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Which is the Best in Early Lung Cancer; Surgery or Stereotactic Body Radiation Therapy?

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ABSTRACT
Despite all improvements in surgical treatment of lung cancer, 25% of early-stage lung cancer patients can either still not undergo safe resection due to medical comorbidities, or they reject surgical treatment. Even though sublober resections were approached with suspicion and even garnered strong reactions in the beginning, it was shown in many studies that results like lobectomy were obtained, and today it has now become a common and safe practice. Based upon the successful results achieved with stereotactic radiosurgery in primary and metastatic brain tumors, due to the technologic advancements, stereotactic body radiation therapy–stereotactic ablative body radiotherapy (SBRT-SABR) practices started to be used at the beginning of the 2000s, which are based on delivering a few fractions of an extremely high radiation dose to a single target. The aim of this study is to evaluate and to discuss the results of clinical interventions in literature about early lung cancer resections and SBRT. The medical literature in the thoracic and cardiovascular surgery and oncology network was reviewed, and studies, cases, and meta-analysis articles that provided early lung cancer treatment even surgical or SBRT outcomes were examined. A discussion was made by also analyzing the survival data in the light of the available guidelines. Surgery is the standard treatment for early-stage lung cancer. SABR is the suitable treatment option in patients that cannot or refuse to undergo surgery. There is no evidence that SABR can be an alternative to surgical treatment in early-stage lung cancer cases with a medically fit condition that do not refuse surgery.
Keywords: Early stage lung cancer, surgery, stereotactic body radiation therapy

INTRODUCTION

About 1.8 million people are diagnosed with lung cancer across the world every year. Despite the increase in smoking cessation programs, scanning programs with low dose CT, and advancements in the field of treatment, it remains as the most prevalent cause of cancer-related deaths, and 1.6 million people die every year due to lung cancer (1, 2).

Due to the developments in imaging methods, and accordingly the increased rate in the application of scanning programs, early-stage lung cancer diagnosis rates have risen to 15%, and long-term survival expectations have increased (1).

Surgical treatment of lung cancer first started in 1933 with pneumonectomy, and lobectomy operations have encouraged the surgery from the 1950s until today. Minimal invasive VATS practices that began in the 1990s due to the advancements in technology were precursors to the VATS lobectomy lung cancer operations that started at the beginning of the 2000s and have begun to be used commonly around the world today with increasing momentum. Along with the imaging methods that are also related with technologic developments, the rates of early-stage lung cancer detection have increased, and sublober resections have started to be performed in peripherally localized tumors smaller than 3cm. Even though sublober resections were approached with suspicion and even garnered strong reactions in the beginning, it was shown in many studies that results similar to lobectomy were obtained, and today it has now become a common and safe practice. Thoracic surgeons have come a long way in the reduction of operative morbidity and mortality during the last decade, surgical mortality has dropped down to rates of lower than 1% today, and patients with medically high risk now have the chance of undergoing surgical treatment (2). During this period, lobectomy rates have decreased from 55% to 50%, whereas pneumonectomy rates have reduced from 3.4% to 1.1%, which, in parallel, has led to an increase in sublober resection rates from 12% to 17% (3).

Despite all these improvements, 25% of early-stage lung cancer patients can either still not undergo safe resection due to medical comorbidities, or they reject surgical treatment (3). The long-term survival results obtained with conventional RT in these cases are extremely bad, and adverse effects related to treatment toxicity are very high. Based upon the successful results achieved with stereotactic radiosurgery in primary and metastatic brain tumors, due to the technologic advancements, sterotactic body radiation therapy – stereotactic ablative body radiotherapy (SBRT-SABR) practices started to be used at the beginning of the 2000s, which are based on delivering a few fractions of an extremely high radiation dose to a single target (4).

