Surgical Treatment is Still Recommended for Patients Over 75 Years with IA NSCLC: A Predictive Model Based on Surveillance, Epidemiology and End Results Database

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Abstract
Background: To determine the populations who suitable for surgical treatment in elderly patients (age ≥ 75 y) with IA stage.

Methods: The clinical data of NSCLC patients diagnosed from 2010 to 2015 were collected from the SEER database and divided into surgery group (SG) and no-surgery groups (NSG). The confounders were balanced and differences in survival were compared between groups using PSM (Propensity score matching, PSM). Cox regression analysis was used to screen the independent factors that affect the Cancer-specific survival (CSS). The surgery group was defined as the patients who surgery-benefit and surgery-no benefit according to the median CSS of the no-surgery group, and then randomly divided into training and validation groups. A surgical benefit prediction model was constructed in the training and validation group. Finally, the model is evaluated using a variety of methods.

Results: A total of 7297 patients were included. Before PSM (SG: n = 3630; NSG: n = 3665) and after PSM (SG: n = 1725, NSG: n = 1725) confirmed that the CSS of the surgery group was longer than the no-surgery group (before PSM: 82 vs. 31 months, P < .0001; after PSM: 55 vs. 39 months, P < .0001). Independent prognostic factors included age, gender, race, marital, tumor grade, histology, and surgery. In the surgery cohort after PSM, 1005 patients (58.27%) who survived for more than 39 months were defined as surgery beneficiaries, and the 720 patients (41.73%) were defined surgery-no beneficiaries. The surgery group was divided into training group 1207 (70%) and validation group 518 (30%). Independent prognostic factors were used to construct a prediction model. In training group (AUC = .678) and validation group (AUC = .622). Calibration curve and decision curve prove that the model has better performance.

Conclusions: This predictive model can well identify elderly patients with stage IA NSCLC who would benefit from surgery, thus providing a basis for clinical treatment decisions.

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Non-small cell lung cancer, surgery, predictive model, SEER database, nomogram

Introduction
Lung cancer is 1 of the most common malignancies worldwide, with high morbidity and mortality. Non-small cell lung cancer (NSCLC) is accountable for more than 80% of lung cancer cases. In the past decades, due to the neglect of health and the constraints of economic and technical conditions, most of lung cancer were found to be in the middle and advanced stage, and the treatment prognosis was poor. In recent years, with the enhancement of the awareness of physical examination and the popularization of multi-slice spiral CT, more and more patients with stage IA lung cancer can be found and diagnosed early.

In the current treatment guidelines, primary tumor resection (PTR) is still the standard operation for the treatment of early lung cancer, which can completely remove the focus, alleviate symptoms and control the disease to a certain extent. Many studies have observed that patients with early cancer can obtain significant survival time after radical resection. This may be the result of surgery reducing the complications (PPCs), indicating that age alone should not be a risk factor for postoperative pulmonary complications (PPCs), indicating that age alone should not be used as a contraindication for surgery.

In conclusion, the choice of treatment for elderly patients with stage IA NSCLC remains controversial. Therefore, the risk of postoperative morbidity and mortality, as well as cancer recurrence and long-term survival, must be carefully weighed in the treatment of this patient population. A study predicts that elderly patients will account for more than 70% of lung cancer cases in the next 10 years.

Therefore, elderly patients over 75 years of age were selected as the study population in this study. A population-based Surveillance, Epidemiology and End Results (SEER) database was used to develop and validate a new predictive model to identify older patients with stage IA NSCLC who could benefit from surgery and to suggest the best treatment option for this population.

Materials and Methods

Data Source and Study Population
Patient Selection in SEER Database. This study used the United States Surveillance, Epidemiology and Outcome Database (SEER), which was established in 1973 and covers 28% of the population in the United States. The information of patients diagnosed with NSCLC ranging from January 2010 to December 2015 was obtained from the SEER database (November 2019 submission).

Patients were included in our study if they met the following inclusion criteria: (1) patients with stage IA NSCLC from January 2010 to December 2015 (n = 38368); (2) Age ≥ 75 years old (n = 13531); (3) There was only 1 malignant primary lesion (n = 7387). Exclusion criteria: (1) Unknown survival time (n = 14). (2) Unknown cause of death (n = 61); (3) Surgical approach is unclear (n = 15).

