Stereotactic Ablative Radiotherapy as an Alternative to Lobectomy in Patients With Medically Operable Stage I NSCLC: A Retrospective, Multicenter Analysis

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Abstract

We report the results of a retrospective analysis of 187 patients with stage I to II NSCLC treated with lobectomy or stereotactic body radiation therapy. No significant difference was found in local control, whereas overall survival was significantly better in patients treated with lobectomy. No difference for overall survival was observed between operable patients undergoing stereotactic body radiation therapy and lobectomy.

Background: Stereotactic ablative body radiation therapy (SBRT) has evolved as the standard treatment for patients with inoperable stage I non–small-cell lung cancer (NSCLC). We report the results of a retrospective analysis conducted on a large, well-controlled cohort of patients with stage I to II NSCLC who underwent lobectomy (LOB) or SBRT. **Materials and Methods:** One hundred eighty-seven patients with clinical-stage T1a-T2bNoMO NSCLC were treated in 2 academic hospitals between August 2008 and May 2015. Patients underwent LOB or SBRT; those undergoing SBRT were sub-classified as surgical candidates and nonsurgical candidates, according to the presence of surgical contraindications or comorbidities. **Results:** In univariate analysis, no significant difference was found in local control between patients who underwent SBRT and LOB, with a trend in favor of surgery (hazard ratio [HR], 0.27; 95% confidence interval [CI], 0.07-1.01; $P < .053$). Univariate analysis showed that overall survival (OS) was significantly better in patients who underwent LOB (HR, 0.44; 95% CI, 0.23-0.85) with a 3-year OS of 73.4% versus 65.2% for surgery and radiation therapy patients, respectively ($P < .01$). However, no difference in OS was observed between operable patients undergoing SBRT and patients who underwent LOB (HR, 1.68; 95% CI, 0.72-3.90). Progression-free survival was comparable between patients who underwent LOB and SBRT (HR, 0.61; $P = .09$). **Conclusion:** SBRT is a valid therapeutic approach in early-stage NSCLC. Furthermore, SBRT seems to be very well-tolerated and might lead to the same optimal locoregional control provided by surgery for patients with either operable or inoperable early-stage NSCLC.

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Introduction

Non–small-cell lung cancer (NSCLC) represents 85% of lung neoplasms,[1] and it is responsible each year for 1.3 million new cases and 1.2 million deaths on a global scale.[2] Early-stage NSCLC is diagnosed approximately in 15% to 25% of cases, allowing a radical treatment with curative intent.[3] Still, surgery represents the treatment choice for stage I to II NSCLC, yielding survival rates of 60% to 80% for stage I and 30% to 50% for stage II lesions, according to different series.[4] Lobectomy (LOB) is the recommended surgical approach over sublobar resections and nonsurgical treatments, owing to reported local control in excess of 90%, according to the American College of Chest Physicians Evidence-based Clinical Practice Guidelines of 2013.[5] Nevertheless, about 15% to 20% of patients are deemed medically unfit to undergo LOB, or they refuse surgery.[6] No therapeutic alternative was available until the emergence of stereotactic ablative body radiation therapy (SBRT) in the past decade. SBRT should now be considered the standard treatment for patients with inoperable early-stage NSCLC.[7-9] Local control rates with SBRT ranged between 80% and 100%, and there was a 3-year overall survival (OS) between 40% and 80%.[10] A biologically effective dose (BED) superior to 100 Gy is related to a better outcome in terms of disease control.[11] Unfortunately, the STARS (Stereotactic Ablative Radiotherapy (SABR) in Stage I Non-small Cell Lung Cancer Patients Who Can Undergo Lobectomy) and ROSEL (Trial of Either Surgery or Stereotactic Radiotherapy for Early Stage (IA) Lung Cancer) phase III randomized clinical trials, comparing SBRT with surgery, were prematurely closed owing to low accrual; therefore, no direct, randomized comparison is currently available.[12,13]

We report the results of a retrospective analysis conducted on a large, well-controlled cohort of consecutive patients with stage I to II NSCLC who underwent LOB or SBRT in 2 academic Italian centers.

