Zeng et al.
European Journal of Medical Research (2025) 30:173
https://doi.org/10.1186/s40001-025-02436-3

European Journal of Medical Research

RESEARCH

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Survival benefit of surgery vs radiotherapy alone to patients with stage IA lung adenocarcinoma: a propensity score-matched analysis

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Abstract

Objectives We compared the overall survival (OS) and cancer-specific survival (CSS) of patients who received radiotherapy and surgery, respectively, in a large population.

Methods In this study, we counted the patients diagnosed with stage IA lung adenocarcinoma in the SEER database from 2015 to 2019. We compared the overall survival (OS) and cancer-specific survival (CSS) through Kaplan Meier analysis, balanced the differences of primary data through propensity score matching (PSM), screened independent prognostic factors through Cox regression analysis, and then compared the survival differences of different treatment methods through hierarchical analysis.

Results Among 11,159 patients with stage IA lung adenocarcinoma, 4254 patients chose radiotherapy alone (38.1%), and 6688 patients were finally included through the propensity score matching. The median survival time for patients with radiotherapy alone was 53 months, while the patients with surgery alone did not reach the median survival time ($p < 0.001$). Multivariate analysis showed that age, sex, tumor size, and household income affected the prognosis of patients. The results of the stratified analysis showed that, except in the subgroup of age ≤ 50 years, almost all subgroup analyses showed that surgical treatment achieved better results.

Conclusions Radiotherapy alone can be used as an option for patients with stage IA lung adenocarcinoma who cannot tolerate surgery, but the benefit to patients is limited, and surgical treatment may still be the best choice.

Keywords Lung adenocarcinoma, Radiotherapy, Surgery, Prognosis, SEER database

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Introduction

The development of high-resolution computed tomography has dramatically improved the early lung cancer detection rate [1]. In 2020 alone, about 2.2 million new lung cancer cases were confirmed, accounting for 11.4% of all cancer cases [2]. Among them, lung adenocarcinoma (LUAD) is one of the most common types, accounting for about 40% of all lung cancer and leading to many patient deaths [3, 4]. Despite significant progress has been made in treatment in recent years, the prognosis of LUAD is still abysmal, and the overall 5-year survival rate is about 18% [5].

For a long time, surgery has been recommended as the first choice for the treatment of early non-small cell lung cancer, including LUAD [6, 7], but not all patients can tolerate surgery. Some patients also benefit from non-surgical treatment, including radiotherapy and radiofrequency ablation [8, 9]. With the development of radiotherapy technology, new technologies represented by three-dimensional conformal radiotherapy and stereotactic body radiotherapy (SBRT) have been applied [10]. They increased the radiation to tumor tissues, reduced damage to normal tissues through accurate positioning and radiation concentration [11], and achieved good local control and overall survival rate in lung cancer patients [12, 13].

To determine the preferred treatment, we compared the overall survival (OS) and cancer-specific survival (CSS) of stage IA lung adenocarcinoma patients who received radiotherapy and surgery, respectively, in the SEER database by means of propensity score matching (PSM).

Materials and methods

Data sources

The Surveillance, Epidemiology, and End Results (SEER) database (https://seer.cancer.gov/), supported by the National Cancer Institute, covers approximately 28% of the U.S. population and is currently the largest publicly available cancer database [14].

We selected the Incidence–SEER Research Plus Data, 17 Registries, Nov 2021 Sub (2000–2019) database, and used SEER*Stat software (version 8.4.0, National Cancer Institute, Bethesda, Maryland, USA) to download the relevant clinical information on lung cancer from 2015 to 2019, the relevant data on lung adenocarcinoma were screened by the International Classification of Tumor Diseases Third Edition (ICD-O-3) histological code 8140/3 (adenocarcinoma, NOS).

The data from 2015 to 2017 were based on the 7th edition of the American Joint Committee on Cancer (ACJJ) staging principles. In addition, the data from 2018 to 2019 were based on the 8th edition of the American Joint Committee on Cancer (ACJJ) staging. However, there was no difference in their definition of stage IA, and both were T1N0M0. Finally, we determined the inclusion criteria as follows: (1) Stage IA; (2) pathologically diagnosed with lung adenocarcinoma; (3) no previous radiotherapy or surgery for cancer; (4) no chemotherapy this time; and (5) have a complete follow-up date and a survival time greater than 0 day.