Patient demographic characteristics (gender, age, marital status, race), tumor characteristics (histology type, tumor location, tumor laterality, grade, stage), CSS, and treatment details (type of surgery) were collected. In this study, histology types of NSCLC were classified as LUAD, LUSC, and other (large cell carcinoma, adenosquamous carcinoma, and sarcomatoid carcinoma). Depending on the type of surgery, surgical patients are further classified as segmentectomy, lobectomy, pneumonectomy.

In this study, cancer specific survival (CSS) was calculated from the date of diagnosis to the date of cancer specific death. Deaths due to lung cancer were regarded as events, and deaths from other causes were regarded as censored observations.

In addition, this study was licensed to access these research data (SEER stat user name: liuyf, 13981-Nov2020) and conducted in accordance with the Helsinki Declaration (revised in 2013). This study was conducted in accordance with the principles of the Helsinki Declaration. It has been approved by the Medical Ethics Committee of Tumor Hospital of Anhui University of Technology (No:2022-KY-FZZX-03). The research process is shown in Fig 1.

Statistical Analysis
Continuous variables were expressed as mean ± standard deviation and P-values were derived from Kruskal Wallis rank sum test; categorical variables were expressed as percentages and P-values were derived from Fisher’s exact probability test. The study population was divided into surgery group and...
no-surgery group according to whether they received radical surgery. Age, gender, race, marital status, tumor location, laterality, grade, T stage, histology, and surgery were included as independent variables with tumor specific survival time (CSS) as the intended event.

Calculated propensity score matching (PSM) was used to reduce the difference between groups by adjusting all independent variables, setting the caliper value to 0.01 and taking the population of 1:1 as the standard. Kaplan-Meier method and log-rank test were used to estimate CSS of patients before and after PSM.

Univariate and multivariate Cox proportional hazards regression analysis was performed in the population after PSM to determine independent prognostic factors. The risk ratio (HR), 95% confidence interval (CI) and P value were calculated and displayed using forest map. In the graph, the blue dots indicate the risk ratio (HR) and the solid black line indicates the 95%CI. When both the upper and lower 95% CI limits of HR values were on the same side of the Y-axis, they were protective or risk factors affecting prognosis (left: protective factors; right: risk factors). When the 95%CI interval of the HR value of the variable is across the Y-axis, it means that the variable is not statistically significant.

All statistical analyses were performed using power stats (version 2.2) and R software (version 4.0.5). All statistical tests were two-sided, P < .05 was considered statistically significant.

Establishment and Validation of the Nomogram

Referring to the median CSS of the no-surgery population, the surgery population was divided into surgery-benefit and surgery-no benefit groups. And patients in the surgery population were divided into training and validation sets according to 7:3 using benefit and no-benefit as dependent variables.

Based on the training group, factors that independently affect CSS in multivariate Cox analysis are included, and a prediction model is constructed by using logistic regression, and the nomogram is used to visualize the model. The nomogram are used as a quantitative tool to calculate which NSCLC patients will benefit from surgery. Scores for each clinical variable was calculated and summed to obtain the patient’s total score. The total score corresponds to the probability that the patient will benefit from the procedure. Patients with a probability of >50% are the ones who benefit from PTR.

ROC analysis shows the performance of the classification model. The AUC values of the training group and the validation group are calculated respectively to verify the discrimination of the model (AUC <.5, not significant; .5 < AUC <.7, low significant; .7 < AUC < 1.0, high significance).16

Draw calibration curve to evaluate the calibration degree of the model. If the model calibration is correct, dots on the calibration plot should be close to a 45° diagonal line, shows calibration performance as measured by the Brier score (lower is better). If the Brier score = 0, the model was considered to have perfect overall performance, and the predicted and actual values were in perfect agreement. If the Brier score is > .25, the model was considered to have no value.

Clinical Application

Decision curve analysis (DCA) was used to evaluate the clinical utility of the model in decision-making. DCA evaluates the clinical benefit of the prediction model by plotting the net benefit (NB) within the range of clinical reasonable risk threshold.18

According to the calculation of the prediction model, all elderly patients with stage IA NSCLC in SEER database after PSM were divided into 3 groups (surgery-benefit group, surgery-no benefit group and no-surgery group). The CSS of
the 3 groups were compared by K-M survival analysis to evaluate whether the surgery-benefit group screened by the prediction model can really benefit.

