Surgery in patients with small cell lung cancer: A period propensity score matching analysis of the Seer database, 2010-2015

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Patients and methods

This was a retrospective, population-based study using cases registered in the SEER database made publicly available through online access. Data were retrieved using the Surveillance Research Program, National Cancer Institute SEER*Stat software (seer.cancer.gov/seerstat) version 8.3.5. Informed consent from the study population was waived, as the authors had no access to the identities of the patients, and no identifiable patient information was included.

Data collection. The following database was used for selection of cases: SEER Program (www.seer.cancer.gov) SEER*Stat Database: Incidence-SEER 18 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2017 Sub (2000-2015) <Katrina/Rita Population Adjustment> - Linked To County Attributes-Total U.S., 1969-2016 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2018, based on the November 2017 submission. Only patients with SCLC [based on International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) (7) codes: 8041-3/8045/3] between January 2010 and December 2015 were included in the present study. The exclusion criteria were: i) An ambiguous or unknown classification of observed clinical characteristics, ii) cause of death to site (COD) recode not as ‘Alive’ or ‘Lung and Bronchus’, iii) distant metastasis at the brain, liver and lung, iv) M1, v) T0 and finally vi) a survival time of <1 month (Fig. 1). Individual data for each case were retrieved from the database including sex, age at diagnosis, race, histology, grade, surgery to primary site (SPS), Tumor-Node-Metastasis (TNM) stage (8), COD and survival time.

Subgroup definitions. In the SEER database, grades were recorded as follows: i) Grade I, well differentiated; ii) grade II, moderately differentiated; iii) grade III, poorly differentiated and iv) undifferentiated and anaplastic. SPS was divided into: i) Non-surgery, no surgery of primary site; ii) Sublobectomy, Partial/Wedge/Segmental Resection, Lingulectomy, Partial Lobectomy, Sleeve Resection iii) lobe/s, lobectomy or bilobectomy; iv) Pneumonectomy. The T, N, M and Stage were recorded in the database according to the AJCC cancer staging manual, 7th ed. (8).

Statistical analyses. Statistical analysis was performed using Stata 15.0 (Stata Corp. LLC). The propensity score matching was performed using the ‘psmatch2’ module in the software. Student’s t-test was used to analyze the differences of means between two samples. Differences of cause-specific survival (CSS) between subgroups and the role of surgery in each subgroup was estimated using the Kaplan-Meier product method and compared by a log-rank test. Cox regression analysis was used to evaluate the effects of multiple variables on survival. The difference of incidence of COD was examined using $\chi^2$ test. Quantitative data were converted into categorical data, with the exception of survival time. All statistical tests were two-sided and $P<0.05$ was considered to indicate a statistically significant difference.
combined small cell carcinoma in histology; Grade I, II, IV; T1b and T2a. Similar survival benefits in patients who received lobe/s compared with sublobectomy were observed in the following clinicopathological subgroups (Fig. 7): 60-70 years, 70-80 years in age; male and female in sex; African descent and Caucasian in race; small cell carcinoma with NOS and
Table I. Propensity score matching test between the surgery groups.

