



Original Research



Comparison of long-term survival outcomes between stereotactic body radiotherapy and sublobar resection for stage I non-small-cell lung cancer in patients at high risk for lobectomy: A propensity score matching analysis

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Abstract Background: The aim of this study was to perform a survival comparison between stereotactic body radiotherapy (SBRT) and sublobar resection (SLR) in patients with stage I non-small-cell lung cancer (NSCLC) at high risk for lobectomy.

Methods: All patients who underwent SBRT or SLR because of medical comorbidities for clinical stage I NSCLC were reviewed retrospectively. Propensity score matching (PSM) was performed to reduce selection bias between SLR and SBRT patients based on age, gender, performance status, tumour diameter, forced expiratory volume in 1 second (FEV1) and Charlson comorbidity index (CCI).

Results: One hundred and fifteen patients who underwent SBRT and 65 SLR were enrolled. The median potential follow-up periods for SBRT and SLR were 6.7 and 5.3 years, respectively. No treatment-related deaths were observed. Before PSM, the 5-year overall survival (OS) was 40.3% and 60.5% for SBRT and SLR, respectively ($P = 0.008$). PSM identified 53 patients from each treatment group with similar characteristics: a median age of 76 years, a performance status of 0–1, a median tumour diameter of ~20 mm, a median FEV1 of

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~1.8 L and a median CCI of 1. The difference in OS became insignificant between the matched pairs (40.4% and 55.6% at 5 years with SBRT and SLR; $P = 0.124$). The cumulative incidence of cause-specific death was comparable between groups (35.3% and 30.3% at 5 years, $P = 0.427$).

Conclusion: SBRT can be an alternative treatment option to SLR for patients who cannot tolerate lobectomy because of medical comorbidities.

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1. Introduction

Lung cancer is the leading cause of cancer-related deaths worldwide [1]. The number of cases of stage I lung cancer is expected to increase when low-dose computed tomography (CT) screening is introduced because CT can detect more stage I cancer cases than chest radiography [2]. The U.S. Preventive Services Task Force recommends annual low-dose CT screening in individuals with a specific smoking history [3]. The treatment of stage I non-small-cell lung cancer (NSCLC) detected by CT screening is of increasing importance, particularly in high-risk operable patients [4–6]. Although lung cancer mortality has tended to decline over the last decade according to the age-adjusted incidence, the crude rate of lung cancer deaths remains high in the elderly [7,8]. As such the optimum treatment of early stage NSCLC in elderly individuals or those with medical comorbidities remains unclear.

Lobectomy remains the standard treatment for patients with clinical stage I NSCLC who can tolerate the type of surgery [9,10], even in the elderly. According to a recently updated opinion paper by the European Organisation for Research and Treatment of Cancer (EORTC) and the International Society of Geriatric Oncology (SIOG), surgical treatment should not be denied to elderly patients simply because of their age [11]. However, the percentage of patients undergoing surgery decreases with advancing age, even in patients with no comorbidities [12]. The EORTC/SIOG paper also refers to consideration of limited resections in the elderly, as well as stereotactic body radiotherapy (SBRT) in individuals who are medically inoperable.

Sublobar resection (SLR) is thought to result in inferior survival compared with lobar resection based on the results of a randomised trial [13]. This type of surgery is considered for patients with major comorbidities, and as well as individuals with a peripheral nodule of ≤ 2 cm with favourable findings [10]. In addition, Rami-Porta and Tsuboi reported that lobectomy and wedge resection result in similar survival in patients aged ≥ 71 years [14]. The American College of Surgeons Oncology Group (ACOSOG) Z4032 and Z4099 defined criteria of ‘high risk’ for lobectomy that included pulmonary function as the major criterion, and age and other medical comorbidities as minor criteria.

SBRT is being a standard treatment option for compromised patients who are medically unfit for any type of surgery due to advanced age or comorbidities [10]. Multicentre prospective trials revealed that SBRT was safe and effective in patients with inoperable stage I NSCLC [15–17]. The introduction of SBRT decreased the number of untreated elderly Dutch patients with early stage NSCLC [18].

The optimal treatment for high-risk operable patients who might tolerate surgical intervention but not lobectomy remains controversial [19,20]. To resolve this issue, an inter-group randomised trial (Radiation Therapy Oncology Group [RTOG] 1021/ACOSOG Z4099) comparing SBRT with SLR in high-risk patients with stage I NSCLC was initiated. However, it was closed in May 2013 due to slow patient enrolment. Therefore, there are no available data comparing SBRT and SLR based on a prospective randomised trial. The aim of the current study was to perform retrospective survival comparisons between SBRT and SLR in patients who underwent treatment due to medical comorbidities.

2. Methods

2.1. Patient population

This study retrospectively reviewed consecutive patients who underwent SBRT or SLR because of medical comorbidities for clinical stage I NSCLC. Data were obtained from databases maintained by the Departments of Radiation Oncology and Thoracic Surgery of Kyoto University Hospital. Clinical stage was determined using CT and 18F-fluorodeoxyglucose positron emission tomography (FDG-PET), or with CT alone. Patients with a tumour diameter > 50 mm or those without histological confirmation of NSCLC were excluded. The type of recurrence was classified according to RTOG 1021/ACOSOG Z4099. Local recurrence (LR) included primary tumour recurrence and recurrence in the involved lobe. Regional recurrence (RR) was defined as ipsilateral nodal recurrence in hilum or mediastinum, or as recurrence in the ipsilateral lung. Distant recurrence (DR) was recurrence other than LR or RR. Primary tumour recurrence was diagnosed on the basis of histologic confirmation or enlargement of the local tumour on CT that continued for at least 6 months. FDG-PET was consid-

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