Original Article

Questionnaire survey comparing surgery and stereotactic body radiotherapy for lung cancer: lessons from patients with experience of both modalities

Atsuya Takeda[1], Naoko Sanuki[1], Yuichiro Tsurugai[1], Masataka Taguri[2], Nobuyuki Horita[3], Yu Hara[3], Takahisa Eriguchi[1], Takeshi Akiba[1,4], Akitomo Sugawara[4], Etsuo Kunieda[4], Takeshi Kaneko[3]

[1]Radiation Oncology Center, Ofuna Chuo Hospital, Kamakura, Kanagawa, Japan; [2]Department of Data Science, Yokohama City University School of Data Science, Yokohama, Kanagawa, Japan; [3]Department of Pulmonology, Yokohama City University Graduate School of Medicine, Yokohama, Kanagawa, Japan; [4]Department of Radiation Oncology, Tokai University School of Medicine, Isehara, Kanagawa, Japan

Contributions: (I) Conception and design: A Takeda, N Sanuki; (II) Administrative support: A Sugawara, E Kunieda, T Kaneko; (III) Provision of study materials or patients: A Takeda, Y Tsurugai; (IV) Collection and assembly of data: A Takeda, Y Tsurugai, T Eriguchi, T Akiba; (V) Data analysis and interpretation: A Takeda, N Sanuki, Y Tsurugai, M Taguri, N Horita, Y Hara; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Atsuya Takeda, MD, PhD. Radiation Oncology Center, Ofuna Chuo Hospital, 6-2-24 Ofuna, Kamakura, Kanagawa 247-0056 Japan. Email: takeda@1994.jukuin.keio.ac.jp.

Background: Currently, there is some controversy regarding indications for stereotactic body radiotherapy (SBRT) for lung cancer patients. We investigated the treatment preferences of patients with experience of both surgery and SBRT using a questionnaire survey.

Methods: Of lung cancer patients treated with SBRT between 2005 and 2017, we identified those who also previously underwent surgery for lung cancer. These patients were asked about their experiences of surgery and SBRT including perceived condition, distress, stress, convenience, adverse effects, and satisfaction during and after treatment. Participants were also asked about treatment decision-making for hypothetical scenarios.

Results: Of 653 lung cancer patients treated with SBRT, 149 also underwent surgery for lung cancer, 52 of whom participated in this questionnaire. The median age at the time of this survey was 76 years (range, 59–91 years). Significantly more participants had a favorable impression of SBRT during and after treatment (all question items; P<0.01). In terms of overall satisfaction, 27 patients preferred SBRT and three patients preferred surgery. In a hypothetical scenario (equivalent treatment outcomes) aged 70 years and faced with decision-making for first-time lung cancer treatment, significantly more patients selected SBRT (P<0.01): 38 patients selected SBRT. In a scenario with 20% better survivals for surgical resection, 14 patients selected SBRT, 12 selected surgery, and 26 were indecisive (P=0.47). In a scenario at age 80 years, significantly more patients selected SBRT (P<0.01).

Conclusions: Most patients with experience of both surgery and SBRT for lung cancer prefer SBRT. This information would be helpful at treatment decision-making.

Keywords: Shared decision making; decision aid; stereotactic body radiotherapy (SBRT); SABR; stereotactic ablative body radiotherapy; standard treatment

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Introduction

Lung cancer is the most frequently diagnosed cancer and the leading cause of cancer deaths (1). Approximately 25% of patients with lung cancer have early-stage disease and indication for local therapy (2). This rate is likely to increase following screening recommendations (3). Surgical resection with mediastinal lymph node dissection is the standard therapy for operable, early-stage non-small cell lung cancer (NSCLC). However, patients with lung cancer are often elderly and present with comorbid conditions, meaning they are high-risk patients for surgical resection and may hesitate to be treated. Up to 45% of these patients who are offered operative treatment reject surgical treatment (4,5).

Stereotactic body radiotherapy (SBRT) is the standard treatment for medically inoperable patients with early-stage NSCLC (6,7). SBRT has achieved a good local control rate and low incidence of severe toxicities (8-11). Radiation use has increased in recent decades, and more than 25% of patients aged ≥60 years with stage I NSCLC are treated with radiation in the United States (12).

