, Poland, between 1998 and 2009. Table 1 summarises patient characteristics. The patients met the Centre's eligibility criteria for radical radiotherapy, which included: histopathological confirmation of NSCLC, Karnofsky performance status (KPS) of over 70%, no weight loss exceeding 10% over 6 months prior to treatment, adequate pulmonary function to be able to undergo radical radiotherapy and ineligibility for surgical treatment due to medical reasons or due to refusal of consent. In very few cases we considered patients with poor performance status or with a weight loss exceeding 10% due to non-malignant causes eligible for radical radiotherapy.

In order to stage the tumour each subject underwent the following: clinical examination, blood tests (complete and differential blood cell counts, kidney and liver function tests, coagulation tests), chest X-rays in the posteroanterior and lateral views, a brain CT or MRI scan, and — if distant metastases were being suspected — bone scintigraphy. Nine patients (7%) had undergone a baseline PET-CT scan for the purposes of staging and establishing treatment. Eleven patients (8%), prior to radiotherapy, had received an average of 3 (range: 2–6) courses of platinum-based chemotherapy (cisplatin plus vinorelbine [PN] or carboplatin plus vinorelbine [KN]).

Radical radiotherapy regimens in NSCLC changed several times during the study period. Our patients received conventional radiotherapy (total doses of 60–74 Gy in fractions of 2 Gy, 5 days a week), accelerated hyperfractionated radiotherapy (total dose of 60 Gy in fractions of 1.5 Gy, 3 times a day, 15 fractions a week) or various forms of accelerated hypofractionated radiotherapy (from a mild hypofractionation of 66 Gy in fractions of 2.2 Gy given 5 times a week through a total dose of 56.7 Gy in fractions of 2.7 Gy given 5–6 times a week, to a total dose of 48–52 Gy in fractions of 4

Table 1. Patients' characteristics

Characteristic	Number (percent) of patients
Sex	
Male	103 (78)
Female	29 (22)
Age (years)	Median: 71,5 (range: 51–89)
Karnofsky performance status (KPS)	
90%–100%	50 (38)
70%–80% [w tym/including: 70]	82 [17] (62)
Weight loss in the previous 6 months	
> 10%	2 (1)
5–10%	10 (8)
No weight loss or < 5%	120 (91)
Comorbidities*	
Yes	125 (95)
No	7 (5)
Histology	
Squamous	58 (44)
Adenocarcinoma	11 (8)
Non-small cell without further specification	59 (45)
No histology	4 (3)
Stage	
I	85 (64)
II	47 (36)
T-category	
T1	43 (33)
T2	54 (41)
T3	35 (26)
N-category	
N0	121 (92)
N1	11 (8)
Side	
Right	71 (54)
Left	61 (46)
Lobe	
Upper	73 (55)
Middle	9 (7)
Lower	47 (36)
All	3 (2)
Neoadjuvant chemotherapy	
Yes	11 (8)
No	121 (92)

*Comorbidities were defined in this study as the need for the permanent drug use because of the chronic disease and/or other malignancy in the history

Gy given 5 times a week). Elective nodal irradiation (ENI) was employed in the earlier period, while in the later period ENI was not used in patients with peripheral tumours and was limited to the hilum in patients with central tumours. The radiotherapy regimens used in our patients are summarised in Table 2.