Patients who met any of the following criteria were also excluded: (1) race unknown; (2) marital status unknown; (3) tumor size unknown (3) tumor anatomical location unknown, (4) neither surgery nor radiation treatment; and (5) received both surgery and radiation therapy at the same time. In the end, 11,159 patients were finally screened for inclusion in the study. The process of filtering data is shown in Fig. 1.

Research variables

Information on variables such as age, gender, year of diagnosis, race, marital status, average household income, tumor anatomical location, tumor size, tumor grade, surgery, radiotherapy, chemotherapy, and survival time were found in the SEER database. In addition, there is no standard for devices used for radiotherapy. We set the primary endpoints as overall survival (OS) and cancer-specific survival (CSS); for OS, death from any cause was considered an event; for CSS, only death from lung cancer was considered.

We divided all patients into five groups for age at diagnosis: ≤50 years, 51–60 years, 61–70 years, 71–80 years, and ≥80 years. For the race, we divided all patients into white, black, and others; for tumor size, all patients were classified as less than or equal to 2 cm and greater than 2 cm but smaller than 3 cm; for marital status, all patients were classified as married and currently unmarried; for family income, all patients were classified as less than $59,999, 60,000 To $74,999 and more than $75,000 in three groups.

Statistics and analysis

All clinical data were performed using SPSS statistical analysis software (version 23.0), and Pearson's chi-square, p value = 0.05, was used as the cutoff value to evaluate the different clinical characteristics between the two groups in the comparison between the surgery therapy group (ST) and the radiotherapy group (RT) [15]. Differences in OS and CSS between surgery and radiotherapy groups were assessed by plotting survival curves.

To reduce selection bias in the two groups of baseline variables, seven variables, including age, gender, race, marital status, household income, tumor location, and tumor size, were subjected to 1:1 propensity score matching (PSM) [16]. The data were then re-analyzed for clinical characteristics and survival. Finally, univariate and multivariate COX regression models were used to estimate hazard ratios and 95% confidence intervals for independent prognostic factors related to OS and CSS in LUAD patients [17]. All survival analyses were performed using R (version 3.6.3), and p values < 0.05 were considered statistically significant.