Patients do not make treatment decisions solely based on reliable evidence of outcomes, but also consider their personal preferences and their clinicians' recommendations (13). Patient decision-making aids have been successful in informing, involving, and empowering patients to participate in decision-making, particularly in decisions regarding cancer treatment (14,15). Recent guidelines from the American Society of Radiation Oncology (16) and the American Society of Clinical Oncology (17) place increasing emphasis on shared decision-making. The shared information includes treatment choices, probability of outcomes, toxicities, morbidity, mortality, and QOL, along with the patient's values and preferences (18). In addition, experience-based views of patients who have experienced both surgery and SBRT for lung cancer are thought to be useful for patients facing treatment decisions. We conducted a questionnaire survey with patients who had undergone both treatment modalities to investigate patients' treatment preferences.

Methods

Patients and survey

From the radiotherapy database in our institution, we extracted patients with lung cancer who were treated with SBRT between 2005 and 2017, and who had also been treated with surgery for lung cancer. We obtained consent to participate in this questionnaire survey from these patients by telephone or directly at a follow-up visit. Questionnaires were mailed to patients who consented to participate, and completed questionnaires were returned to our institution by mail. Alternatively, patients could complete the questionnaire at their follow-up visit. This study was approved by the Ofuna Chuo Hospital Review Board (No. 2017-011).

Participating patients were asked questions relating to quality of life (QOL) for both surgery and SBRT, including their perceptions of condition, distress, stress, convenience, adverse effects, satisfaction during and after treatment, and decision-making for hypothetical scenarios (detailed in *Table 1* and *Figure 1*). The questionnaire is our original and is not validated. We instructed patients to circle appropriate numbers on the questionnaire sheet (*Figure 1A*) with an explanation of the icon arrays (*Figure 1B*). For explanation of 5-point scale (*Figure 1A*) in this study, we instructed patients to choose point 5 when they thought SBRT is better definitely, point 4 when SBRT is relatively better, point 3 when they thought surgery and SBRT are equivalent or they could not decide simply, point 2 when surgery is relatively better, point 1 when surgery is better definitely. In questionnaire, we made hypothetical scenarios. In them, we fixed the 5-year overall survival following surgery as 75% and fluctuated those following SBRT: 75% (equivalent), 70% (5% better OS for resection), 65% (10% better OS for resection) 55% (20% better OS for resection).

Statistical analysis

The frequencies of responses to the scales for each QOL domain were calculated. A one-sample *t*-test was used to investigate which treatment modality was preferred. An independent *t*-test was used to investigate factors that affected favorability of treatment modality. A dependent *t*-test was used to investigate if scales changed for the two situations. For all tests, two-sided P values of <0.05 were considered as statistically significant. Although each scale is a categorical variable, the average score is normally distributed in large samples by the central limit theorem. Thus, we used *t*-tests for the comparisons in this study. Statistical analyses were conducted by SAS program for Windows, version 9.3 (SAS Institute Inc., Cary, NC, USA) and Microsoft Excel 2013 for Windows.

