Original Study

Patient-reported Outcomes After the Treatment of Early Stage Non–small-cell Lung Cancer With Stereotactic Body Radiotherapy Compared With Surgery

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Abstract

Quality of life is an important factor in deciding between stereotactic body radiotherapy and surgery when the expected difference in survival benefit is very small. This Dutch direct comparison of 41 patients treated with stereotactic body radiotherapy and 41 with surgery, revealed no clinical significant differences in quality of life the first year after treatment.

Introduction: As there is increasing evidence for comparable survival after either stereotactic body radiotherapy (SBRT) or surgery for patients with stage I non–small-cell lung cancer (NSCLC), treatment impact on the quality of life (QoL) is essential for well-informed decision-making. Our previous work evaluated health utility between surgery and SBRT in stage I NSCLC. The aim of this secondary analysis is to directly compare QoL in the first year after SBRT and surgery. **Materials and Methods:** QoL was assessed at baseline and 3, 6, and 12 months after treatment. Two prospectively collected databases of patients with clinically proven stage I NSCLC, from 2 large hospitals in the Netherlands, were pooled (n = 306; 265 patients were treated with SBRT and 41 patients with surgery). To correct for confounding, propensity scores were calculated, to be selected for surgical treatment. A mixed model analysis was used to study differences in QoL between the 2 treatments. **Results:** The 41 surgical patients were matched to 41 SBRT patients on propensity score with a 1:1 ratio. At baseline, patients in the surgery group report a lower QoL compared with patients in the SBRT group. However, during the first year after treatment, no clinical meaningful differences were observed, except for role functioning, between patients treated using either modality. **Conclusion:** This study comparing a matched cohort revealed no clinically significant differences in QoL following either SBRT or surgery for early stage NSCLC. These results support the hypothesis that surgery and SBRT are comparable treatments.

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Introduction

Surgical resection is still the recommended-treatment for patients diagnosed with stage I non–small-cell lung cancer (NSCLC). An effective non-surgical treatment is stereotactic body radiotherapy (SBRT).[1] SBRT is nowadays reserved for patients at unacceptably high risk of surgical complications.[2] Beside medical inoperability, there are also patients who refuse surgical treatment for personal motives.[3] The efficacy of SBRT, together with the favorable side-effect profile,[4] has led to several propensity score-matched comparative studies comparing SBRT with surgery. A recent

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meta-analysis of several of these studies by Chen et al observed better overall survival following surgical treatment, but similar disease-specific survival following either treatment. Given the absence of a difference in disease-specific survival, a good explanation for the difference in overall survival may be that, in general, more comorbidities are present in those patients treated with SBRT.[5] Randomized controlled trials that compare SBRT with surgical resection for operable stage I NSCLC have been designed, but were closed prematurely owing to low accrual of patients. In a pooled analysis of 2 of these randomised trials, the estimated 3-year overall survival was 95% after SBRT compared with 79% after surgery.[6] A subsequently designed randomized controlled trial, improving accrual by the use of pre-randomization prior to consent to either surgical resection (sublobar or segmental resection) or SBRT, is still ongoing.[7] Therefore, successfully completed randomized trials providing high-level evidence on the comparability of both treatment modalities are not expected in the near future. Hence, an ongoing debate whether SBRT is equivalent to surgery persists.

In all newly diagnosed patients with lung cancer, treatment should be discussed in a multidisciplinary thoracic oncology team. Regarding surgical treatment, consideration of the perioperative risk and evaluation of performance status, pulmonary function, and maximum oxygen uptake is needed.[8] In patients at high risk but without a strict contraindication to surgery, it is unclear which treatment is preferable. Ideally, clinicians inform these patients about the benefit/risk ratio related to each treatment modality and together they will form a decision for treatment.[9-11] Indispensable input for this shared decision-making process between patients and their providers is the impact of treatment on health-related quality of life (QoL).[12]

Previous studies of QoL after SBRT were reviewed by Chen et al in 2016. In general, QoL after SBRT is preserved.[13] In contrast, a detrimental treatment-effect on QoL was reported in the early post-treatment period following surgery, according to the review of Poghosyan et al.[14] This implies that we may expect a difference in treatment impact between the treatment modalities. However, in the only published comparative study (the secondary analysis of the Radiosurgery Or Surgery for operabele Early stage non-small cell Lungcancer [ROSEL] trial), QoL was comparable in all domains following either surgery or SBRT, and furthermore, after SBRT, an improved global QoL was observed.[15] Large study data providing a direct comparison are lacking.