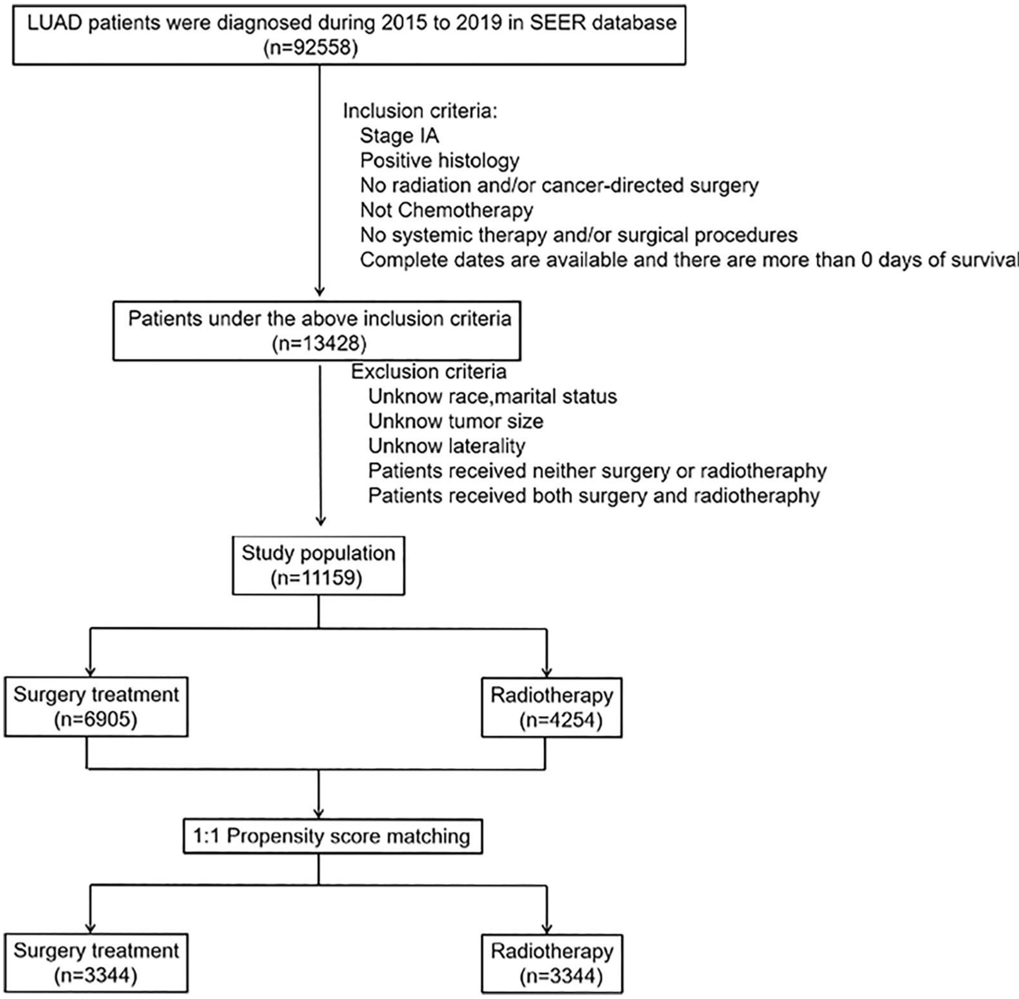

Fig. 1 Workflow of the patient selection process

Results

Demographic and clinical characteristics

We divided 11,159 patients with stage IA LUAD into a surgery therapy group (ST, $n=6905$) and a radiotherapy group (RT, $n=4254$) according to the difference in treatment methods. During the follow-up period, patients in the surgery group did not reach the median survival time, while patients in the radiotherapy group had a median survival time of 53 months. The demographics and clinical characteristics of patients with stage IA LUAD who received different treatment methods are shown in Table S1. The chi-square test results indicated significant differences ($p<0.05$) between the two groups in several variables, including age at diagnosis, gender, race, anatomical location, tumor size, and marital status. However, differences in household income had no significant effect on patients' treatment choices. We also found a significant difference in survival between the groups (Fig. 2), whether in OS or CSS, with significantly better outcomes in the ST than in the RT ($p<0.001$).

Prognostic factors for OS and CSS were identified in a 1:1 PSM sample

To better balance the underlying patient profile, we performed a rigorous 1:1 PSM for variables, such as age at diagnosis, gender, race, anatomical location, tumor size, marital status, household income, and treatment pattern, resulting in 6688 patients (Figure S1). The differences in data at different levels after propensity matching have been significantly adjusted (Table S2). We repeated the survival analysis, and the result showed that the prognosis of the ST was still better than that of the RT, with a significant difference between the two groups (Figure S2).

We performed univariate and multivariate Cox regression analyses for all patients after PSM to assess the relationship between treatment mode and OS and CSS. In