Only those patients were included in the study in whom radiotherapy planning had been conducted entirely with the use of three-dimensional planning and in whom the requirements of conformal radiotherapy had been met. Radiotherapy planning was conducted in accordance with the recommendations of the International Commission on Radiation Units and Measurements (ICRU) Report No. 62 concerning the principles of 3D-CRT use [9]. The dose was prescribed at the ICRU reference point. The minimum and maximum doses to the planning target volume (PTV) were 95% and 107%, respectively (in cases of large PTV, delivering a minimum dose of 90% was acceptable). Target volumes were defined in accordance with the protocol. Gross tumour volume (GTV) was defined as the tumour or, in the case of N1, hilar lymph nodes defined on the pulmonary window. Clinical tumour volume (CTV) was obtained by adding a margin of 5 mm or, in cases of central tumours, by adding a margin of 5 mm and the ipsilateral hilum. PTV was established by adding CTV to an individually selected margin following previous verification of respiratory mobility in three dimensions on a simulator. Elective mediastinal irradiation was used in some patients. The mean dose delivered to the lungs did not exceed 15 Gy for peripheral tumours treated with hypofractionated radiotherapy and 20 Gy for tumours treated using conventionally fractionated radiotherapy. Less than 35% of the lung volume received a dose exceeding 20 Gy. The maximum dose delivered to the spinal cord did not exceed 50 Gy in the case of conventional fractionation and 36 Gy in the case of hypofractionation. A nominal energy of photons X of 6 MV was used and only in exceptional cases a photon energy of 15 MV was utilised. Normally, 3 to 5 coplanar radiation beams were used (with the exception of situations where the field-in-field technique rather than wedge was used).

In order to compare the total doses given to the patients with the use of various fraction doses in various treatment periods we converted the physical doses into biologically equivalent doses (BEDs), taking into account treatment durations and fraction doses. We used the following formula proposed by Fowler [10]:

$$BED = nd\,[1 + d\,(\alpha/\beta)] - \ln 2\,(T - Tk)$$

where n is the number of fractions, d is the fraction dose, T is the total irradiation time, α/β is the ratio of radiation susceptibility and fraction dose (which has been assumed to be equal to 10 for lung cancer), Tk is the time after which accelerated tumour repopulation (increased tumour proliferation) is observed (which we assumed to be 28 days, according to Fowler).

We retrospectively identified the group of patients whose tumours met the eligibility criteria for SBRT. We adopted the Radiation Therapy Oncology Group (RTOG) criteria which define the features of lung tumours eligible for SBRT using ablation doses, such as 3 × 20 Gy, namely T1–L2 N0 tumours or T3 tumours (chest wall), whose longest diameter was below 5 cm and whose location was peripheral (i.e. without any connection with the mediastinal structures or the pulmonary hili on imaging studies) [11].

Table 2. Radiotherapy schedules

Radiotherapy schedule	Number (percent) of patients
Conventional radiotherapy schedule, total dose: 60–74 Gy	
Without elective nodal irradiation	32 (24)
With elective nodal irradiation	24 (18)
Accelerated hyperfractionation with elective nodal irradiation	
Dose per fraction 1,5 Gy, 3 × daily; total dose 60 Gy	6 (5)
Hypofractionation	
Dose per fraction 2,2 Gy; total dose 66 Gy (elective irradiation of ipsilateral hilum)	10 (8)
Dose per fraction 2,7–2,8 Gy; total dose 56,7–58,8 Gy (with elective nodal irradiation)	2 [1] (1)
Dose per fraction 4 Gy; total dose 48–52 Gy (only tumor with margin)	58 (44)

The statistical analysis was performed using Statistica PL (version 6.0). The mean values were compared using the t-Student test. Overall survival, tumour-related survival, local progression free survival and distant metastasis free survival were estimated using Kaplan-Meier methodology and compared using a log-rank test for the group eligible for SBRT and the group ineligible for SBRT. All the survival times were calculated from the date of radiotherapy commencement. Index events for the assessment of tumour-related survival included tumour-related death, treatment toxicity and death from other causes in patients with recurrent disease. Death from a lung-cancer-unrelated cause without previous disease progression was considered a censored observation for tumour-related survival. Isolated regional recurrence (IRR) was diagnosed if metastases were discovered in previously uninvolved hilar lymph nodes or mediastinal or supraclavicular lymph nodes without prior or concurrent local progression. We evaluated the effects of potential prognostic factors (KPS, weight loss, age, sex, possible eligibility for SBRT, histologic type, peripheral versus central location of the tumour, stage, GTV, radiotherapy regimen, BED) on overall survival and local progression free survival using the log-rank test. Overall survival and local progression free survival were additionally compared between the group eligible for SBRT and the group ineligible for SBRT. The factors affecting these two types of survival in univariate analysis at the p value of < 0.2 were then included in multivariate analysis (Cox regression model).