Materials and Methods

One hundred eighty-seven patients with clinical stage T1a-T2bN0MO NSCLC (according to the American Joint Committee on Cancer TNM staging system, Eighth edition) were consecutively treated between August 2008 and May 2015. All patients provided written informed consent before undergoing the treatment recommended by physicians. Before submitting these data, the institutional review board/ethics committee of the University Hospital of Modena (as coordinator center), Italy (Protocol No. 22077/2017), approved the study. Patients underwent LOB or SBRT; those undergoing SBRT were sub-classified as "surgical" candidate and "nonsurgical" candidates. Both centers agreed on the definition of surgical candidates: they were patients with forced expiratory volume in 1 second $>$ 1.5 L/min or $<$ 60%, diffusion lung carbon monoxide $>$ 60%, cardiopulmonary test with a maximum oxygen consumption $>$ 20 mL/Kg/min, and shuffle walk test $>$ 25 shuttles with a desaturation $<$ 4%. The choice of SBRT was proposed by the multidisciplinary team of each center and was also performed when the patient denied consent to surgery owing to higher self-perceived risk of side effects. On the other hand, patients were declared nonsurgical candidates if they could not undergo surgery owing to their performance status, major comorbidities (severe emphysema or other chronic obstructive pulmonary disease, myocardial infarction within the past 6-8 weeks, etc), or severe functional contraindications, such as prior pulmonary surgery, forced expiratory volume in 1 second $<$ 1 L/min, cardiopulmonary test with a maximum oxygen consumption $<$ 10 to 15 mL/kg/min, shuffle walk test of $<$ 25 shuffles, or desaturation $>$ 4%.

In the SBRT group, patients treated without cytohistologic confirmation of malignancy, positron emission tomography (PET) positivity, and increasing dimensions on computed tomography (CT) scans were considered to present diagnostic criteria of tumor presence.

Characteristics such as gender and age were recorded, as well as histology, cT stage, cN stage, and performance status (PS, using the Eastern Cooperative Oncology Group scale). Before treatment, all patients were completely staged, using chest and upper abdomen CT scan with contrast enhancement, brain CT scan or magnetic resonance imaging, and total body 18-fluordeoxyglucose (FDG) PET/CT scan. Invasive mediastinal staging procedures—that is, mediastinoscopy, endobronchial ultrasound, or transbronchial fine-needle aspiration—were performed in 10 patients who were listed to undergo LOB (upon suspicion of lymph node involvement on CT or PET/CT scan) and in 8 patients scheduled for SBRT, with enlarged (more than 1 cm in major diameter) nodes shown by CT scan. Conversely, candidates for SBRT with negative radiologic staging did not receive any invasive procedure. Patients who underwent surgery could therefore be classified as pN0, whereas patients who underwent SBRT were classified as cN0. Before undergoing SBRT/LOB, 175 (93.5%) of 187 patients were functionally classified in accordance with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) scale.[14]

In both centers, treatment planning was performed using 4-dimensional (4D) CT scans with 3-mm slice thickness, and an internal target volume was delineated taking into account breathing movements. The planning target volume was defined as internal target volume plus 5 mm laterally and 5 to 10 mm craniocaudally. Treatment was administered with volumetric modulated arc therapy on a Synergy Linac (Elekta AB, Stockholm, Sweden) or a TomoTherapy system (Accuray Inc, Sunnyvale, CA). No breathing control system was used during radiotherapy (RT) delivery. Patient positioning was verified by cone beam CT or megavolt CT (depending on the machine used in each center) before each fraction. Dose schedules were prescribed to reach a BED of at least 100 Gy (with an alpha/beta ratio of 10), and fractionation was chosen depending on lesion site and dimensions, according to the American Association of Physicists in Medicine report.[15] All BED values refer to the dose at the isocenter, with the 95% isodose encompassing the planning target volume. The use of immobilization devices (such as thermoplastic thoracic body mask) was just strongly suggested; image-guided radiation treatment was performed by means of daily online cone-beam or megavolt CT.

To evaluate the response to SBRT, Response Evaluation Criteria in Solid Tumors 1.1 criteria were used. The appearance of one or more new lesions was considered progression of disease. Locoregional control (LC) was described as an absence of relapse within the tumor treatment site, ipsilateral hilum, and ipsilateral mediastinum. Distant control was classified as the lack of recurrence in any location outside of LC areas.[16] OS and progression-free survival (PFS) were defined as the time from the start of treatment to death or last assessment of vital status and local or distant progression, respectively.