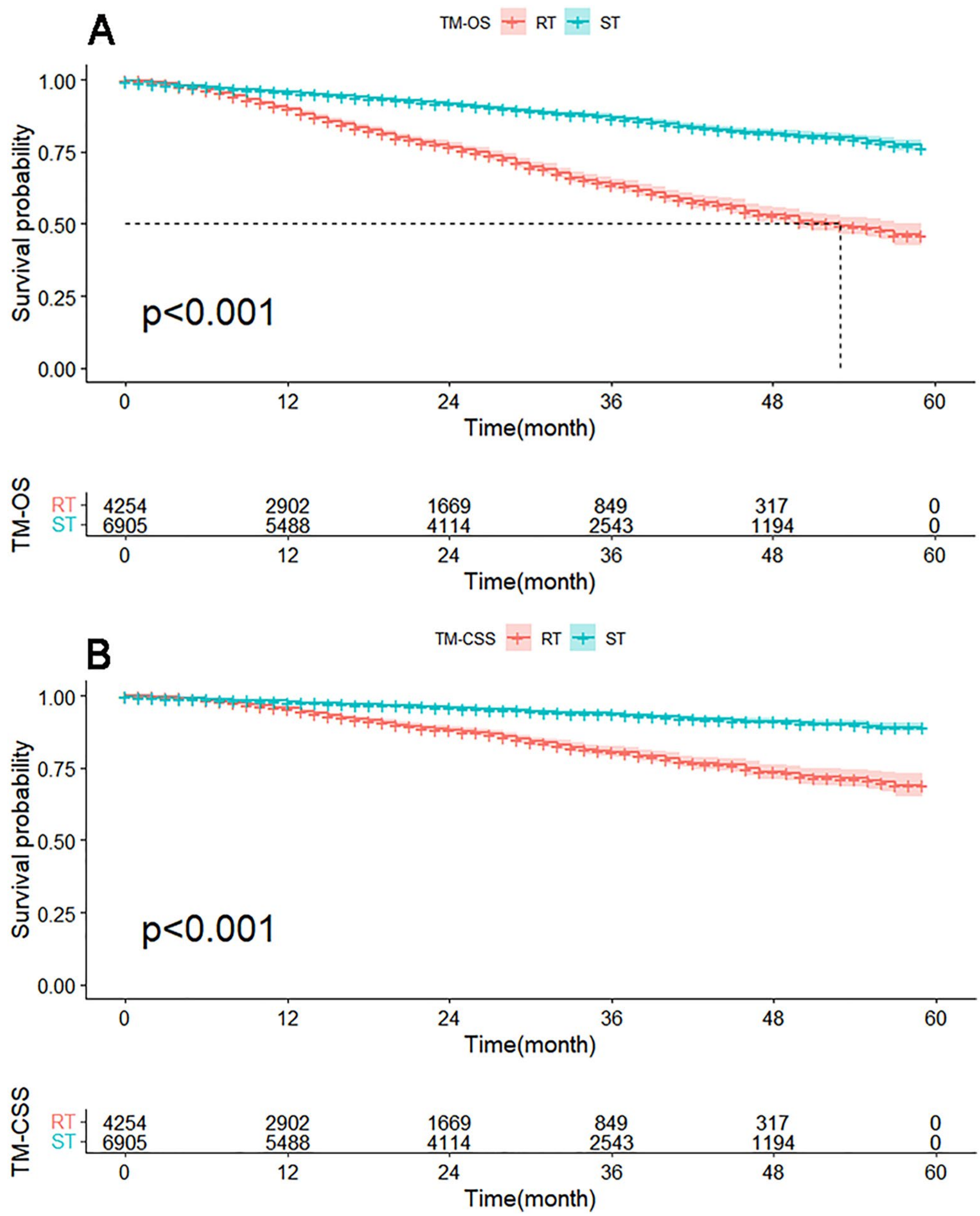

Fig. 2 Survival analysis: the survival analysis of 11,159 patients with stage IA lung adenocarcinoma, **A** the difference of overall survival (OS); **B** the difference in cancer specific survival (CSS)

addition, we found that age, sex, tumor size, household income, and treatment modality to were independent risk factors. Surgery significantly improved the OS (vs "radiotherapy"; HR = 2.38, 95% CI 2.12–2.68, $p<0.001$) and CSS (vs "radiotherapy"; HR = 2.47, 95% CI 2.08–2.95, $p<0.001$) (Table S3).

Effects of independent risk factors on OS and CSS

To further explore the impact of independent risk factors on patient outcomes, we performed subgroup analyses of age, sex, tumor size, and household income. We divided the age into five groups. The results showed that in the age group of 50 or less, the difference in treatment mode had no significant effect on the CSS of the patients ($p=0.115$), but there was a significant difference in the OS of the two groups of patients ($p=0.019$). In the remaining four groups of patients, the OS and CSS bacteria of the patients in the surgery group were better than those in the radiotherapy group, and there were significant differences ($p<0.001$) (Figure S3). Regarding gender, we found that patients treated with surgery had better OS and CSS than those treated with radiotherapy ($p < 0.001$), regardless of whether they were male or female (Fig. 3). In terms of tumor size, we found that whether the tumor was less than or equal to 2 cm or greater than 2 cm but less than 3 cm, surgery was a better choice and could benefit the patient ($p < 0.001$) (Fig. 4). Regarding household income, patients with different household incomes had significantly higher benefits from surgery than from radiotherapy ($p < 0.001$) (Fig. 5).

Cause of death analysis

We also analyzed the causes of death of patients. In the original data, 1874 patients died, of which lung cancer accounted for the most, accounting for 46.85%, followed by cardiovascular and cerebrovascular diseases, accounting for about 13.66%. The proportion of patients who died from other respiratory system diseases was 9.82%. For patients who underwent PSM, a total of 1233 patients died. Lung cancer was still the leading cause of death, accounting for 46.72%, followed by cardiovascular and cerebrovascular diseases, accounting for 13.06%. The proportion of patients who died from other diseases of the respiratory system rose, reaching 10.06% (Figure S4).