Results

Median follow-up for living patients was 33 months (range: 14–122 months). Median GTV in the study population was 43 cm^3 (range: 3–319 cm^3). Median BED in the study population was 74 Gy (range: 58–82 Gy). A total of 68 out of 132 patients were eligible for SBRT. These patients had significantly lower mean GTV than did ineligible patients (36.5 cm^3 v. 88.8 cm^3, $p < 0.00001$). Patients eligible for SBRT received higher doses. The mean BED values for patients eligible and ineligible for SBRT were 74.6 Gy and 72.0 Gy, respectively ($p = 0.01$).

The estimated 2- and 3-year overall survival rates were 51% and 37%, respectively, and 95 patients died during observation. There was 1 toxic death due to radiation pneumonia 2 months after treatment. A total of 24 patients (18%) died within 7–89 months following radiotherapy (median: 20 months) from causes unrelated to the underlying malignancy. The estimated 2- and 3-year tumour-related survival rates in the study population were 59% and 47%, respectively. The overall survival curve for the study population is shown in Figure 1. Univariate analysis demonstrated that the following factors affected overall survival in a statistically significant manner: GTV (tumours with GTV values < 43 cm^3 and ≥ 43 cm^3 were associated with 3-year survival rates of 50% and 28%, respectively, $p = 0.0002$), performance status (3-year survival rates of 48% and 31% for KPS of 100–90% and 80–70%, respectively, $p = 0.0006$), disease stage (3-year survival rates of 45% and 22% for stage I and stage II disease, respectively, $p = 0.003$) and weight loss (3-year survival rates of 22% and 40% for patients with a weight loss of $> 10\%$ and the remaining patients, respectively, $p = 0.03$). No statistically significant relationship was demonstrated between the dose and overall survival, although the 3-year overall survival rates in patients receiving BED of at least 74 Gy and those receiving lower doses were 50% and 30%, respectively ($p = 0.1$). There was no difference in overall survival between patients eligible and ineligible for SBRT (3-year survival rates of 39% and 35%, respectively, $p = 0.3$). The radiotherapy regimen did not affect overall survival. Table 3 presents the detailed results of the univariate analysis with respect to overall survival. Multivariate analysis, in addition to the factors significantly associated with survival in the univariate analysis, demonstrated a significant negative correlation between age above 70 years and survival. The results of the multivariate analysis in terms of overall survival are summarised in Table 4.

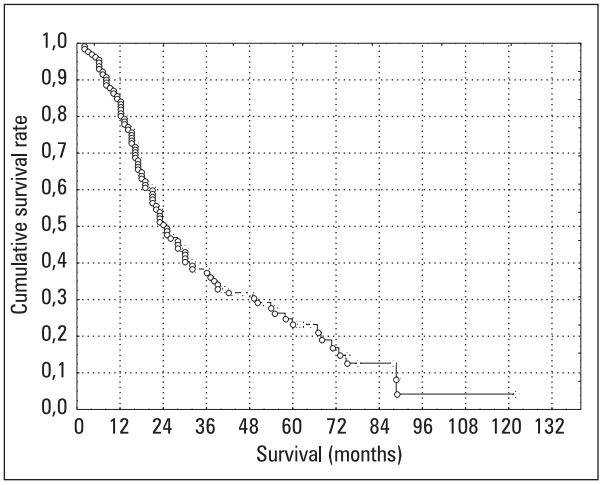

Figure 1. Overall survival for all patients

The estimated 2- and 3-year local progression free survival rates in the study population were 63% and 50%, respectively. The local progression