In view of these results, Wolff et al performed a comparative analysis of health utility in a carefully matched cohort of patients with stage I NSCLC. Health utility measures QoL with a single scale. No clinically meaningful difference in health utility between surgically treated patients and patients treated with SBRT was observed.[16] The purpose of the current follow-up study of Wolff et al is to compare the different QoL domains and symptom items in the first year after either SBRT or after surgery.

Materials and Methods

Patient Population and Selection

This was a secondary analysis of 2 prospectively collected databases of patients with stage I NSCLC. The first cohort was sampled at the Sint Antonius Hospital Nieuwegein, the Netherlands, between March 2013 and January 2016, including patients who were treated with SBRT (delivered in an outpatient setting at the University Medical Center Utrecht) or surgery. The second cohort consists of patients who were all treated with SBRT at the VU University Medical Center Amsterdam, The Netherlands, between April 2003 and November 2008.[17]

Patients were included if they had clinically proven stage I NSCLC, evaluated using the National Comprehensive Cancer Network guidelines. Tumor staging was carried out according to the seventh edition of the tumor, node, metastasis classification.[18] A biopsy-proven diagnosis before receiving SBRT was not always performed, owing to risks of complications in these patients who often have poor pulmonary function.[19] The single pulmonary nodule score of Herder et al was calculated to estimate the probability of malignancy.[20] Patients were excluded when there was one of the following: (1) previous malignancy, (2) second primary lung tumor, (3) chronic obstructive pulmonary disease Global Initiative for Obstructive Lung Disease (GOLD) grade ≥ 3, or (4) an Eastern Cooperative Oncology Group (ECOG) performance score ≥ 3.

Treatment

Before treatment, all patients were discussed in a multidisciplinary meeting. This team consists of a pulmonologist, thoracic surgeon, radiation oncologist, and a nuclear physician. Depending on the localization of a tumor and on patient characteristics, a pulmonary resection including nodal resection according to the European Society of Thoracic Surgeons guidelines was carried out via video-assisted-thoracic surgery or via thoracotomy.[21]

SBRT was delivered in an outpatient setting. Different stereotactic regimens were used, depending on tumor size and location: 3 fractions of 18 Gy or 20 Gy, 5 fractions of 12 Gy, or 8 fractions of 7.5 Gy. Patients received SBRT in 3 to 8 treatment sessions, spread over 3 times a week. They all received a biological effective dosage $>$ 100 Gy. The clinical practice did not change between 2003 and 2016.

Patient-reported Outcomes (PROs) and QoL Instrument

QoL was measured using PROs. To collect PROs, the standardized European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ-C30) and the lung cancer-specific supplementary questionnaire (QLQ-LC13) was used. This questionnaire incorporates 5 functional domains, 3 symptom scales, and 6 single items. From the symptom scales and items, we have only included pain, dyspnea, and fatigue. We decided to exclude symptom items that are related to side effects of chemotherapy. Dyspnea and pain scores (a single item as well as a symptom scale) were pooled because the scoring approach is identical. Patients were asked to complete the questionnaires before clinical visits at baseline and at 3, 6, and 12 months after treatment. Patients were included in our analysis when they completed the questionnaire at least once. Follow-up time was 12 months because the incidence of most toxicities after both treatment modalities is expected to be seen in this time period.[4,22]

For the purpose of this analysis, QoL data was censored after a recurrence was detected or when adjuvant treatment started. The reason is that the current study focusses on the impact of surgery and SBRT on patients' functioning and symptoms, and not the

impact of disease progression. For the same reason, only dyspnea, fatigue, and pain symptom items were included. All of the domains and items have a score in the range of 0 to 100. A high score on a functional domain reflects a high level of functioning, whereas a high score on a symptom item represents a high level of symptoms.