Discussion

Although the treatment of non-small cell lung cancer has been continuously developed, surgical treatment has always occupied a central position; whether it is radiotherapy, chemotherapy, targeted therapy, or immunotherapy, it is more considered complementary to surgical treatment than a complete alternative. However, with the maturity of SBRT technology, we have noticed the value of radiotherapy alone for early stage lung adenocarcinoma. Therefore, we counted the patients diagnosed with stage IA LUAD in the SEER database from 2015 to 2019 and systematically analyzed the effects of surgery alone and radiotherapy alone on the overall survival (OS) and cancer-specific survival (CSS) by propensity matching.

This study found that surgery remains the treatment of choice for stage IA LUAD, in line with clinical guidelines, and radiotherapy may be a potential treatment. However, it is far from being an alternative to surgery. Previous studies have suggested that the emergence of techniques such as SBRT has brought new hope to patients who

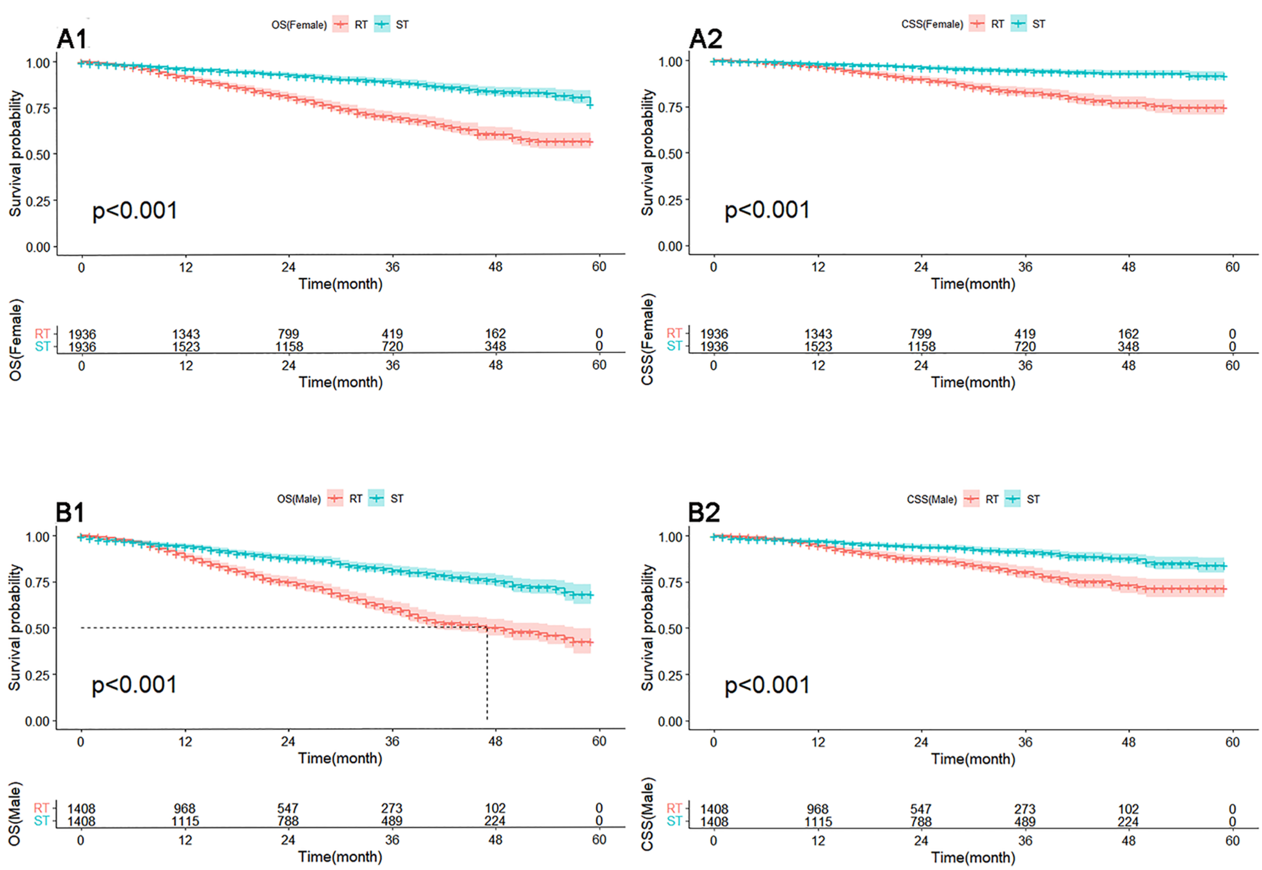

Fig. 3 Survival analysis stratified by gender: **A** for female, **B** for male, 1 for overall survival (OS) and 2 for cancer-specific survival (CSS)

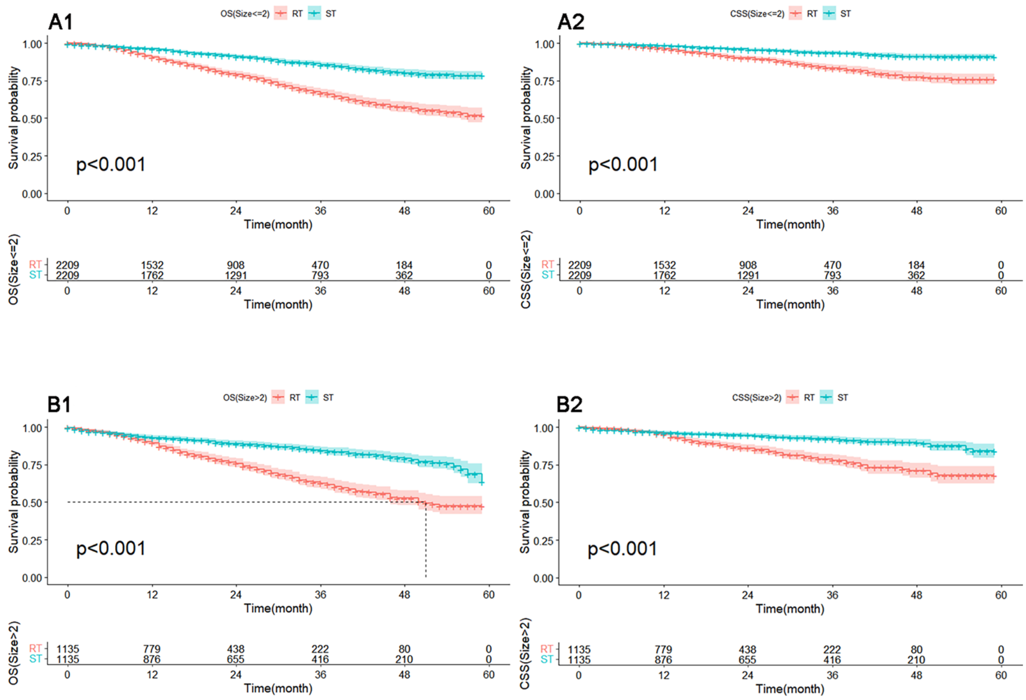

Fig. 4 Survival analysis stratified by tumor size: **A** represents a tumor less than or equal to 2 cm and **B** represents a tumor greater than 2 cm but smaller than 3 cm; 1 represents overall survival (OS), 2 represents cancer-specific survival (CSS)