Table 3. Overall survival: results of the univariate analysis

Factor	Three-year overall survival rate	p-value
Gross tumor volume (GTV)		
< 43 cm^3 (median)	50%	
≥ 43 cm^3 (median)	28%	0.0002
Karnofsky performance status (KPS)		
100%–90%	48%	
80%–70%	31%	0.0006
Clinical stage		
I	45%	
II	22%	0.003
Weight loss in the previous 6 months		
$< 5\%$	40%	
$\geq 5\%$	21%	0.03
Sex		
Female	50%	
Male	35%	0.05
Histology		
Squamous	68%	
Adenocarcinoma	42%	
Non-small cell without further specification	28%	
No histology	50%	0.1
Age (years)		
≤ 70	46%	
> 70	31%	0.1
Biologically equivalent dose (BED)		
< 74 Gy (median)	30%	
≥ 74 Gy (median)	50%	0.1
Meeting inclusion criteria for SBRT		
Yes	40%	
No	38%	0.32

free survival curve for the study population is presented in Figure 2. In univariate analysis, the following factors significantly improved local control: a lower GTV ($p = 0.002$), stage I disease ($p = 0.004$) and KPS of 90–100% ($p = 0.02$). Patients eligible for SBRT also had a significantly superior local control with 3-year local progression free survival rates of 58% compared to 35% in patients ineligible for SBRT ($p = 0.04$). The local progression free survival curves for patients eligible and ineligible for SBRT are presented in Figure 3. The effect of the dose, broken down into doses equal to or higher than median BED (74 Gy) and doses lower than median BED, on local progression free survival did not reach statistical significance (3-year local progression free survival rates of 64% and 43%, respectively, $p = 0.1$). The results of the multivariate analysis in terms of local progression free survival are summarised in Table 5.

The estimated 2- and 3-year distant metastasis free survival rates in the study population were 71% and 62%, respectively. This endpoint did not differ significantly between patients eligible and ineligible for SBRT. A total of 5 cases of IRR were identified during the follow-up of 4 to 25 months (3 cases in the first year after treatment). The 3-year risk of IRR in the study population was 6%. IRR was identified in 3 patients eligible for SBRT (5%) and in 2 patients from the remaining group (4%). Two patients with IRR received elective irradiation of the mediastinum and in 3 cases radiotherapy was limited to the tumour with the margin.

Table 4. The multivariate analysis of factors determining overall survival

Factor	*Relative risk (RR) of death [95% confidence interval (CI)]*	*Level of statistical significance*
Karnofsky performance status (KPS)		
100%–90%	RW (RR): 0.42; PU (CI) (0.27–0.68)	
80%–70%	RW (*RR*): 1.0	p = 0.0004
Gross tumor volume (GTV)		
< 43 cm^3 (*median*)	RW (*RR*): 0.44; PU (*CI*) (0.28–0.70)	
≥ 43 cm^3 (*median*)	RW (*RR*): 1.0	p = 0.005
GTV as a continuous variable	RW (*RR*): 1.004 (cm^3); PU (*CI*) (1.001–1.007)	p = 0.02
Clinical stage		
I	RW (*RR*): 0.48; PU (*CI*) (0.30–0.78)	
II	RW (*RR*): 1.0	p = 0.003
Weight loss		
≥ 10%	RW (*RR*): 2.36; PU (*CI*) (1.25–4.45)	
< 10%	RW (*RR*): 1.0	p = 0.008
Age (years)		
> 70	RW (*RR*): 1.82; PU (*CI*) (1.15–2.88)	
≤ 70	RW (*RR*): 1.0	p = 0.01