| Surgery                  | Features | Sex  | Un/Matched | Treated | Control | %bias | %reduct bias | t    | P-value | V(T)/V(C) |
|--------------------------|----------|------|------------|---------|---------|-------|--------------|------|---------|-----------|
|                          |          |      |            |         |         |       |              |      |         |           |
|                          |          | U    | 0.43197    | 0.43100 | 0.2     |       | 0.03         | 0.97 |         |           |
|                          |          | M    | 0.43197    | 0.39116 | 8.2     | -4.086.7 |       | 1.00 |         | 0.14      |
|                          |          |      | 4.19730    | 4.19670 | 0.1     |       | 0.01         | 0.99 |         | 0.79      |
|                          |          |      | 4.19730    | 4.37070 | -1.73   | -32.360.8 | -2.15 | 0.032 | 0.87     |
| Age                      |          | U    | 3.35710    | 3.56480 | -33.3   |       | -5.66 <0.001 | 1.63 |         |           |
|                          |          | M    | 3.35710    | 3.30270 | 8.7     | 73.8   | 0.92         | 0.356| 0.90    |           |
| Grade (8)                |          | U    | 2.07480    | 1.16140 | 67.6    |       | 14.41 <0.001 | 5.82 |         |           |
|                          |          | M    | 2.07480    | 1.91160 | 12.1    | 82.1   | 1.16         | 0.248| 1.14    |           |
| Histology                |          | U    | 2.75170    | 4.77570 | -131.9  |       | -21.61 <0.001 | 1.33 |         |           |
|                          |          | M    | 2.75170    | 2.57480 | 11.5    | 91.3   | 1.29         | 0.197| 0.96    |           |
| Stage (8)                |          | U    | 2.54800    | 4.29650 | -113.3  |       | -17.05 <0.001 | 0.80 |         |           |
|                          |          | M    | 2.54800    | 2.43200 | 13.3    | 93.8   | 0.90         | 0.366| 1.00    |           |
| T (8)                    |          | U    | 3.40480    | 3.35000 | 7.9     |       | 0.61         | 0.541| 1.03    |           |
|                          |          | M    | 3.40480    | 3.36900 | 5.2     | 34.8   | 0.33         | 0.742| 0.97    |           |
| Race                     |          | U    | 1.85710    | 2.12500 | 13.3    |       | -1.18 <0.240 | 0.85 |         |           |
|                          |          | M    | 1.85710    | 1.61900 | 13.8    | 11.1   | 0.99         | 0.323| 1.29    |           |
| Stage (8)                |          | U    | 2.64290    | 2.74500 | -6.0    |       | -0.48 <0.631 | 1.37 |         |           |
|                          |          | M    | 2.64290    | 2.55950 | 4.9     | 18.4   | 0.32         | 0.751| 1.34    |           |
| T (8)                    |          | U    | 2.22620    | 2.60500 | -25.8   |       | -2.04 <0.042 | 1.29 |         |           |
|                          |          | M    | 2.22620    | 2.20240 | 1.6     | 93.7   | 0.11         | 0.916| 1.29    |           |
| N (8)                    |          | U    | 0.59524    | 0.60500 | -1.2    |       | -0.09 <0.927 | 1.43 |         |           |
|                          |          | M    | 0.59524    | 0.58333 | 1.4     | -22.0  | 0.09         | 0.929| 1.34    |           |
| Race                     |          | U    | 4.83330    | 4.73500 | 13.3    |       | 0.98         | 0.326| 0.65    |           |
|                          |          | M    | 4.83330    | 4.88100 | -6.5    | 51.6   | -0.50 <0.616 | 1.33 |         |           |
| Stage (8)                |          | U    | 3.90400    | 4.17000 | -23.4   |       | -0.90 <0.360 | 2.42 |         |           |
|                          |          | M    | 3.90400    | 4.20000 | -26.0   | -11.1  | -0.60 <0.556 | 3.02 |         |           |
| T (8)                    |          | U    | 3.10000    | 3.35000 | -31.8   |       | -1.10 <0.270 | 1.63 |         |           |
|                          |          | M    | 3.10000    | 3.20000 | -12.7   | 60.0   | -0.25 <0.806 | 0.91 |         |           |
| Histology                |          | U    | 2.90000    | 2.12500 | 40.6    |       | 1.30         | 0.190| 1.28    |           |
| Stage (8)                |          | M    | 2.90000    | 3.40000 | -26.2   | 35.5   | -0.55 <0.591 | 0.96 |         |           |
| Race                     |          | U    | 3.80000    | 2.74500 | 66.5    |       | 2.10         | 0.040| 1.09    |           |
|                          |          | M    | 3.80000    | 3.80000 | 0.0     | 100.0  | 0.00         | 1.000| 1.2     |           |
| Stage (8)                |          | U    | 3.90000    | 2.60500 | 87.1    |       | 2.90 <0.001 | 1.35 |         |           |
|                          |          | M    | 3.90000    | 4.00000 | -6.7    | 92.3   | -0.14 <0.891 | 0.95 |         |           |
| Lobe/s vs. pneumonectomy |          | U    | 0.80000    | 0.60500 | 25.0    |       | 0.80         | 0.440| 1.05    |           |
| Race                     |          | M    | 0.80000    | 0.80000 | 0.0     | 100.0  | 0.00         | 1.000| 1.56    |           |
| Race                     |          | U    | 4.40000    | 4.73500 | -31.5   |       | -1.20 <0.220 | 2.43 |         |           |
|                          |          | M    | 4.40000    | 4.10000 | 28.2    | 10.4   | 0.53 <0.605 | 0.97 |         |           |