cannot tolerate surgery, especially the elderly [18–21]. However, only a few studies have demonstrated comparable OS in patients who opt for surgery vs SBRT [7, 22]. Multiple studies have shown that the benefits of surgical treatment are more significant in early lung cancer patients. Some studies have shown that the 5-year survival rate of patients with stage IA lung adenocarcinoma after surgical treatment is about 80% to 90%, so the median survival period usually exceeds 5 years, some literature points out that the median survival period of patients with stage IA lung adenocarcinoma can reach 10 years or more, especially for younger patients without other health problems [23–27]. Therefore, it is understandable that we were unable to observe the median survival time of patients in the surgical group in our data. In addition, due to the limitation of follow-up time, we were unable to observe the 5-year survival rate of patients in the surgical group. However, our statistical results show that the 1-year OS rate of patients in the surgical group is 95.6%, and the 3-year OS rate is 86.8%, which is similar to the results of multiple studies. The median survival time of patients in the radiotherapy group was 53 months, with a 1-year OS rate of 89.9% and a 3-year OS rate of 63.6%. This may be due to the poor primary conditions of patients who chose radiotherapy. Many of them have serious chronic diseases, such as heart disease, cerebrovascular disease, and chronic obstructive pulmonary disease. The poor physical condition makes these patients inability to tolerate surgery and opt for radiotherapy, thus biasing the final findings.