Patients were followed using contrast-enhanced chest and abdomen CT every 3 months for the first 2 years; from the third year on, a total body CT scan was requested every 6 months, and suspicious CT progressions were then investigated with an 18FDG-PET/CT scan followed by biopsy (if possible).

Statistical Analysis

Baseline features were compared between treatment groups (SBRT surgical candidate vs. SBRT nonsurgical candidate vs. LOB), using the χ^2 test or the Fisher exact test for categorical variables (ie, gender; age classified as $\leq$ 70 years, 71-75 years, and $\geq$ 76 years; histology; cT and cN status; stage; GOLD; and PS).

Survival curves were calculated using the Kaplan-Meier method. Survival estimates were calculated at 1 and 3 years, along with their 95% confidence intervals (CIs), for the different types of treatment and other relevant prognostic factors.

Hazard ratios (HRs) and their 95% CIs were obtained through Cox models: univariate and multivariate models considering the treatment groups; and the relevant prognostic factors were constructed.

All analyses were performed using STATA 14 (2015, Stata statistical software, release 14. StataCorp, College Station, TX).

Results

The baseline features of our population are summarized in Tables 1 and 2. Among patients treated with SBRT, 30 were defined as surgical candidates and 63 as nonsurgical candidates. No differences in gender distribution were observed ($P = .107$) between the SBR and LOB subgroups. Using a 2-sample t test, we found that patients who underwent LOB were significantly younger, with a mean age of 67.9 years (range, 45-87 years) versus 76.6 years (range, 52-92 years) in the SBRT cohort ($P < .0001$).

All patients in the LOB group had a pathologic confirmation of a malignant neoplasm, whereas in the SBRT group, 71 (76.3%) patients had a biopsy-proven NSCLC, and 22 (23.7%) of 187 patients were treated in the absence of confirming histology. Adenocarcinoma was the most frequent histological subtype (59.3%), followed by squamous cell carcinoma (27.2%); finally, 3 patients (1.6%) had uncommon histologies. At the end of staging procedures, 73 (39.3%) of 187 patients had clinical stage T1a NSCLC, 63 (33.7%) cT1b, 44 (23.5%) cT2a, and 7 (3.8%) were classified as cT2b (according to the Seventh Edition of the American Joint Committee on Cancer Lung Cancer Classification).[17] Concerning nodal staging, all patients who underwent SBRT were clinically, radiologically, and metabolically cN0. Three of 71 patients in the LOB group, staged as cN0 preoperatively, were pN1 (3.2%) upon final pathology.

Patients were not equally distributed in terms of GOLD classification among the LOB and SBRT groups ($P < .0001$). Patients in the SBRT groups, in particular in the nonsurgical candidates group, were more frequently in higher GOLD classes. A total of 134 (71.6%) patients of 187 were in stage IA, 39 (20.9%) in stage IB, and 14 (7.5%) in stage IIA. No difference between the SBRT and LOB groups was observed.

Patients were well-balanced between the LOB and SBRT groups also in terms of stage. No significant differences were found even in terms of histology for patients for whom histologic assessment was available (165/187; 88.2%). PS at diagnosis was significantly better in the LOB group than in the SBRT group ($P < .0001$). Patients in the SBRT group received different fractionation schedules; all patients received a BED of at least 100 Gy: 71% received higher than 150 Gy, 29% received between 100 and 150 Gy.

With a median follow-up of 23 months (range, 6-66 months), 12 local failures were observed (9 in the SBRT group and 3 in the LOB group). Cox regression analysis showed that none of the explored parameters (surgery, operability, gender, histology, stage, GOLD score, and PS at diagnosis) influenced the rate of failures, as shown in Table 3. In univariate analysis, no significant difference was found in local control between patients who underwent SBRT and LOB, though with a trend in favor of surgery (HR, 0.27; 95% CI, 0.07-1.01; $P < .053$). After multivariate analysis, surgery and disease stage were found to be independent factors influencing local