*a*If variance ratio outside (0.79; 1.26) for U and (0.79; 1.26) for M. Lobe/s, Lobectomy or bilobectomy; %bias, standardized percentage bias; %reduct bias, achieved percentage reduction in bias.
Table II. The efficacy of the propensity score matching.

| Group                              | Sample (n) | Ps  | R²  | LR  | P > X² | MeanBias | MedBias | B  | R  | % Var |
|------------------------------------|------------|-----|-----|-----|--------|----------|---------|-----|-----|-------|
| Non-surgery vs. surgery            | Unmatched (1,413) | 0.309 | 484.81 | <0.01 | 58.20 | 50.50 | 157.8<sup>a</sup> | 1.15 | 71.00 |
|                                    | Matched (294) | 0.015 | 12.59 | 0.13 | 9.30   | 8.50   | 29.4<sup>a</sup> | 1.22 | 0.00 |
| Sublobectomy vs. lobe/s            | Unmatched (200) | 0.030 | 10.19 | 0.25 | 11.50  | 11.20  | 41.5<sup>a</sup> | 1.09 | 0.00 |
|                                    | Matched (84)  | 0.011 | 2.53  | 0.96 | 6.00   | 5.10   | 24.50  | 1.40 | 0.00 |
| Lobe/s vs. pneumonectomy           | Unmatched (200) | 0.161 | 12.98 | 0.11 | 42.10  | 31.70  | 111.8<sup>a</sup> | 1.78 | 0.00 |
|                                    | Matched (10)  | 0.353 | 9.78  | 0.28 | 20.10  | 19.40  | 109.9<sup>a</sup> | 7.50<sup>*</sup> | 0.00 |

<sup>a</sup>B > 25%, R outside (0.5; 2); B, absolute standardized difference of the means of the linear index of the propensity score in the unmatched and matched groups; R, ratio of unmatched to matched variances of the propensity score index; % Var, the percentage of continuous variables that have variance ratios that exceed the 2.5th and 97.5th percentiles of the F-distribution; Lobe/s, lobectomy or bilobectomy.

Figure 3. Distribution of survival time and age. Emerald curve, Normal-density plot. Lobe/s, Lobectomy or bilobectomy.
Table III. Demographics of the included patients and results of univariate analysis.

A, Non-surgery vs. surgery group

| Features          | NP  | NE  | NEE | P-value |
|-------------------|-----|-----|-----|---------|
| Age, years        |     |     |     | 0.341   |
| <40               | 3   | 2   | 2.02|
| ≥40, <50          | 22  | 10  | 12.62|
| ≥50, <60          | 114 | 51  | 60.07|
| ≥60, <70          | 214 | 91  | 98.62|
| ≥70, <80          | 178 | 92  | 79.70|
| ≥80, <90          | 53  | 28  | 21.19|
| ≥90, <100         | 4   | 2   | 1.78 |
| Sex               |     |     |     | 0.714   |
| Male              | 252 | 118 | 120.99|
| Female            | 336 | 158 | 155.01|
| Race              |     |     |     | 0.279   |
| Hispanic          | 15  | 5   | 7.69 |
| AI/AN             | 2   | 0   | 0.09 |
| API               | 12  | 7   | 5.15 |
| African descent   | 52  | 17  | 27.18|
| Caucasian         | 506 | 247 | 235.81|
| Unknown           | 1   | 0   | 0.09 |
| Histology         |     |     |     | 0.678   |
| SCC, NOS          | 462 | 222 | 213.83|
| OCC               | 11  | 5   | 5.69 |
| SCC, IC           | 4   | 2   | 2.89 |
| CSCC              | 111 | 47  | 53.59|
| Grade (8)         |     |     |     | 0.149   |
| I                 | 10  | 2   | 3.93 |
| II                | 23  | 7   | 14.32|
| III               | 281 | 127 | 125.92|
| IV                | 274 | 140 | 131.83|
| T (8)             |     |     |     | 0.135   |
| T1a               | 189 | 86  | 92.83|
| T1b               | 128 | 60  | 63.02|
| T2a               | 173 | 77  | 79.92|
| T2b               | 29  | 19  | 10.54|
| T3                | 53  | 25  | 21.82|
| T4                | 16  | 9   | 7.86 |
| N (8)             |     |     |     | 0.007   |
| 0                 | 360 | 150 | 176.48|
| 1                 | 105 | 54  | 45.92|
| 2                 | 116 | 69  | 51.28|
| 3                 | 7   | 3   | 2.33 |
| Stage (8)         |     |     |     | 0.003   |
| IA                | 190 | 77  | 99.00|
| IB                | 112 | 44  | 53.56|
| IIA               | 108 | 56  | 45.88|
| IIB               | 31  | 13  | 13.80|
| IIIA              | 135 | 80  | 57.93|
| IIIIB             | 12  | 6   | 5.84 |

