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LETTER TO THE EDITOR

## Results of surgery versus stereotactic body radiotherapy for lung cancer

*Dear Editor,*

Historically, the best outcomes for early-stage lung cancer have been achieved through surgery, via lobectomy.[1] Nevertheless, stereotactic body radiotherapy (SBRT) has emerged as an effective treatment for stage I lung tumors unsuitable for surgery.[2]

From August 2012 to June 2018, 49 patients with lung cancer were submitted to SBRT and 232 patients underwent surgical resection (pathological stage above IIB and neuroendocrine subtype were excluded). See Table 1 for baseline data. Patients submitted to SBRT were considered not fit for surgery, 32 of them due to severe chronic obstructive pulmonary disease (COPD).

Lobectomy was the most frequent surgery (92.2%). Patients undergoing SBRT were submitted to different schemes, the most frequent being 46—60 Gy in 4 fractions ($n = 19$), followed by 30—34 Gy in 1 fraction ($n = 16$), 42.5—50 Gy in 5 fractions ($n = 12$) and 60 Gy in 3 fractions ($n = 2$).

Patients in the SBRT group were older, showed a higher burden of comorbidities, their mean value of FEV1 was lower and their incidence of COPD was higher, compating to patients in the surgical group. One limitation of our study is that we only distinguished the presence or absence of comorbidities, and not their severity. For tumours in stage IA, the SBRT group had a lower mean FEV1 and a higher incidence of COPD.

Progression was defined by imagiological criteria: 20% increase in unidimensional measurement or appearance of new lesions. All the patients had a computed tomography scan, performed every 6 months for surgical patients and 3—6 months for SBRT patients. Other studies, like positron emission tomography, were performed if doubts over disease progression remained. Twelve patients from the surgical group were lost to follow-up. Median survival comparison for surgical and SBRT groups including the results for stage IA patients are depicted in Table 2.

The groups did not reveal differences in median overall survival (OS) and distant progression free survival (PFS), but there were significant differences between surgical and SBRT groups on PFS and local PFS. For disease in stage IA alone, median survival rates are significantly higher in the surgical group for OS, PFS, local and distant PFS.

A propensity score-matching analysis was applied to reduce potential confounding. We matched 31 pairs of patients, using a propensity score based on age, sex, comorbidities like COPD, FEV1, stage and histology. We were not able to compare the two groups on OS due to zero deaths in one of the groups. No significant differences were found between the two groups for PFS (95%CI=0.1;25.3) [$p = 0.917$], local PFS 95%CI=0.1;20.6) [$p = 0.917$] and distant PFS (95%CI=0.1;279.1) [$p = 0.415$].

Lobectomy remains the standard for surgical management of NSCLC, although sublobar resection for NSCLC is still a controversial issue.[3] Rami-Porta and Tsuboi[3] reported that, in terms of survival, lobectomy and wedge resection are equivalent in patients aged more than 71 years; they also report that, in patients unable to undergo lobectomy, sublobar resection is an alternative that will confer similar prognosis. In our study, sublobar resection was performed in only 4 patients, not allowing a subanalysis.

Different stages had different survival and progression rates.[4] One possible confounding factor regarding the distribution of different stages is that the surgical group had a pathological stage while SBRT patients had a clinical stage. These results could also be biased owing to the very small number of patients included in the SBRT group, resulting in a large sample size difference, which could have significantly influenced the analytical power.

We subanalyzed patients in stage IA. This comparison allowed for a better interpretation of the results, as SBRT and surgical groups were more homogenous. However, patients in the SBRT group still presented a lower mean FEV1 and a higher incidence of COPD, and these could have been why the patients were considered unfit for surgery. Surgery has also the advantage of allowing a definitive pathologic diagnosis, accurate lymph node evaluation, and possible upstaging for adjuvant therapy.[5] The lower number of patients included in the propensity matched analysis raises doubts due to low precision results.