In this study, age was one of the critical factors affecting patient prognosis. However, only in the age group ≤ 50 years of age, the CSS of patients in the RT was not significantly different from that in the ST. However, there were only 26 cases in this population, and there was a large offset. Similar to previous findings, surgery yielded better outcomes in other age groups [28]. In the age group ≥ 81 years, the patients who opted for radiotherapy were about four times more likely to choose the surgery group, and the same was true for the results of the early study [29, 30]. By propensity matching, we included 896 patients in this age group. However, the OS and CSS of the patients in the ST were significantly better than those in the RT, suggesting that the elderly did not benefit more from radiotherapy. It was similar to the results of previous studies [31].

The study by Yaakov Tolwin et al. also showed that women had a higher incidence of adenocarcinoma than men [32], which was consistent with our findings. In this study, women accounted for more than half of the patients. Gender difference is also one of the independent prognostic factors. Our results showed that male patients had a higher risk than female patients (95%CI 1.33–1.67, HR = 1.49). The same was true of previous research [33].

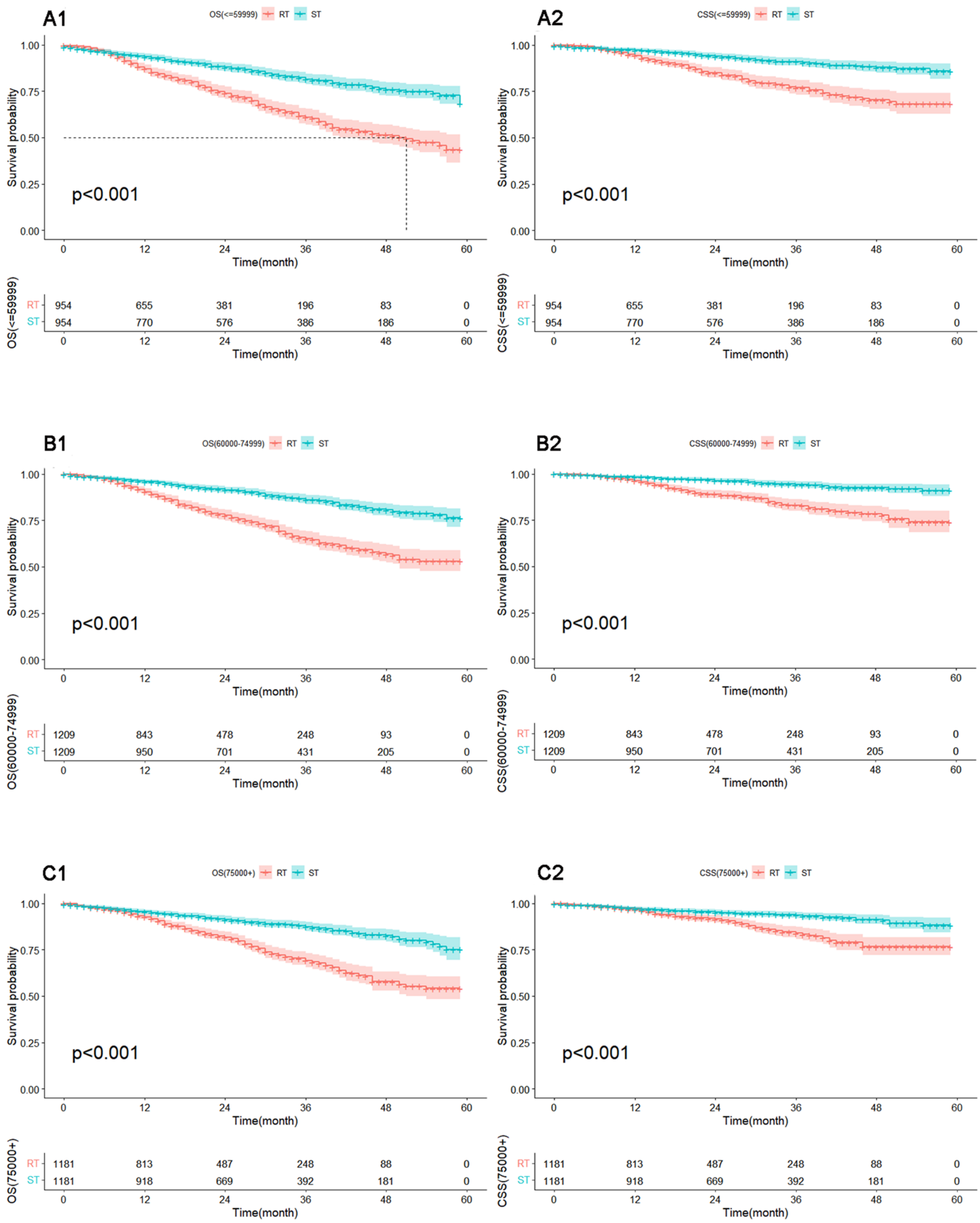

Fig. 5 Survival analysis stratified by household income: **a**–**c** Represent different household incomes (≤ 59,999, 60,000–74,999; ≥ 75,000); 1 represents overall survival (OS), 2 represents cancer-specific survival (CSS)

Household income also has a specific impact on the prognosis of patients. Our results show that the higher the household income, the better the prognosis of patients. A previous study compared the cost difference between radiotherapy and surgery. The results showed that the average cost of surgery was significantly higher than that of radiotherapy [34]. This may affect patients' choice of radiotherapy, and low-income people are forced to choose radiotherapy, which ultimately affects the prognosis.

In multivariate analysis, tumor size is also a factor that cannot be ignored. Our results show that regardless of the tumor size, the surgery has achieved better results. However, a propensity matched data analysis showed no significant difference in cancer-specific survival between sub lobectomy and SBRT in patients with tumor size ≤2 cm [35]. However, another study is similar to our results [36].