Results

Patient Demographics and Survival Analysis

The clinical data of patients with stage IA NSCLC diagnosed from January 2010 to December 2015 were obtained by SEER database. According to the inclusion and exclusion criteria, 7297 elderly patients with stage IA NSCLC were included, of which 3630 (49.75%) underwent surgery and 3665 (50.25%) did not undergo surgery. During PSM, variables were adjusted for age, gender, race, marital, primary location, laterality, tumor grade, AJCC-T, histology, and surgery. A total of 3450 patients were matched, of which 1725 operated and 1725 no-operated elderly patients with stage IA NSCLC were included in the analysis (Table 1).

Cancer-specific survival for Populations With Different Treatment Modalities

Kaplan-Meier survival analysis before PSM found that the prognosis of the surgery group was better than that of the no-surgery group (82 vs. 31 months; P < .0001) (Figure 2A). After PSM, a longer median CSS (55 vs. 39 months; P < .0001) was still observed in patients who underwent surgery than in patients who did not undergo surgery (Figure 2B).

Screening of Independent Prognostic Factors Affecting CSS

In order to explore which factors lead to the difference in survival between the surgery group and the no-surgery group, univariate and multivariate COX analyses were performed on the baseline characteristics of the after PSM population, and visualize it with a forest plot.

Univariate COX regression analysis showed that age, gender, race, marital, grade, histology, and surgery procedure were independent prognostic factors affecting CSS (all P < .05). However, location, laterality, and AJCC-T were not significantly correlated with CSS (Figure 3). The variable with P < .05 was selected to include multivariate Cox analysis. Among them, age, gender, race, marital, tumor grade, histology, and surgery were independent prognostic factors (Figure 4).

In particular, male was an independent risk factor for developing cancer-specific mortality compared to female (HR = 1.719, 95%CI: 1.454-2.033, P < .001). Single patients have a higher risk of cancer-specific death than married patients (HR = 1.331, 95%CI: 1.128-1.570, P = .001). The benefits were not significantly different in LUAD and LUSC (P = .297). However, other rare subtypes benefit more than LUAD and LUSC (HR = .739, 95%CI: .575-.949, P = .017). Among the different surgical approaches, benefits for patients undergoing segmentectomy are significantly better than those for the nonsurgical population (HR = 1.584, 95%CI: 1.268- 1.978, P < .001).

Construction of the Predictive Model

The above independent prognostic factors were included in the analysis of distinguishing the people who benefited from surgery. Firstly, according to the population data after PSM and referring to the median CSS (39 months, n = 1725) of no-surgery patients, patients undergoing surgery were divided into benefit population (survival month > 39 months, n = 1005) and no-benefit population (survival month ≤ 39 months, n = 720).

Secondly, in order to avoid the phenomenon of over fitting or under fitting caused by the construction of a single data model, the benefit population and no-benefit population are randomly assigned to the training group (total N = 1207, surgery benefit n = 763, surgery-no benefit n = 444) and the validation set (total N = 518, surgery benefit n = 242, surgery-no benefit n = 276) according to the ratio of 7:3.

Finally, based on the training group data, a prediction model was established by logistic regression analysis to find the elderly stage IA NSCLC surgery candidates, and the prediction model was visualized by nomogram (Figure 5). The probability of surgical benefit was calculated by adding the scores of each variable. Patients with a prediction probability greater than 0.5 were classified as “surgery-benefit group”. On the contrary, it is the surgery-no benefit group.

The ROC curve is drawn, and the results show that the prediction model has good discrimination in the training group (AUC = 0.678) (Figure 6A). The calibration curve shows a good calibration degree (training group Brier score: 0.211) (Figure 6B). The DCA curves of the training group confirmed the good clinical practical value of the prediction model (Figure 6C).