Table 1 Baseline Characteristics of the Patient Cohort

Patient Characteristics	N (%)
Median age, y	73
Gender	
Male	133 (71)
Female	54 (29)
PS (ECOG)	
0	80 (43)
1	75 (40)
2	32 (17)
GOLD scale	
0	69 (37)
1	45 (24)
2	41 (22)
3	17 (9)
4	3 (2)
N/A	12 (6)
Treatment	
LOB	94 (50)
SBRT	93 (50)
Surgical versus nonsurgical candidate	
Surgical	124 (66)
Nonsurgical	63 (34)
Staging	
Ia	134 (72)
Ib	39 (21)
IIa	14 (7)
Pathology assessment	
Yes	165 (88)
No	22 (12)
Histology	
Adenocarcinoma	111 (59)
Squamous cell	51 (27)
Others	3 (2)
Total	187 (100)

Abbreviations: ECOG = Eastern Cooperative Oncology Group; GOLD = Global Initiative for Chronic Obstructive Lung Disease; LOB = lobectomy; PS = performance status; SBRT = stereotactic ablative body radiation therapy.

Table 2 Distribution of Principal Clinical Features Between the 2 Groups

	LOB, n (%)	SBRT, n (%)	*P*
Mean age, y	67.9	76.6	**< .0001**
Histology			
Adenocarcinoma	60 (73)	42 (59)	.13
SCC	24 (25)	27 (38)	
Others	1 (1)	2 (3)	
T stage			.88
T1a	37 (39)	36 (39)	
T1b	33 (35)	30 (32)	
T2a	20 (21)	24 (26)	
T2b	4 (4)	3 (3)	
Stage			.59
Ia	69 (73)	65 (70)	
Ib	17 (18)	22 (24)	
IIa	8 (8)	6 (6)	
GOLD scale			**< .0001**
0	50 (53)	19 (20)	
1	15 (16)	30 (32)	
2	14 (15)	27 (29)	
3	3 (3)	14 (15)	
4	0	3 (3)	
N/A	12 (13)	0	
PS at diagnosis			**< .0001**
0	62 (66)	18 (19)	
1	29 (31)	46 (49)	
2	3 (3)	29 (31)	

Bold values denote statistically significant.
Abbreviations: GOLD = Global Initiative for Chronic Obstructive Lung Disease; LOB = lobectomy; NA = not available; PS = performance status; SBRT = stereotactic ablative body radiation therapy; SCC = squamous cell carcinoma.

control (HR, 0.14; 95% CI, 0.02-0.93; $P < .042$ and HR, 33.2; 95% CI, 1.95-564; $P < .015$, respectively).

Forty-three (23%) of 187 patients developed distant metastases (24 in the SBRT group and 19 in the LOB group): surgery, histology, and stage did not influence the rate of distant failures.

In the SBRT group, the overall response rate was 90.6%. Complete radiologic response, partial response, or stable disease was observed in 21.5%, 46.2%, or 23.6% of patients, respectively. Six patients experienced progression of disease after the first evaluation.