Table 1 Survey questions

During treatment
How did you feel for your general condition in comparison between surgery and SBRT?
How did you feel for your physical distress, i.e., pain and dyspnea, in comparison between surgery and SBRT?
How did you feel for your mental stress and anxiety in comparison between surgery and SBRT?
How did you think about convenience in comparison between surgery and SBRT?
One year after treatment
How was the recovery in physical condition from pretreatment to one year after treatment in comparison between surgery and SBRT?
How were the adverse effects in comparison between surgery and SBRT?
How did you feel for your mental stress and anxiety in comparison between surgery and SBRT?
How did the treatment interfered you in daily life, i.e., shopping, cleaning, laundry, stroll, car driving in comparison between surgery and SBRT?
Overall impression now
Overall, how were you satisfied with treatment in comparison between surgery and SBRT?
Adoption in hypothetical scenarios
Suppose that you are just diagnosed as early lung cancer in 70 years old at first time. Choose your preference in following situations:
Suppose that, among 100 patients, 75 surgery patients can survive; and, 75 SBRT patients can also survive. Which treatment do you choose, surgery or SBRT?
Suppose that, among 100 patients, 75 surgery patients can survive; in contrast, 70 SBRT patients (5 patients less) can survive. Which treatment do you choose, surgery or SBRT?
Suppose that, among 100 patients, 75 surgery patients can survive; in contrast, 65 SBRT patients (10 patients less) can survive. Which treatment do you choose, surgery or SBRT?
Suppose that, among 100 patients, 75 surgery patients can survive; in contrast, 55 SBRT patients (20 patients less) can survive. Which treatment do you choose, surgery or SBRT?
Suppose that you are just diagnosed as early lung cancer in 80 years old at first time. Choose your preference in following situations:
Suppose that, among 100 patients, 75 surgery patients can survive; and, 75 SBRT patients can also survive. Which treatment do you choose, surgery or SBRT?
Suppose that, among 100 patients, 75 surgery patients can survive; in contrast, 70 SBRT patients (5 patients less) can survive. Which treatment do you choose, surgery or SBRT?
Suppose that, among 100 patients, 75 surgery patients can survive; in contrast, 65 SBRT patients (10 patients less) can survive. Which treatment do you choose, surgery or SBRT?
Suppose that, among 100 patients, 75 surgery patients can survive; in contrast, 55 SBRT patients (20 patients less) can survive. Which treatment do you choose, surgery or SBRT?

SBRT, stereotactic body radiotherapy.

Results

We treated 653 patients with lung cancer with SBRT between 2005 and 2017. *Figure 2* presents a flow chart of study participants. Among the 653 patients, 149 also had a history of lung resection. Of these, 83 patients were deceased at the time of this study, four had dementia, and eight were unable to complete follow-up as outpatients in our institution but were followed by a referral medical doctor. Therefore, we invited 54 patients to complete this questionnaire, and received replies from 52 patients.

Participating patients and tumor characteristics are listed in *Table 2*. As for additional SBRT information, treatment time in each SBRT session was approximately