This study also has some limitations. First, the data in the SEER database is not detailed, such as a lack of information on the patient's physical condition and complications. Elderly patients are more likely to choose radiotherapy alone, which may affect their prognosis; and there is also a lack of data on radiotherapy methods, radiotherapy cycles, and radiotherapy doses, it may affect our judgment of the effectiveness of radiotherapy; what is more, due to the lack of data, we are unable to assess the potential influence of aerogenic noxious factors. Second, this study compared the differences between surgery and radiotherapy, but we did not distinguish the differences in surgical methods, such as wedge resection, segmentectomy, and lobectomy. Different surgical methods may have a certain impact on the prognosis of patients. Finally, because it is a retrospective study, it has obvious limitations, and future research is needed to prove our conclusions. Nevertheless, the SERR database provides very reliable follow-up data and fundamental data. We believe that the conclusions drawn because of the enormous demographic data can be convincing.

Conclusion

Even considering the comorbidities, age, gender, tumor size, and other factors, the benefit of choosing surgery is still more significant for patients with stage IA LUAD. Radiotherapy is an effective treatment option but cannot wholly replace surgery.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s40001-025-02436-3.

Supplementary Material 1

Acknowledgements

We sincerely thank the researchers who provided the data to the SEER database.

Author contributions

DJZ: collection and assembly of data, data analysis and interpretation, writing—original draft. ZCC: collection and assembly of data, data analysis and interpretation. ML: collection and assembly of data, writing—original draft. YJY: data analysis and interpretation. ZYH: collection and assembly of data, data analysis and interpretation. BV: collection and assembly of data. GYS: writing—original draft. CZ: conception and design. JJX: funding acquisition, writing—review & editing. QW: funding acquisition, writing—review & editing. ZWL: conception and design, Funding acquisition, writing—review & editing. Final approval of the manuscript: all authors.

Funding

This study was supported by the Natural Science Foundation of Shanghai Municipality (23ZR1410300) and the National Natural Science Foundation of China (82303442).

Availability of data and materials

The data set analyzed in this study can be queried in the SEER database (https://seer.cancer.gov/).

Declarations

Ethics approval and consent to participate

Not applicable to current research.

Consent for publication

Not applicable to current research.

Competing interests

The authors declare no competing interests.

Received: 12 July 2023 Accepted: 5 March 2025
Published online: 15 March 2025

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