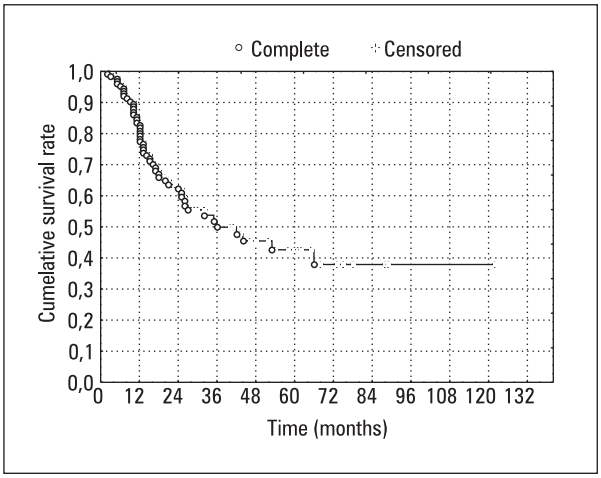

Figure 2. Local progression free survival for all patients

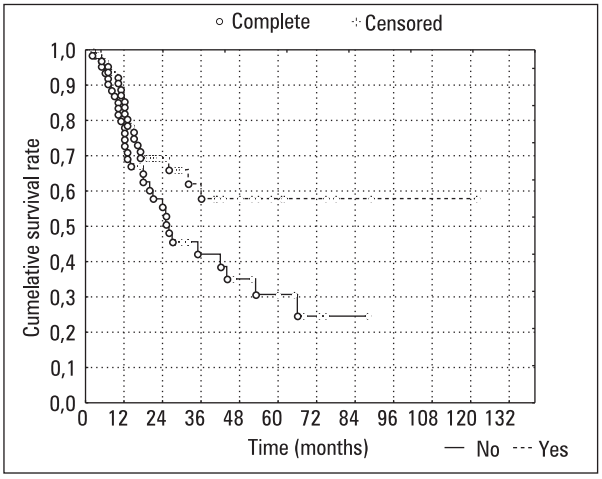

Figure 3. Local progression free survival for patients who met criteria of inclusion for SBRT and the remainder

Discussion

Our results for overall survival and local control following treatment with 3D-CRT in patients with early-stage NSCLC are similar to the results reported in the literature [5]. However, after selecting patients with tumour characteristics consistent with tumour characteristics in patients included in studies investigating SBRT in lung cancer, we observed a superior local control than in the remaining patients, without any differences in survival. Due to the retrospective nature of our study it is difficult to reliably establish whether the severity of co-morbidities in this group was higher than in the remaining patients. It may, however, be assumed that patients with small peripheral tumours who undergo radiotherapy have more contraindications for surgery than patients with larger central tumours. This could have affected the lack of differences in survival between the groups despite a superior local control in the group of patients potentially eligible for SBRT. The superior local control in the group of patients eligible for SBRT is associated with lower tumour volumes in this group. Low tumour volume was the strongest positive prognostic factor in our study, both in terms of local control and overall survival. Many

Table 5. The multivariate analysis of factors determining local progression free survival

Factor	Relative risk (RR) of death [95% confidence interval (CI)]	Level of statistical significance
Karnofsky performance status (KPS)		
100%–90%	RW (RR): 0.46; PU (CI) (0.24–0.82)	
80%–70%	RW (RR): 1.0	p = 0.01
Clinical stage		
I	RW (RR): 0.47; PU (CI) (0.25–0.88)	
II	RW (RR): 1.0	p = 0.02
Gross tumor volume (GTV)		
GTV as a continuous variable	RW (RR): 1.004 (cm^3); PU (CI) (1.001–1.007)	p = 0.04

papers have been published to confirm the negative effect of larger volumes of the lesions (tumour and involved lymph nodes — GTV) on survival in patients with NSCLC treated with radiotherapy [12–16].