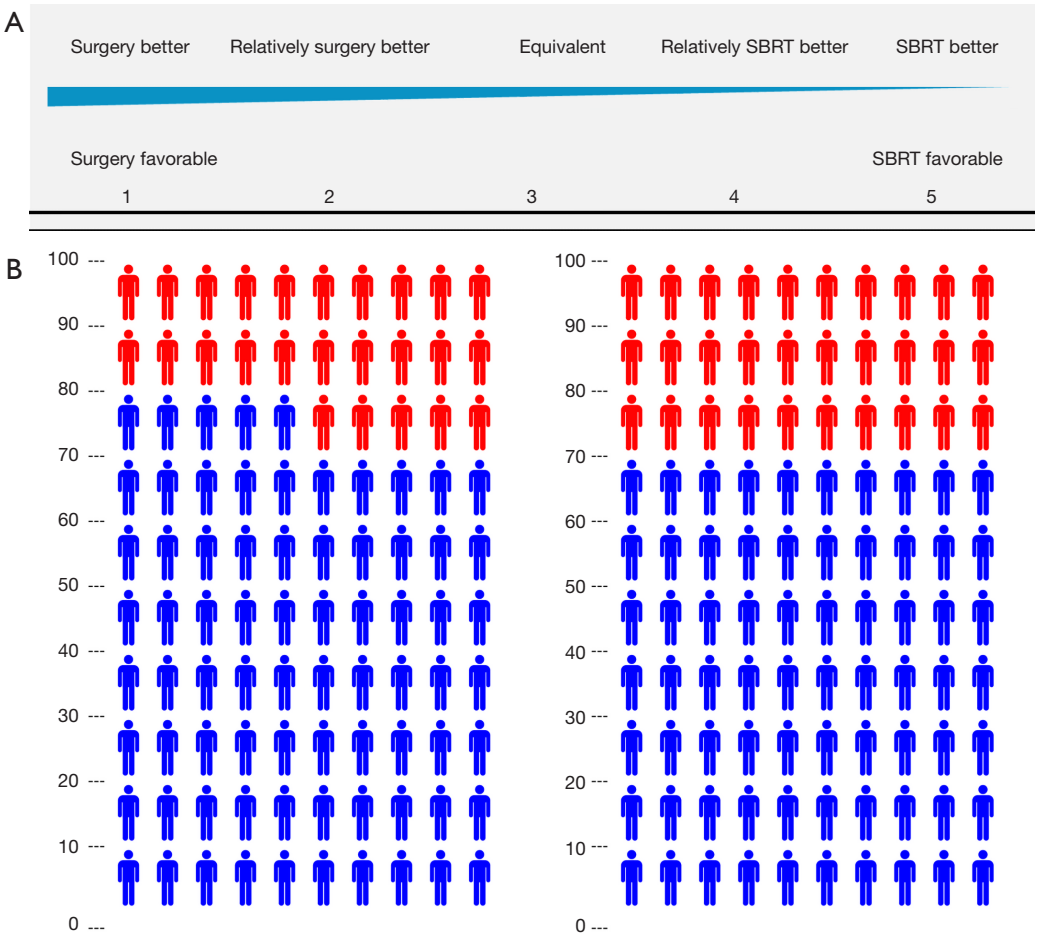

Figure 1 (A) Scales used in the questionnaire. (B) Sample icon arrays (Question 11) used in Question 10–17. The icon arrays are inserted in Questionnaire survey sheets. In the icon arrays, blue and red icons show survivors and deceased persons 5 years after each treatment, respectively. The sample icon indicates that 75 patients are alive and 25 patients are dead 5 year after surgery among 100 patients (left), and that 70 patients are alive and 30 patients are dead 5 year after Stereotactic body radiotherapy (right) (case of Question 11).

30 minutes. And median number of treatment days was 5 [5–10] days. According to the Common Terminology Criteria for Adverse Events (CTCAE) v.4.0., the number of radiation pneumonitis of grade 2 and 3 were 8 and 1, respectively. Grade 2 rib fracture with intercostal neuralgia was observed in 2 patients. No other toxicities were observed. In total, 48 patients had one resection and four had two resections; 46 patients had SBRT once, four had SBRT twice, and two had SBRT three times. All patients had a history of resection before SBRT. No patients had a history of resection after SBRT. Participants' median age at the time of the survey was 76 years (range 59–91 years). The median follow-up from initial resection was 98 months (range, 17–276 months), and from SBRT was 37 months (range, 6–129 months). The median duration between latest resection and initial SBRT was 48 months (range, 2–210 months).

In *Figure 3A*, each column represents the number of patients for each QOL domain (general condition, physical distress, stress and anxiety, and convenience) during treatment. More patients reported favorable impressions of SBRT in terms of general condition (42 patients, 81%), physical distress (45 patients, 87%), mental stress and anxiety (34 patients, 65%), and convenience (48 patients, 92%). For surgery, only one patient (2%) had a favorable impression of general condition, one (2%) had a favorable impression of physical distress, eight (15%) had a favorable impression of mental stress and anxiety, and one (2%) had

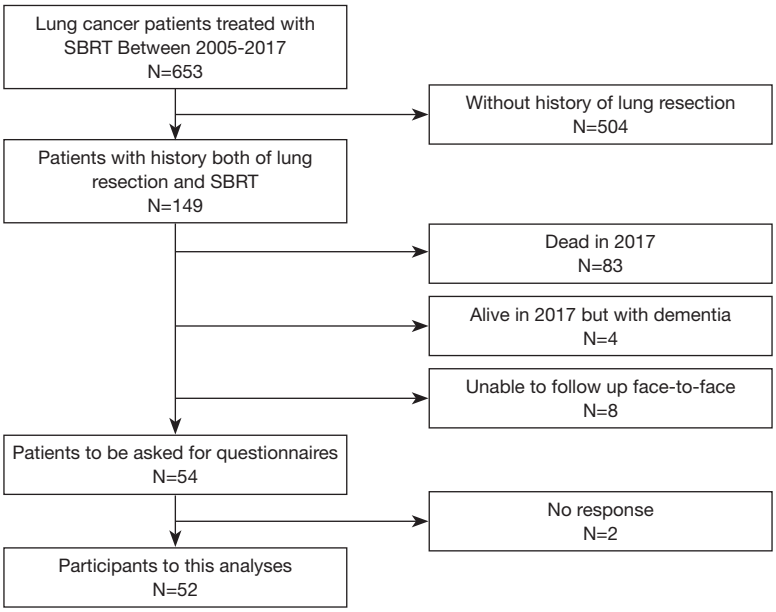

Figure 2 Flow chart of this study.

