Patient-Reported Quality of Life After Stereotactic Ablative Radiotherapy for Early-Stage Lung Cancer

Frank J. Lagerwaard, MD, PhD, Neil K. Aaronson, PhD,† Chad M. Gundy, MSc,†*
Cornelis J.A. Haasbeek, MD, PhD, Ben J. Slotman, MD, PhD,* and Suresh Senan, MRCP, FRCR, PhD**

Background: Deterioration in health-related quality of life (HRQOL) is frequently observed after surgery for stage I non–small-cell lung cancer. As stereotactic ablative radiotherapy (SABR) can result in local control percentages exceeding 90%, we studied baseline and post-treatment HRQOL in SABR patients.

Methods: HRQOL data were collected prospectively using the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire in 382 consecutive patients treated with SABR. Patients were referred from 68 Dutch centers, with 86% judged unfit for surgery, and 14% declining surgery. An SABR dose of 60 Gy was delivered in three-, five-, or eight treatment fractions, depending on tumor diameter and location. HRQOL data were available for 382 patients at baseline (pre-SABR), and for 282, 212, 144, 56, and 43 patients at 3, 6, 12, 18, and 24 months post-SABR, respectively.

Results: Median survival was 40 months, with a 2-year survival of 66%. Local, regional, and distant failure percentages at 2 years were 6%, 13%, and 22%, respectively. Mean baseline global HRQOL and physical functioning scores were 62.9 ± 1.1 and 61.7 ± 1.1, respectively. Baseline symptom scores were highest for dyspnea (47.1 ± 1.7) and fatigue (37.4 ± 1.3). Except for a nonsignificant decrease in 2 to 3 points per year in physical functioning, no statistically or clinically significant worsening of any of the HRQOL functioning or symptom scores at any follow-up time point was observed.

Conclusions: Patients referred for SABR have substantially worse baseline HRQOL scores than those reported in the surgical literature. Clinically relevant deteriorations in HRQOL subscale scores were not observed after SABR.

*Department of Radiation Oncology, VU University Medical Center, Amsterdam, The Netherlands; and †Division of Psychosocial Research and Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands.

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Address for correspondence: Frank J. Lagerwaard, MD, PhD, Department of Radiation Oncology, VU University Medical Center, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands. E-mail: fj.lagerwaard@vumc.nl

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Surgery is considered the standard of care for fit patients with stage I non–small-cell lung cancer (NSCLC). However, lung cancer is increasingly a disease of less fit patients with a median age of 70 years at diagnosis, with one in three patients aged 75 years or older at diagnosis.[1] Several studies of surgically treated patients with early-stage lung cancer have reported compromised health-related quality of life (HRQOL) in the first 6 months postsurgery, with patients aged 70 years and more, and those with poorer pretreatment HRQOL, in particular, failing to show a return to baseline HRQOL levels.[2–6]

Prospective clinical studies of stereotactic ablative radiotherapy (SABR) in stage I NSCLC have reported 3-year local control percentages of 92% to 98%.[7–9] Toxicity is uncommon after SABR for peripheral tumors, and consists mainly of chest pain, rib fractures, and radiation pneumonitis, all of which have been reported in less than 5% of patients.[10] The current experience with SABR has been primarily in elderly patients who are medically inoperable, and there are limited baseline and post-treatment HRQOL data available for this population. The diagnosis of stage I NSCLC is usually made in the absence of tumor-related symptoms, and poorer baseline HRQOL is mostly caused by comorbidities such as chronic obstructive pulmonary disease (COPD).[11,12] As a consequence, preservation of baseline HRQOL can be regarded as the optimal result of treatment for stage I NSCLC.

With the introduction of SABR at the VU University Medical Center (Amsterdam) in 2003, it became institutional policy to prospectively collect serial HRQOL data in all stage I NSCLC patients undergoing this treatment. Local medical ethical committee approval was obtained for collecting these HRQOL data as a standard part of treatment follow-up. In this article, we report the clinical outcomes, treatment toxicities, and HRQOL of patients who underwent SABR for stage I NSCLC.