B, Sublobectomy vs. lobe/s group

| Features          | NP  | NE  | NEE | P-value |
|-------------------|-----|-----|-----|---------|
| Age, years        |     |     |     | 0.384   |
| <40               | N/A | N/A | N/A |
| ≥40, <50          | 2   | 2   | 0.79 |
| ≥50, <60          | 28  | 9   | 13.77|
| ≥60, <70          | 61  | 22  | 21.40|
| ≥70, <80          | 57  | 25  | 23.78|
| ≥80, <90          | 20  | 8   | 6.26 |
| ≥90, <100         | N/A | N/A | N/A |
| Sex               |     |     |     | 0.586   |
| Male              | 56  | 25  | 22.92|
| Female            | 112 | 41  | 43.08|
| Race              |     |     |     | 0.979   |
| Hispanic          | 2   | 1   | 0.70 |
| AI/AN             | N/A | N/A | N/A |
| API               | N/A | N/A | N/A |
| African descent   | 8   | 4   | 4.17 |
| Caucasian         | 157 | 61  | 61.07|
| Unknown           | 1   | 0   | 0.06 |
| Histology         |     |     |     | 0.743   |
| SCC, NOS          | 144 | 57  | 55.32|
| OCC               | 1   | 0   | 0.36 |
| SCC, IC           | N/A | N/A | N/A |
| CSCC              | 23  | 9   | 10.31|
| Grade (8)         |     |     |     | 0.355   |
| I                 | 4   | 0   | 1.38 |
| II                | 5   | 1   | 2.54 |
| III               | 72  | 27  | 29.03|
| IV                | 87  | 38  | 33.05|
| T (8)             |     |     |     | 0.258   |
| T1a               | 85  | 29  | 37.15|
| T1b               | 27  | 11  | 11.03|
| T2a               | 36  | 15  | 11.00|
| T2b               | 2   | 2   | 0.85 |
| T3                | 12  | 6   | 3.82 |
| T4                | 6   | 3   | 2.15 |
| N (8)             |     |     |     | <0.001  |
| 0                 | 108 | 33  | 46.06|
| 1                 | 23  | 12  | 6.44 |
| 2                 | 35  | 19  | 13.11|
| 3                 | 2   | 2   | 0.39 |
| Stage (8)         |     |     |     | 0.006   |
| IA                | 70  | 21  | 32.86|
| IB                | 25  | 6   | 8.97 |
| IIA               | 22  | 12  | 6.30 |
| IIB               | 8   | 3   | 2.76 |
| IIIA              | 39  | 21  | 13.51|
| IIIIB             | 4   | 3   | 1.60 |

Surgery         |     |     |     | <0.001  |
| No               | 84  | 26  | 33.90|
| Yes              | 84  | 40  | 32.10|
combined small cell carcinoma in histology; Grade III and IV; T1a and T1b. Generally, patients who did not receive surgery (P<0.001) or received sublobectomy (P=0.03) were at an increased risk of mortality when compared with patients who received surgery or lobe/s respectively (Table VI). Fig. 8 shows the cumulative survival curves of each group.