Table 2 Participating patients and tumor characteristics

Characteristics	n	%
No. of patients	52	
Male/female (%)	29/23	56%/44%
Median age at questionnaire, year (range)	76	59–91
Median duration between latest resection and initial SBRT month, (range)	48	2–210
SBRT		
Median age at latest SBRT, year (range)	73	53–90
Median follow up from initial SBRT, months (range)	37	6–129
Operable/inoperable at initial SBRT	18/34	35%/65%
COPD at initial SBRT	18	35%
Times of SBRT: 1/2/3 (%)	47/2/3	90%/4%/6%
Metachronous/ postop recurrence (%)	36/16	69%/31%
Stage: I/II/III (%)	46/4/2	88%/8%/4%
Surgery		
Median age at latest resection, year (range)	68	45–84
Median follow-up duration from initial resection, month (range)	98	17–276
Times of resection: 1/2/3 (%)	48/4/0	92%/8%/0%
Stage: I/II/III (%)	46/4/2	88%/8%/4%
Operative procedure: open/video-assisted (%)	39/13	75%/25%
Operative procedure: lobectomy/limited surgery (%)	43/9	83%/17%

SBRT, stereotactic body radiotherapy; COPD, chronic obstructive pulmonary disease.

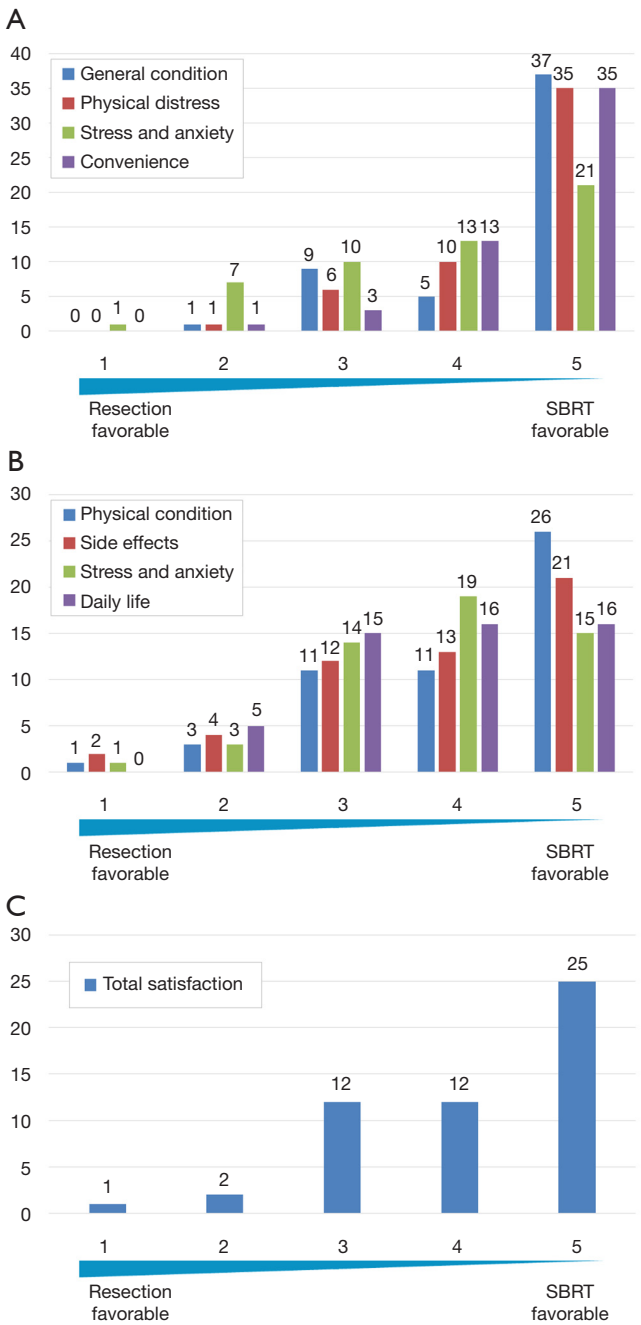

Figure 3 Summary of questionnaire concerning during treatment (A), after treatment (B), and total satisfaction (C). Each column shows the number of patients who selected each response option (number) for each domain: 1, resection favorable; 2, resection slightly favorable; 3, difficult to say which is better; 4, SBRT slightly favorable; 5, SBRT favorable. SBRT, stereotactic body radiotherapy.