MATERIALS AND METHODS

A prospective database containing baseline and follow-up data of all patients treated with SABR for a stage I

NSCLC is maintained at our center. A cohort study was performed in 382 consecutive patients treated between April 2003 and November 2008, with available HRQOL data. Patients had been referred to the VU University Medical Center from 68 hospitals in the Netherlands. Before undergoing SABR, all patients were discussed in a multidisciplinary oncology team, and were considered medically inoperable (n = 323; 86%) or had declined surgery (n = 59; 14%). The group consisted of 230 men (60%) and 152 women (40%), with a median age of 74 years. In general, patients had poor pretreatment pulmonary function, with 72% classified as moderate, severe, or very severe COPD according to the global initiative for obstructive lung disease (GOLD) criteria.[13] In this patient cohort, the incidence of comorbidity was substantial, with a mean-age–adjusted Charlson comorbidity index score of 6.9 (range, 2–12).[14]

Details of the 408 tumors treated in these 382 patients are summarized in Table 1. Included were 255 T1 tumors (63%) and 153 T2 tumors (37%), with a maximum diameter between 10 and 79 mm. Patient staging was performed according to American Joint Committee of Cancer v.6 using computed tomography scans of the thorax and abdomen[18] fluorodeoxyglucose-positron emission tomography scans in all except three patients. Details of target volume delineation, the use of one of three risk-adapted fractionation schemes, all with a biologically effective dose of 100 Gy_{10} or more and SABR delivery technique have been described in our previous report.[9] In brief, patients with a peripheral tumor less than 3 cm (T1) that did not have broad contact with the thoracic wall were treated in three fractions of 20 Gy, whereas patients with T1 lesions abutting the thoracic wall and larger T2 lesions were treated with five fractions of 12 Gy. Lesions adjacent to the heart, hilus, mediastinum, plexus, or esophagus were treated in eight fractions of 7.5 Gy. Patients were routinely followed up at 3 months, 6 months, 12 months, 18 months, and 24 months if their clinical condition permitted this. Computed tomography scans were performed at each follow-up visit and ^{18} fluorodeoxyglucose-positron emission tomography scans were only obtained if clinically indicated. Both early and late toxicity were scored according to the Radiation Therapy Oncology Group (RTOG) toxicity grading system during follow-up visits, and by telephonic consultations.[15]

With the approval of the medical ethics committee, HRQOL data were collected routinely during follow-up visits. HRQOL was assessed with the EORTC QLQ-C30 (version 3.0).[16] The QLQ-C30 consists of 30 questions that assess physical-, emotional-, role-, social-, and cognitive-functioning dimensions of HRQOL, and a range of symptoms (e.g., dyspnea, loss of appetite, fatigue, sleep disturbances, and pain). The questionnaire has been extensively tested and validated.[17] Global HRQOL is measured with two items in the QLQ-C30, one addressing overall health and the other overall HRQOL on a 7-point scale (1 indicating "very poor" to 7 indicating "excellent"). All other questions employ a 4-point scale (1, indicating "not at all" to 4, indicating "very much"). The time frame of the questions is the previous week. The questionnaire was completed by patients before the clinic visit and took approximately 10 to 15 minutes to complete.

TABLE 1. Baseline Characteristics (N = 382)

Sex	
Male	60.2% (n = 230)
Female	39.8% (n = 152)
Median age	74 years (range, 47–91)
T-stage	
IA	60.2% (n = 230)
IB	39.8% (n = 152)
Median-age–adjusted Charlson score	6.9 (range, 2–12)
Median-non-age–adjusted Charlson score	4.1 (range, 0–10)
History of prior lung cancer	
Yes	17.0% (n = 65)
No	83.0% (n = 317)
Tumor location	
Peripheral	80.9% (n = 309)
Central	17.8% (n = 68)
Both	1.3% (n = 5)
Mean tumor diameter (range)	28 (range, 10–79 mm)
COPD GOLD class (N = 361)	
No COPD	15.8% (n = 57)
GOLD 1	12.2% (n = 44)
GOLD 2	36.8% (n = 133)
GOLD 3	28.3% (n = 102)
GOLD 4	6.9% (n = 25)
Performance status (WHO) (N = 380)	
0	11.1% (n = 42)
1	52.9% (n = 201)
2	31.8% (n = 121)
3	4.2% (n = 16)
Median FEV1 (range)	1.46 liter (61% of predicted)
SABR indication	
Refusal of surgery	15.4% (n = 59)
Medically inoperable	84.6% (n = 323)
Fractions SABR	
3	40.1% (n = 153)
5	44.5% (n = 170)
8	15.4% (n = 59)

COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in 1 second; GOLD, global initiative for obstructive lung disease; WHO, World Health Organization.

Statistical Analysis

All scores on the EORTC QLQ-C30 were linearly transformed to a 0 to 100 scale according to the EORTC guidelines. Higher scores on the functional HRQOL scales indicate better functioning, whereas higher scores on the symptom scales indicate more severe symptoms. A 10-point difference on any of the HRQOL scales is generally considered to be a "moderate" difference, which can be regarded as clinically meaningful.[18,19] Mean changes of more than 20 points are considered to be large effects.

The median follow-up duration was 23 months. Multilevel analyses were conducted to evaluate whether there was a statistically significant change in HRQOL scores over