Discussion

As SCLC responds to chemotherapy and radiotherapy, surgical treatment is considered to be an option for stage I-IIA (T1-2, N0, M0) SCLC (9,10). The most recent National Comprehensive Cancer Network (NCCN) guidelines recommend that patients with SCLC at clinical stage I-IIA (T1 -2, N0, M0) after a standard staging evaluation may be eligible for surgical resection (9). After analyzing the SEER database, Schreiber et al (11) concluded that the use of surgery, and particularly lobectomy, in selected patients with limited-stage SCLC was associated with improved survival outcomes. However, there was inherent selection bias in their study (11). Therefore, the present study performed the period propensity score matching analysis using the SEER database to further examine the role of surgery on survival in patients with SCLC.

Following propensity score matching analysis, the present study identified that the clinicopathological features of N stage and surgery were important factors for postoperative CSS in patients who received surgery, including sublobectomy, lobe/s and pneumonectomy. This finding was corroborated by the results of previous studies (5,11,12). The IASLC proposals (12) demonstrated that there was a significant difference in the survival of patients who underwent surgery between N0 patients and those with node-positive disease for both clinical and pathological staging, independent of T category. Takenaka et al (5) reported that the 5-year survival rates of the patients with SCLC with or without surgical resection, according to the clinical stage were as follows: 62 and 25% in stage I (P<0.01), 33 and 24% in stage II (P=0.95) and 18 and 18% in stage III (P=0.35). The study of Schreiber et al (11) also demonstrated that the overall survival for patients with SCLC with N0, N1 and N2 who received surgery were significantly improved, when compared with those who did not receive surgery (P<0.01). In addition, the significance of surgery was corroborated following Cox regression analysis (P<0.001) (Table IV). These results suggested that the role of surgery for patients with SCLC was significant.
To further identify who would benefit from surgery, the survival functions of surgery stratified by the clinicopathological features were analyzed using log-rank tests (Table V). The results revealed that patients who did not receive surgery in any of the subgroups, including sex, histology and grade had an increased risk of COD compared with patients who received surgery. These results suggest that surgery should be performed irrespective of sex, histology, grade and clinicopathological features. Previous studies have reported that increasing age was an independent adverse prognostic factor in SCLC (13-15). However, the results of the present study demonstrated that patients between 50 and 90 years of age benefited from surgery, although analysis was not tested in the subgroups of age <40 years or between 90 and 100 years. Furthermore, age was an independent prognostic factor (P<0.001; Table IV), which suggested that surgery should also be performed even in elderly patients with SCLC. This result was similar with the treatment of thoracic irradiation for limited-stage SCLC, in which it was reported that in the dose range examined, age did not appear to have an effect on the delivery, tolerance or efficacy of TI in the combined modality management of SCLC (16). Concerning T, there was significant difference in the T1a subgroup (P<0.001) and better survival trends in the T1b and T2a subgroups. Furthermore, patients
with SCLC with N0 (P<0.001) and stage Ia (P<0.001) and Ib (P<0.001) would have an increased benefit from surgery. These results, which were in accordance with those reported by the IASLC (12), clarified why the most recent NCCN guidelines...
### Table V. Continued.

#### B. Sublobectomy vs. lobe/s group

| Feature          | Sublobectomy | lobe/s | P-value |
|------------------|--------------|--------|---------|
| Sublobectomy     | NE | NEE  | NE | NEE  |        |
| NE/A             | N/A | N/A  | N/A | N/A  | NS     |
| ≥40, <50         | 2  | 2.0  | NT | NT   | NS     |
| ≥50, <60         | 5  | 5.5  | 4  | 3.5  | 0.75   |
| ≥60, <70         | 12 | 9.6  | 10 | 12.4 | 0.30   |
| ≥70, <80         | 14 | 11.3 | 11 | 13.7 | 0.28   |
| ≥80, <90         | 7  | 4.0  | 1  | 4.1  | 0.03   |
| ≥90, <100        | N/A | N/A  | N/A | N/A  | NS     |

#### C. Lobe/s vs. Pneumonectomy group

| Feature          | lobe/s | Pneumonec- | P-value |
|------------------|--------|------------|---------|
| lobe/s           | NE | NEE  | NE | NEE  |        |
| NE/A             | N/A | N/A  | N/A | N/A  | NS     |
| ≥40, <50         | NT | NT   | 1  | 1.0  | NS     |
| ≥50, <60         | 0  | 0.0  | 1  | 1.0  | 1.00   |
| ≥60, <70         | 6  | 6.7  | 2  | 1.3  | 0.42   |
| ≥70, <80         | NT | NT   | NT | NT   | NS     |
| ≥80, <90         | NT | NT   | NT | NT   | NS     |
| ≥90, <100        | N/A | N/A  | N/A | N/A  | NS     |