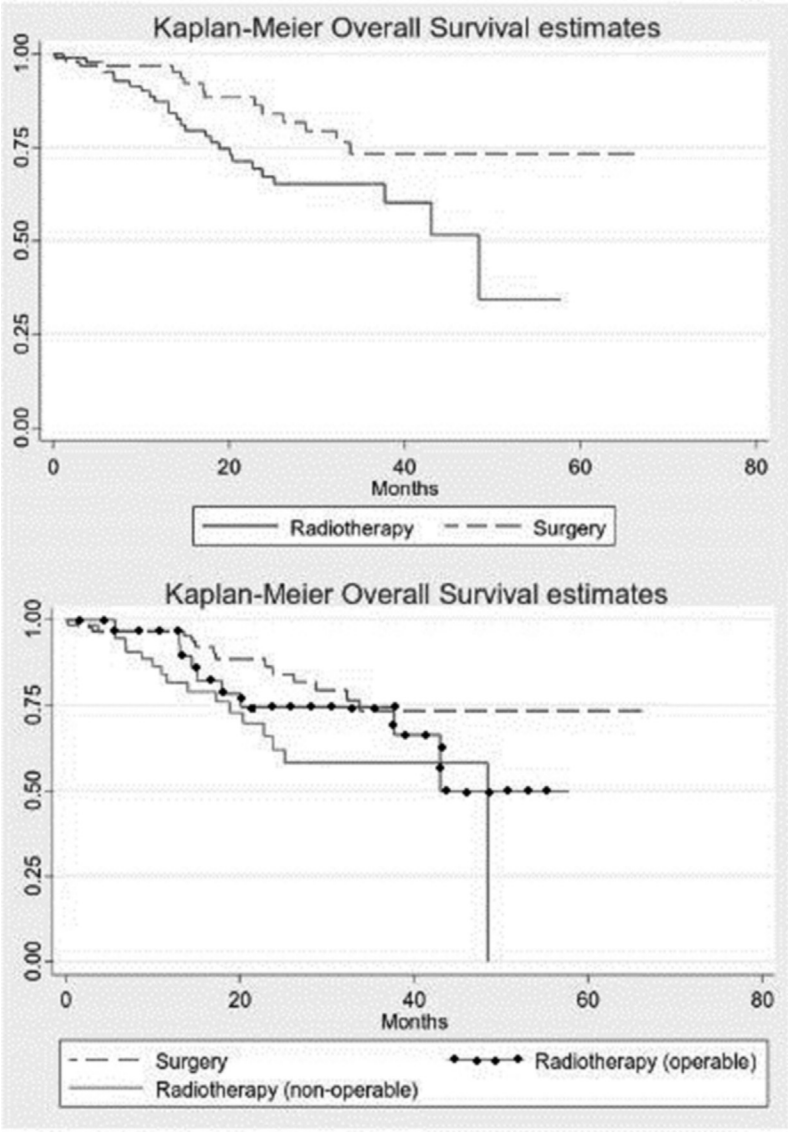
Results for OS and PFS are reported in Figure 1 and Figure 2, respectively. Forty deaths occurred, and the univariate analysis showed that OS was significantly better among the patients who underwent LOB (HR, 0.44; 95% CI, 0.23-0.85) with a 3-year OS of 73.4% ± 6.6% (standard error) and 65.2% ± 6.1% for surgery and SBRT, respectively ($P < .01$). Considering surgical and nonsurgical candidates, however, no difference for OS was observed between operable patients undergoing SBRT and patients undergoing LOB (HR, 1.68; 95% CI, 0.72-3.90). Patients deemed inoperable had a significantly lower OS than patients who underwent LOB (HR, 2.76; 95% CI, 1.35-5.68) (Figure 1). OS was not

Table 3 Influence of Patients' Characteristics on Recurrence Rate

	Hazard Ratio (95% CI)	*P*
Surgery	0.27 (0.07-1.01)	.053
Operability	3.2 (0.71-14.4)	.13
Gender	1.69 (0.53-5.34)	.36
Histology	0.52 (0.11-2.4)	.41
Stage I	2.29 (0.67-7.8)	.18
GOLD score		
1	1.72 (0.45-6.4)	.41
2	0.96 (0.18-4.9)	.96
3	1.53 (0.17-13.6)	.7
4	6.32	1
PS at diagnosis		
1	1.01 (.29-3.5)	.97
2	1.1 (0.22-5.9)	.85

Abbreviations: CI = confidence interval; GOLD = Global Initiative for Chronic Obstructive Lung Disease; HR = hazard ratio; PS = performance status.