Statistical Analysis

To correct for selection bias owing to the non-randomized nature of treatment allocation in this study, propensity score matching was used. Propensity scores, which represent the chance to be selected for surgical treatment, were calculated. The scores are calculated by means of logistic regression using forward treatment selection of the potential treatment confounders: age, gender, stage (IA and IB), dichotomized ECOG score, GOLD stages and forced expiratory volume in 1 second percent predicted. For the final propensity model, age, dichotomized ECOG score and forced expiratory volume in 1 second percent predicted scores were selected. Surgical patients were matched to SBRT patients on propensity score with a 1:1 ratio. Further details of the propensity score matching have been described earlier.[16]

Differences in (baseline) patient characteristics between the 2 treatment groups were assessed using the χ^2 test for categorical variables and the t test for continuous variables. The longitudinal structure of the dataset required the use of a mixed model analysis to correct for correlations between observations with the same patients. The mixed model used fixed effects for treatment, time, and their interaction, and random effects per patient. A Wald test was used to analyze significance of the fixed effects.

The clinical meaningful difference was expected when there were 10 or more points of difference at any time period.[23]

All analysis were performed by using the Statistical Package for the Social Sciences (SPSS) software (version 22.0) and R (version 3.3.1.).

Results

Patient Baseline Characteristics

Among the 471 patients in the 2 cohorts, 302 patients met the inclusion and exclusion criteria. Of these 302 patients, 261 patients were treated with SBRT (40 at the Sint Antonius Hospital; the remaining at the VU University Medical Center) and 41 patients with surgery.[17] The main reasons for exclusion were a COPD GOLD score of ≥ 3 and a previously diagnosed malignancy. The propensity score matching resulted in the selection of a subgroup of 41 SBRT patients that matched the 41 surgical patients. The abovementioned is summarized in Table 1. There were no significant changes between the matched groups. Lobectomy was performed in 32 (78%) patients, and thoracotomy was the most performed procedure.

Health-related Questionnaire Response Rates

Completion rates of the serial evaluation of patient reported outcomes were 75% at 3 months, 70% at 6 months, and 50% at 12 months. There were no significant differences in completion rates between the treatment groups. The missing results are explained as follows: 5 patients had recurrence of disease (in the SBRT group), 9 patients received adjuvant treatment after surgery, and in total, 22 patients were lost to follow-up, mostly owing to back-referral to referring centers (for detailed specifications, see Supplemental Tables 1 and 2 in the online version), and therefore can be seen as missing at random. It should be noted that these patients had no poorer baseline QoL values than patients with available follow-up.

QOL: Differences Over Time Between the SBRT and Surgery Groups

The patients' emotional and cognitive scores showed no significant differences between surgery and SBRT throughout the first year after diagnosis. All other scores showed significant differences between surgery and SBRT at baseline (Figure 1). This difference was largest for role functioning (26.68), with a significant treatment $\times$ time effect ($P < .001$). After-treatment differences between the 2 treatments were insignificant except for role functioning (16.38) and dyspnoea (8.98). Additional analyses with mixed models showed that the average dyspnea score was also significantly lower at 3 months independent of treatment ($P = .034$) (see Supplemental Table 3 in the online version).

Discussion

As there is increasing evidence for comparable survival following either SBRT or surgery for early stage NSCLC,[5,6] treatment impact on QoL may become decisive in choosing the suitable treatment for patients balancing on the edge of acceptable or non-acceptable operable risk. It is against this background that we performed a direct comparison by carefully matching a cohort of patients with early stage NSCLC treated with either SBRT or surgery. To date, we report no clinical meaningful differences in any QoL domain or symptom item between the SBRT or surgery groups. Although role functioning seemed to be in favor of SBRT at 3 months, this is in context of a low baseline level for the surgical cohort but with a rapid rate of change. A counter-intuitive finding was the significantly lower QoL reported in the surgical group compared with the SBRT group before the treatments started. This difference disappeared 6 months after treatment. Although the sample size was small, these results may support the theory that SBRT and surgery are equivalent therapies in terms of QoL.

Our results are in line with the only published direct comparison of QoL after SBRT versus surgical resection for stage IA NSCLC reported from the ROSEL randomised control trial. This trial was prematurely halted owing to low accrual of patients. In these 22 patients QoL was preserved and in favor of SBRT in terms of global QoL.[15]

SBRT

Treatment-related toxicity in patients with early stage NSCLC are different for surgical resection and SBRT.

Radiation pneumonitis and chest wall pain are the main toxicities following SBRT. But radiation pneumonitis of grade ≥ 2, usually seen after a median of 5 months, is reported in less than 10% of the patients.[4,24] Chest wall pain or chest wall syndrome is mainly reported when the peripheral tumor is close to the chest wall and can be minimized with a risk-adaptation scheme.[25-27] In addition to the favorable toxicity profile of SBRT, the principle of organ preservation, its non-invasive nature, and the short treatment time is attractive.