Validation and Clinical Application of the Nomogram

At the same time, the model performance is verified with the validation group data. The ROC curve results showed that the prediction model was equally well distinguished in the validation group (AUC = 0.622) (Figure 6D). The calibration curve shows a good degree of calibration (validation group Brier score: 0.238) (Figure 6E). The DCA curves of the validation group confirmed the good clinical utility of the prediction model (Figure 6F).

Using the constructed prediction model, Kaplan-Meier survival analysis was used to analyze the population after PSM, and the survival results of “surgery-benefit group”, “surgery-no benefit group” and “no-surgery group” in the training group and validation set were displayed respectively. In the training group and validation group, the median CSS of
the surgery benefit group was higher than that of the surgery-no benefit group and no-surgery group (training group: 83 vs 20 vs 39 months, P < 0.0001; validation group: 81 vs 23 vs 39 months, P < 0.0001) (Fig. 7(A), (B)).

### Table 1. Baseline characteristics for overall survival in patients with NSCLC.

| Variable               | Before PSM | Standardize | After PSM | Standardize |
|------------------------|------------|-------------|-----------|-------------|
|                        | No-Surgery |             | No-Surgery|             |
|                        | n = 3665   | Surgery n = 3630 | n = 1725  | Surgery n = 1725 |
| Age(year)              | 81.624 ± 4.532 | 79.115 ± 3.437 | 81.439 ± 4.470 | 79.318 ± 3.518 |
| Survival months        | 33.211 ± 23.663 | 52.656 ± 26.947 | 37.625 ± 24.947 | 47.841 ± 28.913 |
| Gender                 | 2152 (58.718%)  | 2158 (59.449%)  | 1012 (58.667%)  | 1088 (63.072%)  |
| Female                 | 1513 (41.282%)  | 1472 (40.551%)  | 713 (41.333%)  | 637 (36.928%)  |
| Race                   | 3158 (86.166%)  | 3181 (87.631%)  | 1523 (88.290%)  | 1467 (85.043%)  |
| White                  | 265 (7.231%)   | 196 (5.999%)   | 100 (5.797%)   | 121 (7.014%)  |
| Black                  | 242 (6.603%)   | 253 (6.970%)   | 102 (5.913%)   | 137 (7.942%)  |
| Marital                | 1426 (38.909%)  | 1859 (51.212%)  | 750 (43.478%)  | 771 (44.696%)  |
| Married                | 2079 (56.726%)  | 1627 (44.821%)  | 921 (53.391%)  | 857 (49.681%)  |
| Location               | 160 (4.366%)   | 144 (3.967%)   | 54 (3.130%)    | 97 (5.623%)  |
| Left                   | 2209 (60.273%)  | 2168 (59.725%)  | 1033 (59.884%)  | 1027 (59.536%)  |
| Right                  | 162 (4.420%)   | 206 (5.675%)   | 83 (4.812%)    | 85 (4.928%)  |
| Unspecified            | 1205 (32.879%)  | 1215 (33.471%)  | 591 (34.261%)  | 587 (34.029%)  |
| Laterality             | 89 (2.428%)    | 41 (1.129%)    | 18 (1.043%)    | 21 (1.507%)  |
| Grade                  | 1.242 < .001   | .019 .583      | .031 .934      |
| G1                     | 361 (9.850%)   | 967 (26.639%)  | 344 (19.942%)  | 325 (18.841%)  |
| G2                     | 395 (16.235%)  | 1552 (42.755%) | 568 (32.928%) | 585 (33.913%)  |
| G3                     | 658 (17.954%)  | 802 (22.094%)  | 518 (30.029%)  | 517 (29.971%)  |
| G4                     | 23 ( .628%)    | 22 ( .606%)    | 14 ( .812%)    | 15 ( .870%)  |
| G5                     | 2028 (55.334%)  | 287 (7.906%)  | 281 (16.290%)  | 283 (16.406%)  |
| Histologic type        | .366 < .001   | .156 .169      | .037 .562      |
| LUAD                   | 1045 (28.513%)  | 891 (24.545%)  | 529 (30.667%)  | 548 (31.768%)  |
| LUSC                   | 1696 (46.276%)  | 2262 (62.314%) | 1003 (58.145%) | 900 (52.174%)  |
| Other                  | 924 (25.211%)  | 477 (13.140%)  | 193 (11.188%)  | 277 (16.058%)  |
| AJCC-T                 | .199 < .001   | .037 .562      |
| T1a                    | 27 (.737%)     | 10 (.275%)    | 5 (.290%)      | 9 (.522%)  |
| T1b                    | 1837 (50.123%)  | 2165 (59.642%) | 938 (54.377%) | 934 (54.145%)  |
| TINOS                  | 1801 (49.141%)  | 1455 (40.083%) | 782 (45.333%) | 782 (45.333%)  |