Despite the relatively small tumour volumes in the group of patients eligible for SBRT, the demonstrated local control in this group (updated 3-year local progression free survival rate of 58%) is much worse than that in SBRT, in which case the 3-year local control rate, defined similarly to us as absence of disease progression, is 80–100% [6]. The doses given using the SBRT technique, especially in cases of peripheral tumours, are equivalent to biological doses exceeding 100 Gy and are therefore equivalent to doses that are much higher than the dose range used in our study (BED: 58–82 Gy). No effect of dose on outcomes within the employed dose ranges was shown. Martel et al. [17] suggest that doses necessary to cure NSCLC should exceed 84 Gy. This largely explains the difference in outcomes between 3D-CRT and SBRT. With 3D-CRT, administration of such high doses is difficult due to a lower conformality index (the dose decrease outside the treated tumour). Conventional fractionation, which is most commonly associated with using 3D-CRT, also leads to the prolongation of treatment duration, which results in decreased treatment efficacy when attempts to escalate the dose using this technique are made [18]. Shortening of the treatment duration is a factor that increases the biological efficacy of radiotherapy and, at the same time, by shortening the time spent by the patient travelling to the related radiotherapy sessions or hospitalisations, makes the treatment more comfortable and less expensive for the population of elderly and otherwise unwell patients. For this reason, at our centre, we used accelerated hypofractionated radiotherapy. The study regimen was taken from a study by Slotman et al. [19], who delivered 48 Gy in 12 fractions. The good tolerability of the treatment made it possible to increase the dose, with time, to 52 Gy in 13 fractions. The outcomes observed using this regimen are no different from those observed with conventionally fractionated radiotherapy regimens, although do not result in outcomes possible thanks to SBRT. Treatment with SBRT should be the treatment of choice for patients who are eligible for this method.

Our study has obvious methodological limitations because of its retrospective nature and the arbitrary division of patients into those eligible and those ineligible for SBRT. In real life, many other patient- and tumour-related factors would affect patient assignment to the two treatment groups. In addition, the outcomes of SBRT are often based on short follow-up periods and early development of fibrosis following a high dose of SBRT may confound the evaluation of local control, hence the outcomes may be worse than those reported in the literature. Similar objections may be raised with reference to our study, where the median follow-up period was 30 months and the assessment of local control was based on the absence of radiological progression. Despite that the outcomes were still inferior to those obtained using SBRT. SBRT seems to be an appropriate method of treatment intensification in a population of patients ineligible for surgery, such as patients with multiple co-morbidities and often elderly patients, as this method is characterised by low toxicity provided that the tumours are appropriately qualified for the treatment [20]. All the other forms of treatment intensification, such as radiochemotherapy or alternative fractionation regimens, failed to improve the outcomes in this group of patients compared to conventional radiotherapy alone [21].

The main type of failure in our study was local recurrence, which is consistent with the results of all the studies investigating radiotherapy in patients with NSCLC. Isolated mediastinal nodal recurrences were rare, which justifies the generally adopted approach to skip elective mediastinal irradiation in early-stage NSCLC [22]. Furthermore, the incidence of this failure was not reduced by using elective irradiation. Three out of 5 isolated regional recurrences developed within the first year after treatment. Only a few patients in the study population had undergone PET-CT prior to radiotherapy, which could have led to unsatisfactory outcomes. One of our prospective studies of 100 patients demonstrated that PET-CT before radical radiotherapy planning led to disqualification of 25% of patients from treatment, while in 27% of patients eventually considered eligible for radiotherapy, the irradiation field was modified following the PET-CT scan due to the identification of additional pathological lesions [23]. This is most likely another potential method to improve the outcomes of radiotherapy, also in patients with early-stage NSCLC.

Conclusions

The retrospective nature of our study limits the conclusions. However, in view of the absence of prospective studies of 3D-CRT in patients eligible for SBRT, it seems that based on our results the following practical conclusion may be drawn: given the poorer local control following 3D-CRT compared to the known outcomes of SBRT reported in the literature, patients with early-stage NSCLC who are ineligible for surgery but who are eligible for SBRT should be offered treatment with SBRT rather than with 3D-CRT.

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