Figure 1 Kaplan-Meier Overall Survival Curves



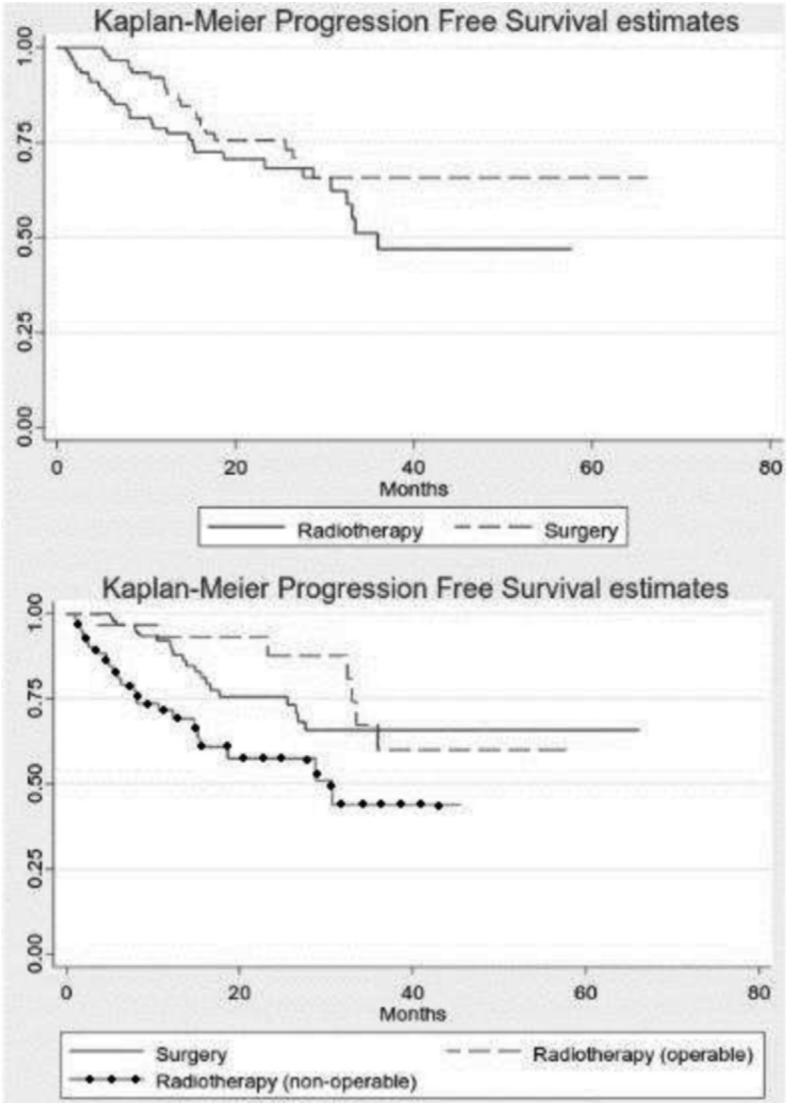
affected by gender, histology, T dimension, clinical stage, or GOLD score, whereas a higher risk of death was observed in patients with a PS equal to 2 (HR, 4.05; 95% CI, 1.77-9.26). Indeed, the 3-year OS was 53.3% ± 10.1% in this subgroup of patients (Eastern Cooperative Oncology Group PS = 2), significantly poorer if compared with the same parameter in patients with PS equal to 0 or 1 (respectively, 81.1% ± 6.2% and 64.9% ± 7.5%). In a multivariate analysis, only a PS equal to 2 was associated with an increased risk of death (HR, 3.11; 95% CI, 1.09-8.86).

Fifty-one of 187 patients progressed during follow-up; PFS was comparable between patients who underwent LOB and SBRT (HR, 0.61; $P = .09$), with a 3-year PFS equal to 65.8% ± 6.8% and 46.9% ± 8.3%, respectively ($P < .08$). Inoperable patients who underwent SBRT had a significantly lower PFS rate than those who underwent LOB did (HR, 2.48; 95% CI, 1.22-5.05), whereas surgical candidates had a PFS comparable with patients who underwent LOB (HR, 1.57; 95% CI, 0.68-3.64) (Figure 2). Gender, histology, cT stage, and GOLD class did not influence PFS. As for OS, PFS was significantly lower in patients with a PS of 2 (HR, 3.66; 95% CI, 1.60-8.36). In a multivariate analysis, no considered prognostic factors were significantly associated with PFS.

Discussion

Studies comparing LOB and SBRT in patients with inoperable and operable NSCLC have been performed by several authors. Despite limitations related to patient imbalances in the treatment arms, that is, age, comorbidities, and/or the studies' retrospective design, all analyses consistently suggested the absence of significant differences in terms of local control. Furthermore OS does not seem inferior in patients who undergo SBRT when treatment groups were