Indeed, SBRT did not influence QoL over 12 months in our patient group. A small increase in dyspnea, fatigue, and pain was

Table 1 Patient Characteristics

	Population Statistics, n (%)			Propensity Score Matched, n (%)	
	Surgery (n = 41)	SBRT (n = 261)	*P*	SBRT (n = 41)	*P*
Age, y (SD)	66.7 (7.6)	74.3 (8.1)	<.001	69.8 (8.3)	.080
Gender			.53		.494
Male	24 (58.5)	166 (63.6)		27 (65.9)	
Female	17 (41.5)	95 (36.4)		14 (34.1)	
Stage			.47		.206
IA	28 (68.3)	163 (62.5)		33 (80.5)	
IB	13 (31.7)	98 (37.5)		8 (19.5)	
ECOG score			<.001		.199
0	35 (85.4)	51 (19.5)		33 (80.5)	
1	5 (12.2)	140 (53.6)		3 (7.3)	
2	1 (2.4)	70 (26.8)		5 (12.2)	
GOLD			.03		.195
0	20 (48.8)	74 (28.4)		13 (31.7)	
1	5 (12.2)	47 (18.0)		10 (24.4)	
2	16 (39.0)	140 (53.6)		18 (43.9)	
FEV1%	84.3 [17.4]	78.0 [19.4]	.05	82.7 [18.7]	.696
Surgery					
VATS (lobectomy)	5 (12.2)				
Thoracotomy	36 (87.8)				
Lobectomy	32 (78)				
Bilobectomy	2 (4.9)				
Wedge	1 (2.4)				
Pneumonectomy	1 (2.4)				
SBRT fractionation					
3 × 20 Gy		81 (31.2)		15 (36.6)	
3 × 18 Gy		7 (2.7)		4 (9.8)	
5 × 12 Gy		128 (49.2)		18 (43.9)	
8 × 7.5 Gy		44 (16.9)		4 (9.8)	

This table is reproduced with permission from the Journal of Thoracic Oncology.
Abbreviations: ECOG = Eastern Cooperative Oncology Group; FEV1 = forced expiratory volume in 1 second; GOLD = Global Initiative for Chronic Obstructive Lung Disease; SBRT = stereotactic body radiation therapy; VATS = video assisted thoracoscopy.