a favorable impression of convenience. Similarly, *Figure 3B* shows that more patients preferred SBRT for physical condition (37 patients, 71%), adverse effects (34 patients, 65%), mental stress and anxiety (34 patients, 65%), and daily life (32 patients, 62%). Fewer patients had more favorable impressions of surgery: physical condition (four patients, 8%), adverse effects (six patients, 12%), mental stress and anxiety (four patients, 8%), and daily life (five patients, 10%). In terms of total satisfaction, 37 patients had a more favorable impression of SBRT and three patients had more favorable impression of surgery (*Figure 3C*). In addition, patients had a significantly more favorable impression of SBRT during and after treatment, with average scores ranging from 3.8–4.6, by one-sample t-tests against the null values of 3 point scores which meant equivalent value to both of the treatments (all question items; P<0.01). For total satisfaction, older patients (aged ≥76 years) had a significantly less favorable average score (3.8 *vs.* 4.5) (P=0.02). The other background factors investigated (sex, age, stage at surgery/SBRT, open thoracotomy or video-assisted thoracic surgery, lobectomy or limited surgery, postoperative adjuvant chemotherapy or not, SBRT for postoperative recurrence or metachronous lung cancer, current cancer status, operability or not at initial SBRT, chronic obstructive pulmonary disease or not at initial SBRT) did not significantly affect the score.

In a hypothetical scenario with equivalent treatment outcomes where patients were aged 70 years and faced with decision-making for first-time lung cancer treatment (*Figure 4A*), the average score was 4.0 under equivalent treatment OS and it showed patients significantly preferred SBRT (P<0.01); 38 (73%) patients preferred SBRT, and only four (8%) patients preferred surgery. Under a scenario of better outcomes for resection, more patients were indecisive, more selected surgery, and average scores significantly declined (3.7, 3.4, and 3.1 for 5%, 10%, and 20% better outcomes for resection, respectively) (P<0.01). However, in a scenario with 20% better outcomes for resection, the preference was statistically insignificant (P=0.47), with 14 (27%) patients preferring SBRT and 12 (23%) preferring surgery.

In a scenario for age 80 years, even more patients preferred SBRT compared with the 70-year-old scenario (*Figure 4B*). Average scores significantly declined for scenarios with 0% (4.4), 5% (4.2), 10% (3.8), and 20% (3.6) better outcomes for surgery (P<0.01). These scores