Discussion

The standard surgical treatment for early-stage NSCLC has been lobectomy, in which individual units of the lung lobes are removed along with their specific regions of the hilum and mediastinal lymphatics. A previous diagnosis and treatment guideline proposed that in the treatment of early NSCLC, surgery has better survival time and lower recurrence rate. However, not all patients with early NSCLC are suitable for surgery. Statistics showed that the incidence rate and mortality rate of elderly people increased exponentially compared with younger patients. In clinical treatment, surgeons are often reluctant to recommend lobectomy for patients with older age, complications or poor pulmonary function. Preoperative multiple complications and poor pulmonary function may lead
Figure 2. Kaplan–Meier plots show the specific survivals of NSCLC patients according to the group before PSM (A) or after PSM (B).

| Characteristics       | N (%)     | HR (95% CI)            | P value |
|-----------------------|-----------|------------------------|---------|
| Age                   | 80.4 ± 4.2| 1.058 (1.040, 1.077)    | <0.001  |
| Gender                |           |                        |         |
| Female                | 2100 (60.9)| ref                    |         |
| Male                  | 1350 (39.1)| 1.510 (1.304, 1.750)   | <0.001  |
| Race                  |           |                        |         |
| White                 | 2990 (86.7)| ref                    |         |
| Black                 | 221 (6.4)  | 0.844 (0.635, 1.122)    | 0.242   |
| Other                 | 239 (6.9)  | 0.369 (0.282, 0.482)    | <0.001  |
| Marital               |           |                        |         |
| Married               | 1521 (44.1)| ref                    |         |
| Single                | 1778 (51.5)| 1.281 (1.109, 1.480)   | 0.001   |
| Other                 | 151 (4.4)  | 0.773 (0.551, 1.085)    | 0.136   |
| Location              |           |                        |         |
| Upper lobe            | 2060 (59.7)| ref                    |         |
| Middle lobe           | 168 (4.9)  | 0.850 (0.613, 1.178)    | 0.329   |
| Low lobe              | 1178 (34.1)| 0.900 (0.775, 1.047)   | 0.172   |
| Main broucher         | 44 (1.3)   | 0.718 (0.391, 1.319)    | 0.286   |
| Grade                 |           |                        |         |
| G1                    | 669 (19.4)| ref                    |         |
| G2                    | 1153 (33.4)| 1.623 (1.327, 1.986)   | <0.001  |
| G3                    | 1035 (30.0)| 2.015 (1.632, 2.489)   | <0.001  |
| G4                    | 29 (0.8)   | 1.658 (0.724, 3.799)    | 0.232   |
| Unknown               | 564 (16.3)| 0.398 (0.316, 0.501)    | <0.001  |
| Laterality            |           |                        |         |
| Left                  | 1510 (43.8)| ref                    |         |
| Right                 | 1940 (56.2)| 0.975 (0.846, 1.124)   | 0.73    |
| Histology             |           |                        |         |
| Lusc                  | 1077 (31.2)| ref                    |         |
| Luad                  | 1903 (55.2)| 0.571 (0.484, 0.673)   | <0.001  |
| Other                 | 470 (13.6)| 0.576 (0.458, 0.726)    | <0.001  |
| AJCC–T                |           |                        |         |
| T1a                   | 14 (0.4)   | ref                    |         |
| T1b                   | 1872 (54.3)| 1.001 (0.334, 3.000)   | 0.998   |
| TINOS                 | 1564 (45.3)| 1.148 (0.383, 3.443)   | 0.605   |
| Surgery               |           |                        |         |
| No surgery            | 1725 (50.0)| ref                    |         |
| Segmentectomy         | 604 (17.5)| 1.316 (1.072, 1.615)   | 0.009   |
| Lobectomy             | 1112 (32.2)| 0.759 (0.649, 0.887)   | 0.001   |
| Pneumonectomy         | 9 (0.3)    | 1.745 (0.361, 8.429)    | 0.488   |

Figure 3. Univariate Cox regression analysis of factors affecting CSS.
to high recurrence rate and mortality, resulting in poor surgical treatment effect. Therefore, it is urgent to establish a reliable and simple discrimination method for elderly stage IA NSCLC.