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The first phase II study on this subject was performed by RTOG, and 3-year primary tumor control rate, locoregional control rate and survival rate were reported as 97.6%, 87.2% and 55.8%, respectively, with 54 Gy SBRT in three fractions. Excellent and provocative results obtained in medically inoperable patients led the specialized field of radiation oncology to perform investigations on SBRT practice in operable early-stage patients. The patient group that were medically suitable for surgical treatment but refused it constituted the basis of these investigations. In the first study performed on this patient group with 45-72.5 Gy SBRT practice in 7-10 fractions, 5 year local control rate was reported as 92% and 73% in T1 tumors and T2 tumors, respectively, and the survival rate was reported as 72% and 62% in Stage IA and Stage IB, respectively, with the results being claimed to be similar to those in surgical series (1).

The emergence of successful results obtained with SBRT both in medically inoperable and operable patients gave rise to an interest in surgery-SBRT comparison studies. It was seen that a healthy comparison could not be made from studies that were conducted on a retrospective series and population basis (1). Two prospective studies were commenced for this purpose.

1. STARS (StereoTActic Radiotherapy vs Surgery):
Group 1. Patients with clinical Stage I ≤4 cm tumor whose mediastinal lymphatic gland sampling was performed with surgical resection

Group 2. 54Gy SABR practice in 3 fractions on peripheral tumors
50Gy SABR practice in 4 fractions on central tumors

Histologic diagnosis was established in all patients in this study

2. ROSEL (Radiosurgery Or Surgery for operable Early stage Lung cancer)

Group 1. Surgical resection (lobectomy or sublober) on patients with Clinical Stage I ≤ 3cm tumor

Group 2. 54Gy SABR in 3 fractions on peripheral tumors
60Gy SABR in 5 fractions on tumors in contact with the central or thoracic wall

There was no histologic diagnosis condition in this study.

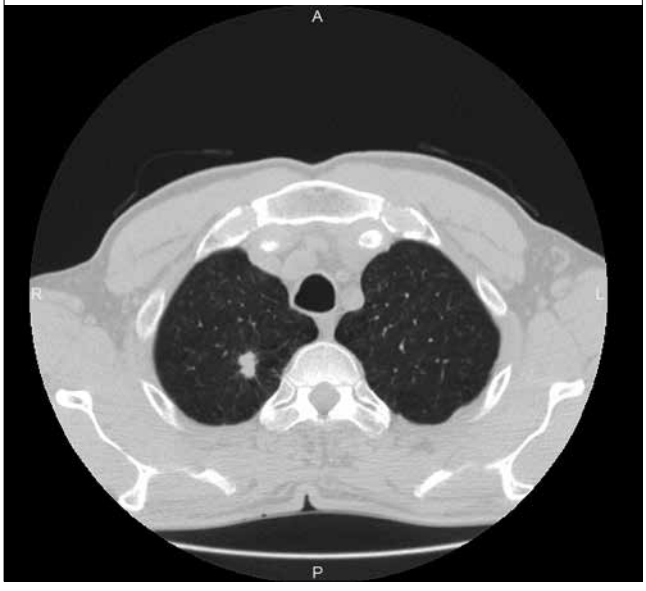
These two prospective studies were terminated early due to the lack of sufficient number of patients. STARS and ROSEL studies were terminated on 36 and 22 patients, respectively. An assessment attempt was made based on these 58 patients, and it was reported that toxicity in SABR was less and results were not worse than surgery; however, no evidence could be presented.

The reason for non-performance of surgery could be determined in only 25% of the patients that decided to take non-surgical treatment. It is not known why surgery could not be performed in 75% of the patients that received non-surgical treatment. While surgically high-risk definitions have been made with various evaluation and scoring systems, the definition of the difference between surgically high risk and medically inoperable concepts is not clear (3). In order to decide that a lung cancer patient is medically inoperable, a thoracic surgeon must be present within the multidisciplinary team.