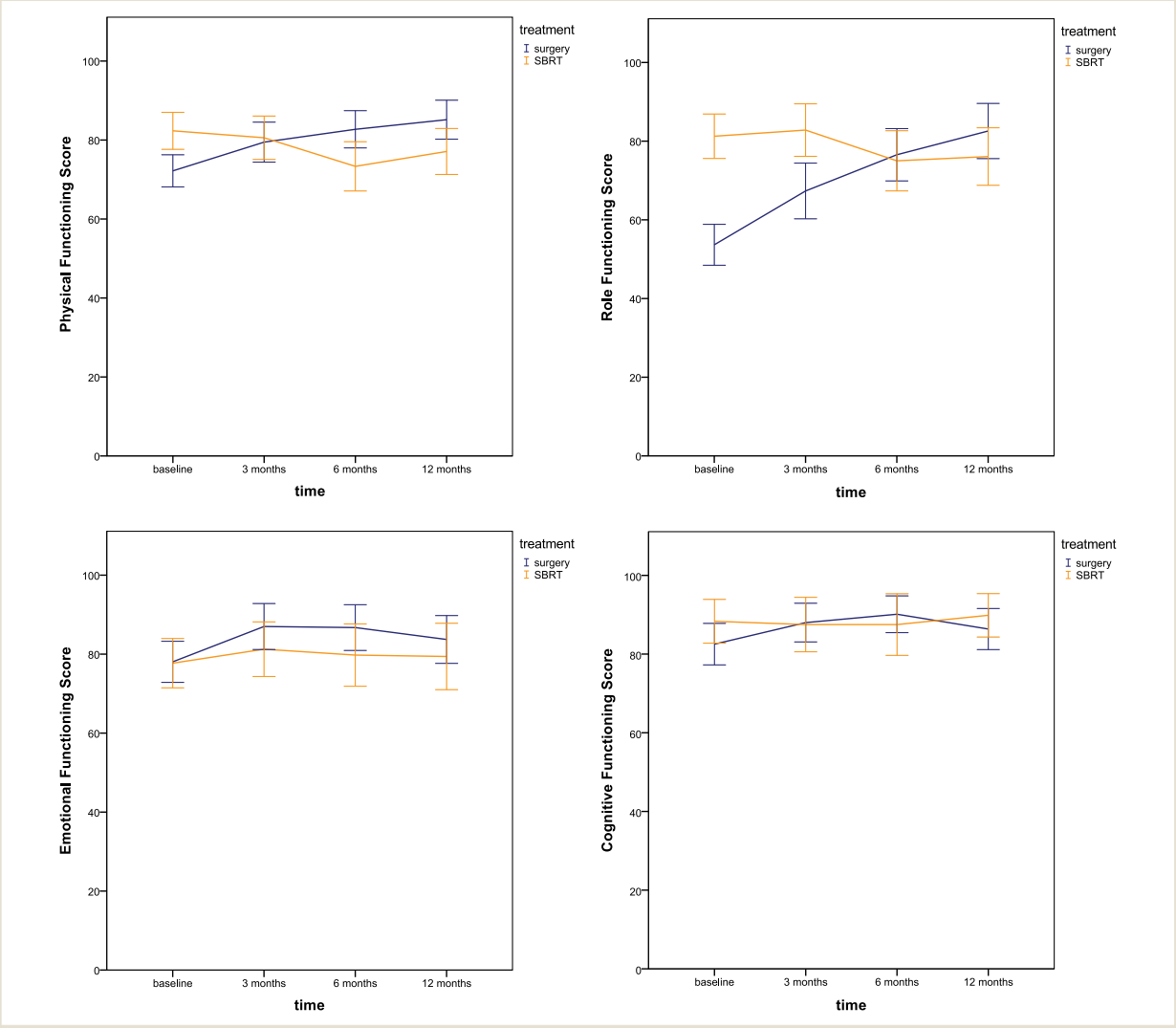
observed after treatment, but did not reach the threshold of clinically significant difference. This finding is supported by previous studies examining QoL after SBRT. Chen et al reviewed 9 prospective studies between 2010 and 2015. The median follow-up length was 20 months. The median number of patients studied was 39 patients (range, 19-382 patients). From the included studies that examined QoL changes over time, 5 studies reported no differences in QoL compared with baseline. The only reported clinically significant negative effects were an increase in fatigue after 135 days reported in a small study of Ferrero et al (n = 30) and a clinically significant increase in dyspnea 2 years after SBRT. Furthermore, the results of van der Voort van Zyp showed a positive effect on QoL, with a moderate improvement in emotional functioning at 12 months (difference on average, 12 points).[13,28,29] Toxicities were not included in our analysis. In light of the preserved QoL, we have no indications that our SBRT cohorts deviate from the average toxicity rates. In summary, SBRT has shown to be an overall well-tolerated treatment modality in terms of patient-reported health-related QoL.

Surgery

Surgery is an invasive therapy, with a corresponding hospital stay of, on average, 4 to 7 days. After a video assisted thoracoscopy procedure, the length of hospital stay tends to be less compared with an open surgical procedure.[30-32] We hypothesized that surgery would negatively influence QoL in the early post-treatment period. Complications of surgery include pneumonia and persistent air leak.[22] The estimated 30-day mortality rate from lobectomy is 2.07% versus 0.73% after SBRT.[33] Furthermore, patients are given advice on lifestyle modification during the first 4 to 6 weeks after the operation in our center. They are recommended to restrict activities, not to carry weights more than 1.5 kilogram, and not to travel by airplane during the same period.[34]

There have been a number of studies evaluating QoL after surgical resection for NSCLC. Poghosyan et al reviewed 19 studies, including both FACT-L questionnaires as well as EORTC-QLQ-C30. The inclusion criteria were stage I to III NSCLC. Contrary to our results, in this review, patients had a poorer mental QoL and

Figure 1 Baseline and Follow-up Patient-Related Outcomes. Baseline is Pre-treatment. A High Score on a Functional Domain Reflects a High Level of Functioning, whereas a High Score on a Symptom Item Represents a High Level of Symptoms



Abbreviation: SBRT = stereotactic body radiation therapy.

a decreased physical function after surgery compared with pre-treatment values, which persisted at 2-year follow-up.[14] The impaired QoL in most of the domains/items in patients waiting for surgical resection is described in one study only.[35]