We constructed a prediction model and proposed several findings. First, NSCLC patients who underwent surgery survived longer than those who did not, which is consistent with previous studies. Second, although surgery can improve the survival of elderly patients with stage IA NSCLC to some extent, not all patients with surgery have a longer survival than those without surgery. We established a visual nomogram to screen the patients who benefit most from surgery and prolong their survival time; at the same time, patients who are not suitable for surgery can also be screened in order to reduce the additional physical and economic burden. Finally, the effectiveness and stability of the model are verified internally.

According to our model, age, gender, race, grade, histological type, Marital and surgery methods are predictive variables to estimate whether elderly patients with stage IA NSCLC can benefit from surgery. Among them, surgery methods, tumor grade, gender and age have the greatest impact on the benefit of surgery.

Among various surgical procedures, pneumonectomy is a traditional treatment modality that allows complete resection of tumor tissue, but also excessive removal of normal lung tissue. The lung function of the elderly is inherently poor and the surgical tolerance is not strong, so total pneumonectomy for the elderly is usually considered with caution, and total pneumonectomy is only considered when partial resection cannot remove the complete lesion. This usually means that the primary lesion is large or has metastasized, and the prognosis is usually poor. In a retrospective study, it was found that lobectomy and segmental resection have similar clinical efficacy in the treatment of early NSCLC patients, but segmental resection can maintain healthy lung tissue as much as possible, with less trauma, protect lung function, and

| Characteristics | N (%) | HR (95% CI) | P value |
|-----------------|-------|-------------|---------|
| Age             | 80.4 ± 4.2 | 1.061 (1.040, 1.082) | <0.001 |
| Gender          |       |             |         |
| Female          | 2100 (60.9) | ref |         |
| Male            | 1350 (39.1) | 1.719 (1.454, 2.033) | <0.001 |
| Race            |       |             |         |
| White           | 2990 (86.7) | ref |         |
| Black           | 221 (6.4) | 0.792 (0.585, 1.071) | 0.13    |
| Other           | 239 (6.9) | 0.337 (0.254, 0.448) | <0.001 |
| Marital         |       |             |         |
| Married         | 1521 (44.1) | ref |         |
| Single          | 1778 (51.5) | 1.331 (1.128, 1.570) | <0.001 |
| Other           | 151 (4.4) | 0.716 (0.500, 1.024) | 0.067   |
| Grade           |       |             |         |
| G1              | 669 (19.4) | ref |         |
| G2              | 1153 (33.4) | 1.544 (1.241, 1.919) | <0.001 |
| G3              | 1035 (30.0) | 1.747 (1.385, 2.203) | <0.001 |
| G4              | 29 (0.8) | 1.706 (0.723, 4.024) | 0.222   |
| Unknown         | 564 (16.3) | 0.345 (0.271, 0.439) | <0.001 |
| Histology       |       |             |         |
| Lusc            | 1077 (31.2) | ref |         |
| Luad            | 1903 (55.2) | 0.905 (0.749, 1.092) | 0.297   |
| Other           | 470 (13.6) | 0.739 (0.575, 0.949) | 0.017   |
| Surgery         |       |             |         |
| No surgery      | 1725 (50.0) | ref |         |
| Segmentectomy   | 604 (17.5) | 1.584 (1.268, 1.978) | <0.001 |
| Lobectomy       | 1112 (32.2) | 0.923 (0.776, 1.097) | 0.363   |
| Pneumonectomy   | 9 (0.3) | 2.627 (0.454, 15.213) | 0.281   |

Figure 4. Multivariate Cox regression analysis of factors affecting CSS.
Figure 5. Nomogram was used to identify patients with NSCLC who would benefit from surgery.