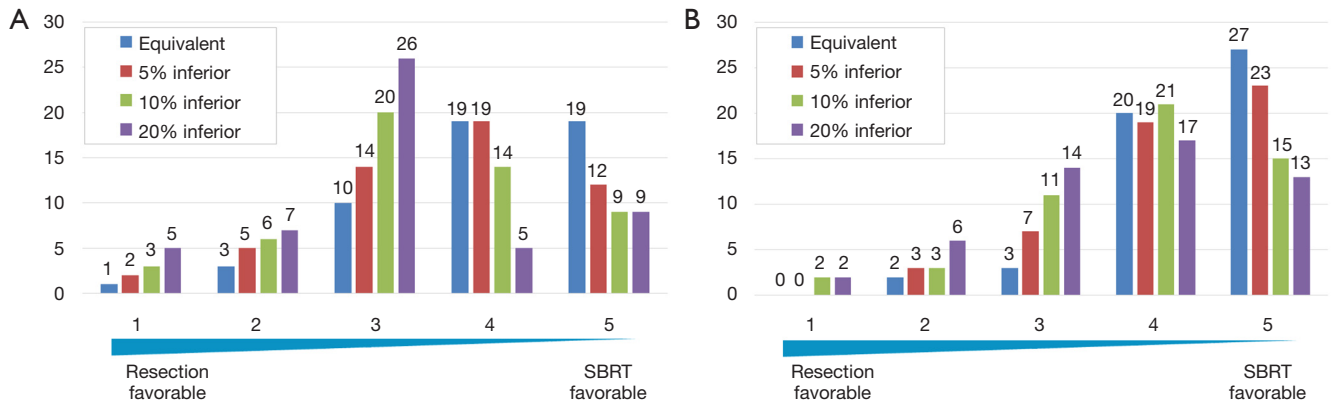

Figure 4 Summary of preferences for surgery and SBRT at age 70 years (A) and 80 years (B). Patients were asked which treatment they would select when treatment outcomes (5-year overall survival) for resection were 0%, 5%, 10%, and 20% better than those for SBRT. Each column shows the number of patients who selected each number for each state: 1, resection favorable; 2, resection slightly favorable; 3, difficult to say which is better; 4, SBRT slightly favorable; and 5, SBRT favorable. SBRT, stereotactic body radiotherapy.

were significantly increased compared with those under the hypothetical scenario involving a 70-year-old patient (P<0.01).

Among the background factors, stage at surgery significantly affected average scores. Patients who were stage II or III at surgery had significantly lower scores than those who were stage I; in patients with stage I, average scores for survival gaps of 0%, 5%, 10%, and 20% (assuming age 70 years) were 3.9, 3.5, 3.2, and 3.0, respectively. In contrast, in patients who were stage II or III, average scores were 4.4, 4.3, 4.1, and 3.6, respectively. No other background factors had a significant effect on score. The 80-year-old scenario showed similar results, with no other background factors significantly affecting the score.

Discussion

Currently, there is no reliable evidence of superiority of surgery or SBRT for patients with operable early-stage NSCLC, especially for high-risk operable patients. Three randomized trials were conducted to compare the outcomes of surgery and SBRT for operable early-stage NSCLC, but these trials closed early because of poor accrual (19). This poor accrual might be explained by the totally different nature of the two treatment modalities (20). In this situation, information regarding patients' preferences for both modalities is not sufficient. Shaverdian *et al.* (21) surveyed patient preferences treated with SBRT, and compared them among some part of patients who had experienced both treatment modalities. We also conducted a questionnaire survey with exclusive patients who had experienced both surgery and SBRT for lung cancer and investigated patients' preferences and treatment decision depending on age. To our knowledge, this is the second study to compare patient preferences among patients who had experienced both treatment modalities.

A major concern for patients when making treatment decisions is QOL during and after treatment. QOL studies following SBRT showed little deterioration in functional ability, reported pulmonary symptoms, and other QOL measures (22-25). However, QOL studies following surgery reported distinct deterioration in physical function and general and pulmonary symptoms (26,27), although these were modestly improved with video-assisted thoracic surgery (28). In a direct comparison using an objective index, QOL measures were significantly more favorable with SBRT (29).

This study was based on a questionnaire survey involving patients who had experienced both surgery and SBRT, an uncommon patient group with valuable insights. Their preferences and QOL may be applicable to early lung cancer patients diagnosed at first time, although the participants themselves were somewhat specific. Participants were treated with SBRT for metachronous second primary lung cancer or postoperative stump recurrence. In this study, the reason SBRT was conducted did not significantly affect the scores, and SBRT was effective for both diseases. The risk of metachronous second primary lung cancer in patients with previously treated lung cancer is thought to be 1.10% per patient per year (30). The rate of postoperative

stump recurrence alone is reported to be 3%, even after complete resection (31), and the rate further increased in surgical margin positive patients. To rescue such patients, SBRT plays an important role with high local control (32).

In this study, questions about QOL during and after treatment showed the average scores favored SBRT. These results indicated that patients generally experienced less stress with SBRT, mentally, physically, and comprehensively. A similar result was observed in the previously mentioned study by Shaverdian *et al.* (21). In addition, both studies showed that the more favorable QOL was consistent even if they had SBRT-related toxicities.

Morbidity and mortality are also major concerns in deciding about treatment, and affect QOL after treatment. This information should also be conveyed to patients, as early death is of particular concern. Post-treatment early mortality rates (0–3 months after treatment) were moderately higher following surgery than SBRT (33). In addition, differences in the rates increased with age (33). In the medium term (3–18 months after treatment), mortality rates were also higher following surgery (34), with excess non-cancer deaths also observed more often in the surgical arm.