Interpretation in Terms of Mechanisms

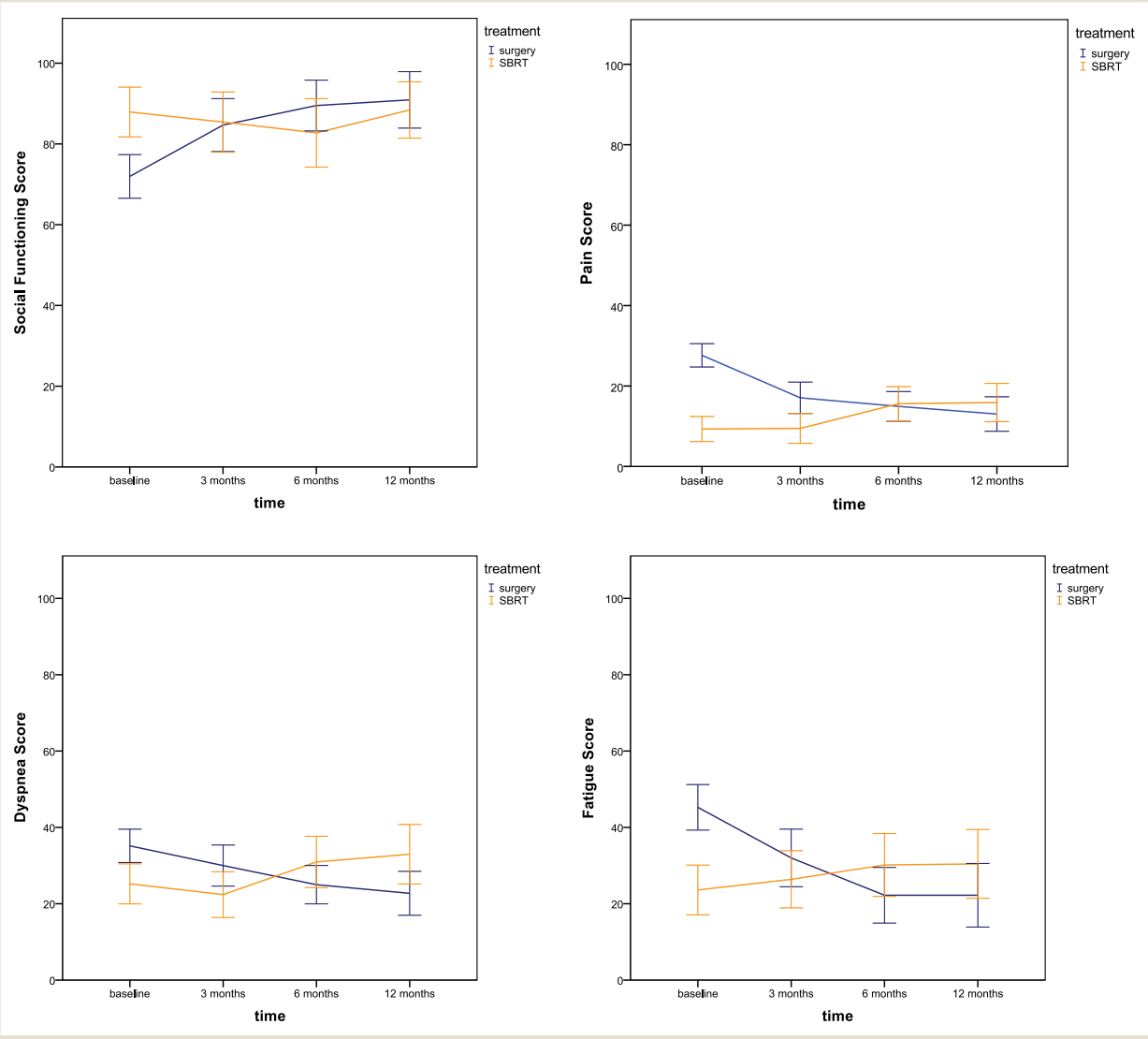
Difference at Baseline

One of the explanations for the low and significantly different baseline values in patients awaiting surgery compared with patients awaiting SBRT might be that, in most patients receiving surgery, the diagnosis was biopsy-proven, whereas in most patients receiving SBRT, there is only a suspicion of lung cancer. This may suggest 2 things: there is potential hope for benign disease in patients submitted for SBRT, and for a biopsy-proven disease, diagnostic examinations including mediastinal staging with risks of complications have taken place.[19,36] However, the influence of pretreatment staging in lung cancer on QoL is not known.