Figure 6. Receiver operating characteristic curve of the nomogram in the training (A) and validation (D) groups. (B) The calibration plots of the training group. (E) The calibration plots of the validation group. Decision curve analysis of training group (C) and validation group (F).
promote postoperative recovery. Several other population-based studies have found that lobectomy has a significant survival advantage over segmental resection. With our results, lobectomy is more beneficial than segmental resection. This may be due to the fact that fewer regional lymph nodes are removed by lung segmental resection and the presence of potentially positive lymph nodes is more likely to lead to postoperative recurrence or distant metastasis of lung cancer, resulting in poorer patient prognosis. Further prospective randomized trials, as well as more detailed stratification, are still needed to explore reasonable surgical treatment modalities.

Previous studies have shown that tumor grade is an independent prognostic factor for patients with non-small cell lung cancer, and the higher the tumor grade, the worse the prognosis. A recent study found that low differentiation of lung cancer is not only associated with low survival rate, but also can predict the survival benefit of cisplatin-based adjuvant chemotherapy after surgery, which is similar to our results. Tumor grade can predict the surgical benefit rate of patients. Our results also show a surgical benefit in patients with stage G4, which may be a false positive due to the fact that this population is too small.

In our prediction model, female can increase the surgical benefit rate. The results were the same as in 2 studies based on the seer database, where male patients underwent surgery with higher lung cancer-related mortality compared to female patients. Another study on the survival rate of elderly lung adenocarcinoma also shows that female patients have a better survival rate. Overage is usually considered as a predictor of poor OS. Different from previous studies, our research focuses on elderly patients (≥75 y). The results show that this law is also applicable to judge whether the operation benefits. The older the elderly patients are, the less likely they will benefit from the operation.

We also found that postoperative survival was better in patients with LUAD than in patients with LUSC, with the result that in the same study based on a Japanese population, patients with LUAD who underwent surgery had a better prognosis than patients with LUSC. Marital status has been shown to be associated with survival in NSCLC patients in many studies, with married patients often having a better prognosis than single patients, possibly because spouses provide strong social support for cancer patients, alleviating their depression and anxiety and increasing their desire to survive.

Our results have some practical implications, as well as implications for future research. First, with the advent of aging, older patients’ may gain more benefit with surgical treatment when clinical guidelines are strictly followed. Second, the variables in this study are only some of the factors affecting prognosis, and more blood and imaging biomarkers are worthy of further exploration to construct a more integrated and comprehensive prediction model. Finally, in this study, the prognostic impact of different procedures also differed, which provides a data reference basis to further promote the study of individualized treatment.

This study has several limitations. First, this study is retrospective, and bias is inevitable. Despite the PSM adjustment, we attempted to reduce this bias with extensive data analysis and rigorous statistical methods. Second, 1 of the undeniable shortcomings of this study is that the SEER database does not document common complications and pulmonary function in older patients that could affect decisions about surgical treatment. Third, the conclusion of this study still needs to include more variables to improve the effectiveness of the model. However, based on the current state of data, seer is the world’s most extensive comprehensive database of study populations. Analysis using this database remains an ideal method for our study of surgical beneficiaries.

Figure 7. Kaplan–Meier analysis of a comparison of benefit candidates, no-benefit candidates and no-surgery patients in the training group (A) and validation group (B) after using our nomogram.
Conclusion

We constructed a simple and effective prediction model to select the best operable elderly patients with stage IA NSCLC who can benefit from surgery. Using our prediction model, clinicians can formulate more accurate treatment strategies for elderly patients with stage IA NSCLC.

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I would like to declare on behalf of my co-authors that the work described was original research that has not been published previously, and not under consideration for publication elsewhere, in whole or in part. All the authors listed have approved the manuscript that is enclosed.

Author Contribution

HD and WJ: conception and design, and study supervision. LY, ZW, ZX, WQ, GJ and ZJ: development of methodology, analysis and interpretation of data, and writing of the manuscript. XY, XJ and WW: review of the manuscript.

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Ethical Approval

This study was conducted in accordance with the principles of the Declaration of Helsinki. It has been approved by the Medical Ethics Committee of the Cancer Hospital of Anhui University of Technology (No. 2022-KY-FZZX-03). Written informed consent is not required in this retrospective analysis.

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Supplemental Material

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