Figure 2 Kaplan-Meier Progression-Free Survival Curves



adjusted for variables that might lead to a selection bias.[18-26] Robinson et al showed that LOB favored OS (29.6% vs. 63.5% at 4 years) despite a higher percentage of T1 patients in the SBRT group.[18] Moreover, patients undergoing surgery or SBRT showed comparable OS if matched by the Charlson comorbidity score (HR, 1.09; 95% CI, 0.50-2.36; $P = .83$).[20] A recent phase II trial, including patients with stage I inoperable NSCLC with peripheral lesions, showed excellent local controls and survival outcome after a follow-up of 36 months, with minimal toxicity (OS rate at 1, 2, and 3 years of 92%, 75%, and 66%, respectively).[27] Chen et al recently conducted a meta-analysis, including only propensity score studies about SBRT versus surgery comparison. Despite favorable results in terms of OS reported in surgical subgroups (HR, 1.48; 95% CI, 1.26-1.72; $I^2 = 80.5\%$), SBRT and surgery did not show any difference in terms of lung cancer-specific survival (HR. 1.17; 95% CI, 0.92-1.50; $I^2 = 18.6\%$).[28] Nodal staging remains an important issue in early-stage NSCLC; in the Robinson et al series, 32.7% of patients were upstaged after surgery, and adjuvant chemotherapy was prescribed in 20% of cases.[18] Adjuvant systemic therapy may be considered with good PS in younger patients with high-risk features. Notably, no invasive staging was systematically performed in our study population; accurate nodal assessment could be suggested for younger patients theoretically fit for surgery but candidates for SBRT, especially taking into account more recent data from available literature about mediastinal upstaging in cN0 patients after surgery.[28,29] Wink et al recently published a systematic review on this issue, emphasizing that regional recurrence after SBRT and surgery was comparable despite more elaborate pre- and intraoperative nodal staging. The authors concluded also that no evidence was available to justify more invasive nodal staging in inoperable patients with stage I disease before SBRT. However, these conclusions were based on retrospective data, including mainly

patents who underwent SBRT deemed inoperable, and this should be taken into consideration.[30]

These encouraging results, particularly after the publication of the combined analysis of the insufficiently recruiting STARS/ROSEL trials,[12,13] stimulated a challenging debate on whether SBRT might replace surgery as the first-line treatment of early-stage NSCLC. In particular, the STARS analysis compared CyberKnife-based SBRT (50-54 Gy in 3-4 fractions) with anatomic lobectomy with ipsilateral hilar lymphadenectomy in a phase III randomized 1:1 clinical trial with the aim of obtaining the same local control and OS. The study was prematurely closed owing to very slow accrual, so clear information is not expected.[12] Taking into account the limitation of this analysis, it showed no difference between enrolled populations in age, gender, PS, histology, T stage, or tumor site. Despite a statistically significant difference in OS, no difference in locoregional control, distant metastases, or recurrence-free survival was found between LOB and SBRT.

Supporters of surgical treatment claim that surgery allows ruling out occult lymph node involvement and performing pathologic evaluation of disease at the same time, whereas SBRT relies on PET/CT assessment of nodal involvement and pretherapeutic biopsy.[29] On the other hand, SBRT advocates report a low incidence of nodal relapse following treatment[25] and no impact of histology on main clinical outcomes.[23,31-35] Cost-effectiveness results are controversial and seem to depend on the adopted evaluation scale and calculation model.[36,37]

Data from our current analysis, with all limitations inherent to such a retrospective approach, confirm that survival differences between patients who underwent LOB and SBRT may predominantly be a consequence of a treatment selection bias and provides further insight into the interplay of prognostic factors, therapeutic choices, and outcomes.

Patients deemed fit for surgery had a clinical outcome that was comparable with surgery (as well in terms of OS and PFS). These findings may suggest that, for operable patients, SBRT and LOB may be considered efficient, effective, and safe alternative options in a real-practice scenario. This result is quite high and rather uncommon, considering also that all lesions were treated with a BED of at least 100 Gy. Performance status was 0 in 80 (42.7%), 1 in 75 (40.1%), and 2 in 32 patients (17.1%), showing a different distribution in the 2 groups: only 18 of 80 patients in the SBRT group had PS = 0, whereas 29 patients in the same group (vs. just 3 in the LOB group) had a PS = 2. These features resulted in a worse PS for patients who submitted to SBRT, with a $P < .0001$ in the Pearson χ^2 test. PS was found to have a statistically significant impact on OS, whereas stage and histology did not, confirming again that surgery and SBRT are both reasonable options in medically fit patients.