Changes Over Time and the Process of Denial and Stigmatization

We can only speculate why baseline results are not the same in this carefully matched cohort of patients treated with SBRT or surgery. Also, the increase in QoL following surgery is remarkable. At the time of diagnosis, there are usually no symptoms in patients with early stage disease produced by the disease itself.[37] The confrontation with lung cancer is predominantly a stressful event. Denial in patients with cancer is often seen and associated with

Figure 1 Continued



better social outcomes (role functioning, social functioning) and less anxiety and depression than in patient with a low level of denial.[38] The aspect of denial might be more dominant in patients offered SBRT than surgery, but this aspect has not been studied so far.

In the light of the abovementioned, the same mechanism applies to lung cancer stigma (including feelings of shame, regret about one's lung cancer) and is related to poorer psychological outcomes throughout the cancer trajectory.[39] Lung cancer stigma might be less pronounced in SBRT patients, given the potential hope of benign disease, than in surgically treated patients.

Furthermore, well-being may fluctuate and change after successful treatment.[40] This could explain the increase in QoL 6 months after surgery in this study. Whether there is reason to believe that this process is different for patients undergoing surgical resection or SBRT is not known.

Strengths and Limitations

This study is a direct comparison between surgery and SBRT and gives insight in the different QoL domains and symptom scales after treatment. Direct comparisons in this field are scarce.

The retrospective nature of the analysis and small study population, after matching had been applied, are limitations of this study. Another limitation is the increasing number of missing questionnaires over the follow-up time. Ten patients were censored because of recurrence of disease or adjuvant therapy. The remaining missing questionnaires were mainly because of the fact that the VU Medical

Centre is a referral center for patients, and after treatment, patients were referred to their local hospitals for follow-up.[17] Although video assisted thoracoscopy is associated with better short-term outcomes, the most performed procedure in this selected cohort was thoracotomy, without an observed detrimental effect on QoL.[41]

Conclusion

In conclusion, no clinically significant differences in QoL were observed in a matched cohort of patients diagnosed with early stage NSCLC and treated with either surgery of radiotherapy during the first year after treatment. However, at baseline, QoL in patients who underwent surgery was significantly lower than in patients who underwent SBRT. This was restored 6 months after treatment. These results support the hypothesis that SBRT and surgery are equivalent treatment options. All these patient-relevant aspects of the treatment should be weighted and considered during shared decision-making.

Clinical Practice Points

- SBRT is an effective alternative treatment modality for patients with inoperable stage I NSCLC. High-level evidence about equal (or comparable) survival outcomes following either SBRT or surgical resection in operable patients is still pending.
- Meanwhile, the influence of treatment on QoL is essential for the future shared-decision making process. Many studies have investigated QoL after surgery and SBRT. In general, QoL after SBRT is preserved. In contrast, a detrimental treatment-effect on QoL was reported in the early post-treatment period following surgery. However, direct comparisons are scarce.
- In this study, we compared the impact of treatment on QoL by using PROs in a matched cohort of patients with stage I NSCLC treated with either SBRT or surgery. No clinically significant differences in QoL were observed the first year after either SBRT or surgery for an early stage NSCLC.
- These results support the hypothesis that surgery and SBRT are comparable treatments. This information provides input for shared decision-making whether patients with operable early stage NSCLC should receive treatment with SBRT or surgical resection.

Acknowledgment

Table 1 and the contents in our appendix are reused from Wolff HB, Alberts L, Kastelijn EA, et al. Differences in longitudinal health utility between stereotactic body radiation therapy and surgery in stage I non-small cell lung cancer. *J Thorac Oncol* 2018; 13:689-98, under the terms of the Journal of Thoracic Oncology.

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Disclosure

The authors have stated that they have no conflicts of interest.

Supplemental Data

Supplemental tables accompanying this article can be found in the online version at https://doi.org/10.1016/j.cllc.2019.04.001.

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Supplemental Data

Supplemental Table 1 Completed Questionnaires

Selection	Treatment	0 Months	3 Months	6 Months	12 Months
Propensity score match	Surgery	41	25	27	22
	SBRT	40	32	28	23

The numbers of complete questionnaires available for analysis per time point. The completion rates at each time point are compared between the 2 treatment groups using the χ^2 test. No significant differences in completion rates were found ($P = .88$).
Abbreviation: SBRT = stereotactic body radiation therapy.