Comparison of SABR with surgery using the retrospective series involves highly important restrictions. The significant differences between the patient populations of the two groups are quite clear. On the other hand, the two methods applied are very different from each other. While real pathological staging is performed with surgical resections, and hilar mediastinal lymphatic gland dissection or sampling, staging can be made only for the T stage with SABR, and histological diagnosis of the tumor is not often seen as a criterion. An SPN that is evaluated as malignant can be benign or a carcinoid tumor, and these cases are included in the long-term survival rates in the SABR series (Figure 1). Occult lymph node metastasis is identified at a rate of 15-20% in early-stage lung cancer. As lymph node condition cannot be determined in SABR, patients lose the chance of adjuvant treatment. Considering the evaluation of post-treatment relapse, definition of relapse is also quite different between the two methods. Residual parenchyma scar and tumors cannot be distinguished precisely in the computerized tomography during the follow-up of SABR patients. Post-treatment relapse is considered a relapse not only for those in the same lobe, but also for those in different lobes, and the definition of local follow-up varies between these two methods (4).

The low rate of adverse effects and complications in SABR is often emphasized as the advantage of this method. However, studies showing that the method might have some severe complications have also been published. Complications might be seen

Figure 1. A lesion with a spiculated contour of 16x9 mm in the right upper lobe, wedge resection with SUV max 3.2 in PET CT Pathology: Rheumatoid nodule+coal workers' pneumoconiosis (Caplan Syndrome) (From the archive of Department of Thoracic Surgery, Ankara University School of Medicine)



such as esophageal stenosis and fistula, brachial plexus neuropathy, large vascular aneurysm, stenosis or fistula in the trachea or main bronchi, skin ulcerations, rib fracture, and pneumonitis (5). In terms of early adverse effects and mortality, SABR seems to be superior to surgery in elderly patients that are believed not to be able to tolerate surgery, however when considered in the long-term, late complications may arise two years later, and surgery might become superior to SABR in terms of survival (6). On the other hand, a remarkable decrease has been seen in the surgical complication rates with the common administration of minimal invasive surgery and sublober resections starting from the beginning of the 2000s, and it has been determined through many studies that there are effective methods that are suited to oncologic surgery principles. The fact that the lobectomy results were better in the surgical series than those in SABR was identified as statistically significant (7, 8). Apart from that, it has been suggested that the results of segmentectomy, or even wedge resection, are better than those of SABR in a statistically significant way (9-11).

Survival depends on the stage of disease in lung cancer. Therefore, both tissue diagnosis and metastasis studies are very important. Computerized tomography and PET are extremely valuable in this evaluation; however, the false negativity ratio is 5-15% while false positivity ratio is about 50% in staging. Therefore, it is required to use invasive mediastinal staging methods such as TBNA, mediastinoscopy, and VATS. To make a healthy comparison between the two methods, the non-surgical treatment branch must also follow this strategy in the future (2).

Stereotactic ablative body radiotherapy is a suitable treatment method in medically inoperable Stage I lung cancer cases. In patients whose medical condition is fit for surgical treatment, mediastinal lymph node dissection or sampling together with lobectomy is the standard treatment method. This allows patients to obtain a local control and annual survival chance of over 90% and 80.5%, respectively. In patients with medical comorbidities, minimal invasive surgery methods and sublober resections can be administered, and patients thus have the chance to undergo effective treatment. Naturally, there must be a thoracic surgeon in the team to make the decision regarding medical operability.

CONCLUSION

Today, the appropriate approach in identifying the most suitable treatment option is believed to include the presence of a multidisciplinary cooperation, and a discussion carried out between a thoracic surgeon and radiation oncology specialist on the advantages and disadvantages of the treatment method to decide for each patient. Such cooperation will contribute to the studies to be conducted in the future.

To conclude, surgery is the standard treatment for early-stage lung cancer. SABR is the suitable treatment option in patients that cannot or refuse to undergo surgery. There is no evidence that SABR can be an alternative to surgical treatment in early-stage lung cancer cases with a medically fit condition that do not refuse surgery.

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