Surgery was the primary treatment and only unfit patients were submitted to SBRT, in accordance with guidelines. In RTOG 0236 (a multicenter phase II study),[6] 52 patients with medically inoperable NSCLC were treated with 60 Gy delivered in 3 fractions; long-term results showed an

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**Table 1** Clinicopathologic characteristics of the patients submitted to surgery and SBRT included in the study.

| | Thoracic Surgery Patients *n* = 232 | SBRT Patients *N* = 49 | p |
|---|---|---|---|
| Sex | **n (%)** | **n (%)** | **0.017** |
| Male | 154 (66.4%) | 41 (83.7%) | |
| Female | 78 (33.6%) | 8 (16.3%) | |
| | **Median (range)** | **Median (range)** | <**0.001** |
| Age (years) | 65.5 (35−88) | 71 (54−88) | |
| ECOG PS | **n (%)** | **n (%)** | 0.649 |
| 0 | 150 (64.7%) | 30 (61.2%) | |
| 1 | 82 (35.3%) | 17 (34.7%) | |
| 2 | 0 | 2 (4.1%) | |
| | **Median (range)** | **Median (range)** | <**0.001** |
| FEV1 | 96 (29.5−115) | 69.5 (32−121) | |
| Comorbidities | **n (%)** | **n (%)** | |
| COPD | 35 (15.1%) | 32 (65.3%) | <**0.001** |
| CVD | 43 (18.5%) | 5 (10.2%) | 0.159 |
| CKD | 11 (4.7%) | 2 (4.1%) | 0.174 |
| ILD | 5 (2.2%) | 1 (2.0%) | 0.719 |
| Histology | **n (%)** | **n (%)** | <**0.001** |
| Adenocarcinoma | 205 (88.4%) | 33 (67.3%) | |
| Squamous | 27 (11.6%) | 16 (32.7%) | |
| Stage | **n (%)** | **n (%)** | <**0.001** |
| IA | 99 (42.7%) | 41 (83.7%) | |
| IB | 87 (37.5%) | 5 (10.2%) | |
| IIA | 5 (2.2%) | 2 (4.1%) | |
| IIB | 41 (17.7%) | 1 (2.0%) | |

Table1 − CKD-chronic kidney failure; COPD-Chronic Obstructive Pulmonary Disease; CVD: Cardiovascular disease; ECOG PS- Eastern Cooperative Oncology Group Performance Status; FEV1-Forced Expiratory Volume in 1 S; ILD: Interstitial Lung Disease.

**Table 2** Median survival (months) in patients submitted to surgery versus SBRT.

| | Surgical patients -Median (95%IC) | SBRT Patients Median (95%IC) | p |
|---|---|---|---|
| OS | 68.243 (64.497−71.990) | 43.355 (36.028−50.682) | 0.099 |
| PFS | 69.625 (65.816−73.435) | 31.039 (24.063−38.014) | <**0.001** |
| Local PFS | 73.400 (69.979−76.821) | 34.494 (25.394−43.594) | <**0.001** |
| Distant PFS | 74.347 (71.116−77.578) | 42.948 (35.548−50.349) | 0.062 |
| | **Surgical Stage IA patients-Median (95%IC)** | **SBRT Stage IA Patients Median (95%IC)** | **p** |
| OS | 70.568 (65.153−75.983) | 42.949 (35.507−50.391) | **0.038** |
| PFS | 77.032 (71.728−81.337) | 32.588 (25.301−39.875) | <**0.001** |
| Local PFS | 77.904 (73.899−81.910) | 36.014 (26.508−45.520) | <**0.001** |
| Distant PFS | 78.710 (74.982−82.439) | 43.738 (36.345−51.131) | **0.009** |

OS of 40% after a median follow-up of 4 years, and 13% experienced locoregional recurrence at 3 years. In another study (RTOG 0618),[7] 33 operable patients were also treated with 60 Gy delivered in 3 fractions; the 2-year local failure rate was 8%. We expect further data on SBRT outcomes in patients fit to undergo surgery. Results of prospective randomized clinical trials are awaited.

Our cohort represents tumours in stages I-II and most of the patients were submitted to surgery (232 patients, versus 49 submitted to SBRT). SBRT was the preferred treatment in patients deemed unfit for surgery. Survival analysis showed significantly higher values in the surgical group, especially in stage IA, but SBRT remains a suitable option for inoperable patients.

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