#### Age, years

| Age, years | Sublobectomy | Pneumonec- |        |
|------------|--------------|------------|--------|
| <40        | N/A          | N/A        | NS     |
| ≥40, <50   | NT           | NT         | NS     |
| ≥50, <60   | 0            | 1.0        | 1.00   |
| ≥60, <70   | 6            | 2.7        | 0.53   |
| ≥70, <80   | NT           | NT         | NT     |
| ≥80, <90   | NT           | NT         | NT     |
| ≥90, <100  | N/A          | N/A        | NS     |

#### Sex

| Sex | Sublobectomy | Pneumonec- |        |
|-----|--------------|------------|--------|
| Male| 17           | 14.9       | 0.38   |
| Female| 23         | 17.7       | 0.09   |

#### Race

| Race  | Sublobectomy | Pneumonec- |        |
|-------|--------------|------------|--------|
| Hispanic | 1           | 1.0        | NS     |
| AI/AN | N/A          | N/A        | NS     |
| API   | N/A          | N/A        | NS     |
| African descent | 3 | 2.8       | 0.81   |
| Caucasian | 36      | 28.4       | 0.05   |

#### Histology

| Histology     | Sublobectomy | Pneumonec- |        |
|---------------|--------------|------------|--------|
| SCC, NOS      | 32           | 25.1       | 0.06   |
| OCC           | NT           | NT         | NT     |
| SCC, IC       | N/A          | N/A        | NS     |
| CSCC          | 8            | 6.8        | 0.36   |

#### Grade (8)

| Grade | Sublobectomy | Pneumonec- |        |
|-------|--------------|------------|--------|
| I     | NT           | NT         | NT     |
| II    | 1            | 1.0        | 1.00   |
| III   | 18           | 14.5       | 0.17   |
| IV    | 21           | 17.0       | 0.19   |

#### T (8)

| T   | Sublobectomy | Pneumonec- |        |
|-----|--------------|------------|--------|
| T1a | 14           | 10.7       | 0.52   |
| T1b | 5            | 3.5        | 0.48   |
| T2a | 5            | 1.0        | 0.22   |
| T2b | 1            | 0.6        | 0.32   |
| T3  | 12           | 12.6       | 0.24   |
| T4  | 3            | 3.0        | NT     |

#### N (8)

| N   | Sublobectomy | Pneumonec- |        |
|-----|--------------|------------|--------|
| 0   | 22           | 16.2       | 0.04   |
| 1   | 5            | 1.2        | 10.8   |
| 2   | 11           | 12.2       | 6.8    |
| 3   | 2            | 2.0        | NT     |

#### Stage (8)

| Stage | Sublobectomy | Pneumonec- |        |
|-------|--------------|------------|--------|
| IA    | 14           | 10.7       | 0.14   |
| IB    | 5            | 3.5        | 2.5    |
| IIA   | 5            | 1.0        | 11.0   |
| IIB   | 1            | 0.6        | 2.4    |
| IIIA  | 12           | 12.6       | 8.4    |
| IIIB  | 3            | 3.0        | NT     |

Lobe/s, lobectomy or bilobectomy; NP, Number of Patients; NE, Number of Events; NEE, Number of Expected Events; AI/AN, American Indian/Alaska Native; API, Asian or Pacific Islander; SCC, Small cell carcinoma; OCC, Oat cell carcinoma; IC, Intermediate cell; CSCC, Combined small cell carcinoma; NT, No test possible because of no failures observed; N/A, No observation in the database.
recommend that patients with SCLC with clinical stage I-IIA (T1-2, N0, M0) after a standard staging evaluation may be considered for surgical resection (9).

As with the comparison of non-surgery with surgery, following propensity score matching analysis, the present study identified that the clinicopathological features of N, stage and surgery were important factors in postoperative CSS in patients with SCLC who received sublobectomy compared with those who received lobe/s. However, no independent prognostic factor was identified in the Cox regression model.