Finally, these results are consistent with internationally available literature: survival among patients who underwent SBRT is comparable with that obtained in population-based comparisons using surgery.[22,38,39] Furthermore, the low number of patients upstaged after surgery may be a further indication that an aggressive combination of imaging and invasive staging, as performed in our population, may further improve staging accuracy, as suggested in other contemporary series.[40,41]

In our study, we also analyzed patients' respiratory function at baseline, using the GOLD scale, but it did not significantly affect prognosis. Thus, the overall comorbidity status influenced survival more than lung comorbidity assessment alone, suggesting that residual pulmonary function after ablative therapies is not the only factor to take into account when addressing the right treatment strategies for these patients. Results of the current analysis are consistent with literature data. Indeed, several retrospective series confirmed that comorbidities strongly affect survival among patients treated with lobar or sub-lobar resection or with SBRT.[19]

Regarding SBRT parameters, the rate of local recurrence in this series was too low to explore a correlation between BED and LC. Data from the literature showed that $BED_{10} \geq 100$ is related to significantly better 3-year LC (89% vs. 62%; $P = .0001$),[42] but dose-escalation protocols might further increase LC.[43,44]

A retrospective, matched-pair analysis of 114 patients treated with accelerated radiotherapy (48-60 Gy in 12-15 fractions, BED_{10} about 80-90 Gy) or SBRT (48-52 Gy in 4-5 fractions, $BED_{10} >$ 130 Gy) was recently published.[45] OS and LC were significantly higher in the SBRT group ($P < .0024$ and $P < .009$, respectively), suggesting a dose effect above $BED_{10} > 130$.

Recently, the phase II, randomized, feasibility study named UK-SABRTooth (Comparing stereotactic ablative radiotherapy with surgery in patients with peripheral stage I non small cell lung cancer considered at higher risk of complications from surgical resection) trial was closed to accrual; it compared SBRT with surgery in patients at higher risk of morbidity/mortality from surgery with the aim of investigating the feasibility of conducting a definitive large-scale phase III trial.[46] Results are awaited as soon as possible. Two phase III trials from the United States are ongoing and are expected to deliver remarkable information about the best therapeutic approach between SBRT and surgery. The first one is the VALOR trial (Veterans Affairs Lung Cancer Or Stereotactic Radiotherapy) [ClinicalTrials.gov: NCT02984761], a multicenter, randomized phase III clinical trial involving 670 patients comparing SBRT and surgery (lobectomy/segmentectomy) in stage I peripheral NSCLC. The second one is the Stable-Mates (JoLT-Ca Sublobar Resection (SR) Versus Stereotactic Ablative Radiotherapy (SAbR) for Lung Cancer) trial (Clinicaltrials.gov ID NCT02414334) that is recruiting, with a projected sample size of 272 patients, and it will compare sublobar resection and SBRT in high-risk patients. Finally, the Canadian radiotherapy LUSTRE (Stereotactic Body Radiotherapy Versus Conventional Radiotherapy in Medically-Inoperable Non-Small Lung Cancer Patients) trial is the only phase III randomized controlled trial investigating the role of SBRT in conventionally hypofractionated RT for the treatment of stage I medically inoperable NSCLC.[47] Recent data showed favorable outcomes in terms of patients' global health-related quality of life and indirect costs of therapies[13] in addition to the low impact of SBRT on quality of life[23,35]; prospective data confirming non-inferiority of one treatment strategy to the other, at least in the intermediate term, would expand the number of patients with NSCLC to whom SBRT could be offered as 1 of 2 possible treatment options.

Conclusions

In the absence of randomized data and with the limitations and bias of a retrospective study, this analysis further corroborates the hypothesis of comparable outcomes after SBRT and LOB in

patients with operable stage I to II NSCLC. Furthermore, SBRT might lead to the same optimal locoregional control provided by surgery for both operable and inoperable patients with early-stage NSCLC. Moreover, these results support the consideration of SBRT as a valid therapeutic approach in early-stage NSCLC, awaiting data from randomized trials such as the SABRTooth and LUSTRE projects.

Clinical Practice Points

- We collected data on 187 patients with stage I to II NSCLC. Patients underwent LOB or SBRT. Patients undergoing SBRT were sub-classified as surgical candidates or nonsurgical candidates.
- No significant difference was found in local control between patients who underwent SBRT and LOB, although OS was significantly better in patients who underwent LOB.
- No difference for OS was observed between operable patients who underwent SBRT and patients who underwent LOB.

Disclosure

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

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