In the hypothetical scenarios in the present study, participants generally selected SBRT. In those scenarios, the average score only showed favor of either modality when the difference of the 5-year survival rate of both treatment methods was 20% at the age of 70 years. This result suggests that more patients place importance on better QOL than on good treatment outcomes than physicians may expect. In fact, in the scenario of a 20% difference, the number of patients selecting surgery was small and more than half scored "3", suggesting that patients could not select a modality.

In terms of the influence of background factors, more advanced stage (stage II/III) at surgery encouraged patients to select SBRT. However, interpretation of this result was difficult because no other factors (including invasiveness of surgery (open *vs.* VATS, lobectomy *vs.* limited surgery) and presence of adjuvant chemotherapy) showed significant differences.

Patients' preferences might be quite different between experiencers and non-experiencers. Tong *et al.* (13) performed a conjoint analysis using healthy volunteers to reveal patients' preference in hypothetical stage I NSCLC. The survey respondents were recruited by an open online platform hosted and governed by Amazon, with a self-reported smoking history and age greater than 40 years. They were shown brief characteristics of treatment modalities composed of each numerical values of length of procedure, days in hospital and recovery time at home. Then they answered questions for treatment decision among three treatment options (open operations, minimally invasive operations, and SBRT) with median time of 12 minutes. As results, they preferred minimally invasive operation over SBRT or open operations. Risk of cancer recurrence, as well as treatment modality, were the most important factors associated with treatment preferences. Those results were different from our results. Although many other factors might influence results such as supplied information, characteristics of survey responders (i.e., age, health and comorbidities) and questions, preferences of experiencers are thought to be more persuasive and worth considering for decision making as experience is the best teacher.

Differences in preference and values between patients and physicians may lead to an inappropriate goal in decision-making. As a key part of treatment decision-making, physicians should be aware that their explanations are likely to be biased by their own expertise. It is important to remember that medical specialists disagree on which option is best for patients with early-stage disease. A previous study asked thoracic oncologists to recommend surgery or SBRT for 16 hypothetical patients with stage I NSCLC (35). The results showed limited consistency in the majority of cases, except in the fit of young patients with no comorbidity for surgery. SBRT was recommended more often by pulmonologists and radiation oncologists than by thoracic surgeons. In addition, nearly 55% of thoracic oncologists indicated they considered surgery and SBRT to be equal treatment options. Clinicians who considered surgery and SBRT to be similarly effective were more likely to recommend SBRT.

The present study has several limitations and biases. First, this was a retrospective study performed at a single-institution with a small number of patients, which could not validate the subgroup analyses for any definitive conclusions. Second, all participants were treated with surgery first and SBRT second. There is potential for recall bias and recency bias. Patients might have lost memories of surgery, and evaluate their preferences based on recent memories. Early-death patients were not included in the study sample, which represents potential selection and length bias. Patients were more advanced in age/frailer

and thus preferred SBRT based on their current health state. Third, there may be a bias that some patients had a bad impression to surgical operation because they recurred following surgery and were salvaged by SBRT. Fourth, this study was conducted by staff at a radiation oncology center. Participants' answers might have been different if the study had been conducted by surgeons. Fifth, surgical techniques are progressing and becoming less invasive. With the increase in minimally invasive and robotic surgery procedures, a more contemporaneous cohort would state preferences differently. Sixth, there is no reliable method to compare QOLs after one treatment to those after another. Therefore, we performed this questionnaire with our original method though it is not evaluated objectively. In order to exclude those biases, it would be desirable to prospectively conduct this questionnaire survey closer to the decision time and at fixed times after each treatment with larger population.

The experience-based views of patients who had experienced both surgery and SBRT for lung cancer are valuable and helpful to both physicians and patients in treatment decision-making. Physicians should be aware of and respect these valuable experience-based views, and make an effort to share them with their patients. Patients should be aware of such information to aid discussion and reaching appropriate treatment decisions with their physician. In conclusion, most patients who had experienced both surgery and SBRT for lung cancer prefer SBRT. This information would be helpful to patients and physicians in treatment decision-making.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study was approved by the Ofuna Chuo Hospital Review Board (No. 2017-011). We obtained consent to participate in this questionnaire survey from these patients by telephone or directly at a follow-up visit.

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