When the survival functions of surgery stratified by clinicopathological features were analyzed using log-rank tests (Table V), more patients who received sublobectomy in all subgroups of sex, histology were at risk of COD compared with those who received lobe/s. On the other hand, the results also demonstrated that there were more patients between 60 and 90 years of age, who benefited from lobe/s, although this analysis was not performed in the subgroups ages <50 years, as no failure events were observed, and in the subgroups ages <40 years and between 90 and 100 years, due to the absence of observations.

Another study comparing treatment strategies for stage I SCLC using the National Cancer Database (17) demonstrated that lobectomy was associated with an improved survival compared with limited resection (HR 0.64; 95% CI, 0.53-0.78; P<0.001). Schreiber et al (11) revealed that the median survival time for lobectomy and sublobectomy was 40 and 23 months, respectively.
These results confirmed that, similar with the NCCN recommendation (9), bi-/lobectomy was the preferred operation for SCLC compared with sublobectomy, even in elder patients irrespective of sex and histology. When analyzing T, although

(P<0.001). These results confirmed that, similar with the NCCN recommendation (9), bi-/lobectomy was the preferred operation for SCLC compared with sublobectomy, even in elder patients irrespective of sex and histology. When analyzing T, although
there was no significant difference, it was the patients with SCLC with T1a to T2b, who had received lobe/s, who exhibited better survival trends. Simultaneously, the present study also demonstrated that more patients with N0-1, stage Ia-IIb who received sublobectomy, rather than lobe/s, were at risk of COD. Despite the recommendation in the most recent NCCN guidelines that patients with SCLC with clinical stage I-IIA (T1-2, N0, M0) after a standard staging evaluation may be considered for surgical resection (9) and multiple medical societies concluding that the survival advantage of surgical resection is only observed in patients with stage I disease (5,10,18,19), the results of the present study suggest that patients with SCLC with up to stage IIB (N1) may benefit from lobe/s. Combs et al (20) also stated that patients with stages I, II and III SCLC that underwent surgical resection as part of the initial treatment with chemotherapy may exhibit an improved overall survival rate.

Due to the inclusion criterion, only 10 patients who received pneumonectomy were included in the present study, and therefore results were too limited to be extensively discussed. Despite the large sample size, a limitation of the SEER database, and consequently of the present study, was the lack of information regarding performance and smoking status, which may have an important impact on postoperative survival, and the use of perioperative effective treatments.
including systemic therapy, mediastinal radiation therapy and prophylactic cranial irradiation. In addition, the different surgical types of lobectomy and bilobectomy were recorded as a single category ‘lobectomy or bilobectomy’, and the present study was unable to analyze the difference between them.

In conclusion, surgery should be taken into consideration when initial treatment strategy is made in patients with SCLC with a clinical stage I-IIA (T1-2, N0, M0), and should not be overlooked in patients >50 years, irrespective of sex, histology and the grade of the clinicopathological features. There is also evidence to suggest that certain patients with SCLC with stage IIB (N1) may also benefit from lobectomy or bilobectomy, although further investigation is required. In addition, lobe/s is preferred compared with sublobectomy when surgery is performed. However, the present study was unable to conclusively state the role of pneumonectomy for SCLC.

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Figure 7. Insignificant survival functions of surgery stratified by clinicopathological features when comparing Sublobectomy with Lobe/s. (A) Age, ≥60 and <70 years; (B) age, ≥70 and <80 years; (C) sex, male; (D), sex, female; (E) race, African descent; (F) race, Caucasian; (G) histology, SCC, NOS; (H) histology, CSCC; SCC, small cell cancer; NOS, not otherwise specified; CSCC, combined small cell carcinoma.
Availability of data and materials

The datasets generated during and/or analyzed during the current study are available in the Surveillance, Epidemiology, and End Results (SEER; www.seer.cancer.gov) Program SEER*Stat Database.

Authors' contributions

XD, DT, JX, WL, SY, HZ and JZ participated in the design of the study and performed statistical analysis. LL, ZT and XC contributed to the acquisition and interpretation of data and critically revised the article for intellectual content. All
authors were involved in the writing of the manuscript and approved the final version of the manuscript.

Ethics approval and consent to participate
Not applicable.

Patient consent for publication
Not applicable.

Competing interests
The authors declare that there is no competing interests.

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