Supplemental Table 2 Specification of Censored or Missing Questionnaires

Treatment/Selection	Reason Missing	0 Months	3 Months	6 Months	12 Months
Surgery	Censored	0	8	8	9
	Death	0	0	0	0
	Lost to FU	0	0	0	2
	Other missing	0	8	6	8
	Total	0	16	14	19
SBRT propensity matched	Censored	0	1	3	4
	Death	0	2	2	2
	Lost to FU	0	1	3	6
	Other missing	1	5	5	6
	Total	1	9	13	18

The specification of reasons for censoring or missing questionnaires per time point. Patients were censored because of recurrences (5 times), and adjuvant treatment was given to patients after surgery upstaged to cTNM II or III (5 times), or other high-risk patients according to the National Comprehensive Cancer Network guidelines[1] (3 times), and adjuvant treatment given after a false positive scan (1 time).
Lost to follow-up is defined as that all contact with the patient was lost. Other missing is defined as a missing questionnaire, when there is still contact with the patient.
Abbreviations: FU = follow-up; SBRT = stereotactic body radiation therapy.

Supplemental Table 3 Mixed Model Analysis QLQ-C30 Score Estimates

QLQ-C30 Score	Physical Functioning		Role Functioning		Emotional Functioning		Cognitive Functioning		Social Functioning		Fatigue		Pain[c]		Dyspnea[c]	
Parameter	**Estimate**	**Wald**	**Estimate**	**Wald**	**Estimate**	**Wald**	**Estimate**	**Wald**	**Estimate**	**Wald**	**Estimate**	**Wald**	**Estimate**	**Wald**	**Estimate**	**Wald**
Intercept	76.83	[a]	75.63	[a]	77.98	[a]	88.90	[a]	86.83	[a]	28.42	[a]	14.67	[a]	29.96	[a]
Baseline	5.35	0.05	5.69	0.27	−0.33	0.92	−0.34	0.92	1.22	0.74	−4.90	0.22	−5.56	0.11	−4.44	0.18
3 months	3.54	0.22	7.47	0.17	3.91	0.24	−0.41	0.91	−1.27	0.74	−2.25	0.59	−5.21	0.16	−7.38	0.03
6 months	−2.58	0.38	0.29	0.96	3.62	0.29	0.94	0.80	−2.26	0.57	−0.73	0.87	0.33	0.93	−0.60	0.87
12 months	[b]		[b]		[b]		[b]		[b]		[b]		[b]		[b]	
Surgery	5.66	0.22	3.18	0.67	1.09	0.85	−7.94	0.18	0.02	1.00	−2.40	0.72	−0.55	0.91	−2.55	0.63
SBRT	[b]		[b]		[b]		[b]		[b]		[b]		[b]		[b]	
Baseline × Surgery	−15.64	< 0.001	−30.84	< 0.001	−0.70	0.88	1.91	0.71	−16.12	0.003	24.14	< 0.001	19.07	< 0.001	12.20	0.01
Baseline × SBRT	[b]		[b]		[b]		[b]		[b]		[b]		[b]		[b]	
3 months × Surgery	−6.96	0.09	−19.56	0.01	0.48	0.92	3.85	0.47	−2.29	0.68	9.41	0.12	9.56	0.07	11.53	0.02
3 months × SBRT	[b]		[b]		[b]		[b]		[b]		[b]		[b]		[b]	
6 months × Surgery	2.37	0.57	−3.82	0.63	1.34	0.78	4.67	0.38	3.79	0.50	−0.69	0.91	2.26	0.67	0.91	0.86
6 months × SBRT	[b]		[b]		[b]		[b]		[b]		[b]		[b]		[b]	
12 months × Surgery	[b]		[b]		[b]		[b]		[b]		[b]		[b]		[b]	
12 months × SBRT	[b]		[b]		[b]		[b]		[b]		[b]		[b]		[b]	

Abbreviations: SBRT = stereotactic body radiation therapy; QLQ-C30 = European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire; QLQ-LC13 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Lung Cancer 13.

[a]Intercept is per definition significant.

[b]This parameter is contained within the intercept.

[c]Pain and Dyspnea scores are the combined scores of the QLQ-C30 and QLQ-LC13 questionnaires.

Reference

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