Advanced age is not the decisive factor in chemotherapy of small cell lung cancer: a population-based study

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ABSTRACT

Objective: There is limited research on the impact of chemotherapy on the prognosis of different age group patients with small cell lung cancer (SCLC). The aim of this study was to explore the impact of chemotherapy on survival prognosis of elderly patients with SCLC.

Methods: Based on the Surveillance, Epidemiology and End Results (SEER) database, 57,460 SCLC patients between 2004 and 2015 were identified and divided into a ≤ 80 years group (n = 50,941) and a >80 years group (n = 6,519). Confounding factors were controlled by propensity score matching (PSM) analysis. Kaplan Meier (KM) analysis was performed to determine the impact of chemotherapy on overall survival (OS) and lung-cancer specific survival (LCSS) of the patients. Other variables that could affect survival of SCLC patients were also examined by COX analysis.

Results: KM analysis showed that both OS and LCSS were improved in chemotherapy group compared to those in non-chemotherapy group (log rank P < 0.001) in both age groups after PSM. Cox analysis demonstrated the survival benefit of chemotherapy in both ≤ 80 years group (OS: HR 0.435; 95% CI 0.424–0.447; LCSS: HR 0.436; 95% CI 0.424–0.448) and >80 years group (OS: HR 0.424; 95% CI 0.397–0.451; LCSS: HR 0.415; 95% CI 0.389–0.444). Additionally, the following parameters had a negative impact on survival of elderly patients: male sex, tumor location in main bronchus, increased stage, bilateral tumor, no surgery or radiation, and lower median household income.

Conclusions: Elderly patients with SCLC should be encouraged to receive chemotherapy provided their general conditions permit.

INTRODUCTION

According to the American Cancer Society (ACS), lung cancer is the second most common cancer, with 235,760 new cases diagnosed in 2021 [1]. It is also one of the cancers with the lowest 5-year relative survival rate (21%), especially for small cell lung cancer (SCLC) whose 2-year survival is even lower than that of non-small cell lung cancer (NSCLC) (14–15% vs. 42%) [1]. SCLC accounts for approximately 13% of all lung carcinomas [2]. Compared with NSCLC, SCLC is associated with poorer prognosis, earlier and more frequent brain metastasis [3, 4]. Lung cancer is also a cancer of the elderly, with a median age of about 71 years.
at diagnosis [5], and there is an increasing trend in the proportion of SCLC patients in the age group older than 75 years according to a study from Hebei, China [6].

Over the past three decades, chemotherapy has provided considerable survival benefits for SCLC patients [7], and remains the standard treatment for first- and second-line management of SCLC [8]. Immunotherapy also plays an important role in patients with relapsed SCLC [8]. There have been many clinical trials on immune checkpoints inhibitors (ICIs), tumor vaccines, antigenic targets, and adoptive cellular immunotherapy in SCLC, but the results have been somewhat disappointing so far [9]. Treatment planning and decision mainly depend on the cancer TNM staging system and the Veterans Administration Lung Study Group (VALG) staging system, according to the National Comprehensive Cancer Network Clinical Practice Guidelines for SCLC, the Chinese Society of Clinical Oncology Lung Cancer Guidelines, and the European Society for Medical Oncology Clinical Practice Guidelines for Metastatic SCLC [10]. With the overall population life expectancy improving, treatment for elderly patients has aroused increasing attention. Given the performance status (PS) of the elderly and the associated comorbidities and toxicity, some oncologists are not inclined to using chemotherapy in elderly patients with SCLC [11]. So, whether chemotherapy is beneficial to elderly patients needs to be further confirmed. Several retrospective cohort studies exploring the relationship between age and treatment choice have defined elderly patients as age ≥ 65 [12, 13], ≥ 70 [14, 15] or ≥ 75 years old [11, 16]. There is limited research on patients > 80 years old, much less in elderly SCLC patients older than 80 years. A recent single center retrospective study evaluated the survival outcome associated with the treatment strategies in 56 cancer patients aged over 80 years, but only 7 of them were SCLC patients [17]. The aim of present study is to explore the impact of chemotherapy on survival prognosis of elderly patients with SCLC using the Surveillance, Epidemiology and End Results (SEER) database.

**METHODS**

**Data source**

We performed this study to verify the relationship between chemotherapy and the survival prognosis of SCLC patients of different ages. All the data were based on the Surveillance, Epidemiology, and End Results (SEER) database, which was established in 1973 and collects information on cancer incidences and survival in the United States (US), covering 17 population-based cancer registries, accounting for about 28% of the current US population [18].

**Study population**

From 74,294 SCLC patients initially identified from the SEER database between 2004 and 2015, we included 57,460 patients for final analysis after excluding 13,544 patients without first malignant primary indicators, 167 with unknown survival months and 3,123 with incomplete data according to the inclusion and exclusion criteria (Figure 1). They were divided into two age groups: ≤ 80 years group (n = 50,941) and >80 years group (n = 6,519), and each group was further divided into chemotherapy group (n = 37,136 for ≤ 80 and 2,774 for >80 years) and non-chemotherapy group (n = 13,805 for ≤ 80 and 3,745 for > 80 years).

**Covariates**

Baseline clinical characteristics including median age at diagnosis, gender, race, region, year of diagnosis, primary site, grade, laterality, stage, radiation, surgery, marital status, education level and median household income were collected.

**Statistical analyses**

Continuous variables were compared using t-test, and categorical variables were compared using chi-square. Potential deviation between chemotherapy and non-chemotherapy groups was controlled by propensity score matching (PSM) analysis. Kaplan-Meier (KM) analysis and the log rank test were applied to compare overall survival (OS) and lung-cancer specific survival (LCSS) between patients with or without chemotherapy. To study whether other variables could affect survival of SCLC patients, COX analysis was performed in each group. Statistical significance was set at a two-tailed P value < 0.05. All analyses were performed with IBM SPSS version 25.0.

**RESULTS**

**Study cohort characteristics**

Demographic and clinical characteristics of the patients are included in Table 1. Among these, 50,941 were ≤ 80 years old and 6,519 were >80 years old, and their median age at diagnosis was 65 years (interquartile range, 59–72 years) and 83 years (interquartile range, 81–85 years) respectively. Both groups of patients were distributed roughly equally by gender (men 50.4%, women 49.6% in ≤ 80 years group; men 47.0%, women 53.0% in >80 years group). Most patients were Caucasian (86.9% in ≤80 years group; 87.8% in >80 years group), and from the East (50.8% in ≤80 years group; 41.6% in >80 years group) or Southwest (36.5% in ≤80 years group; 45.1% in >80 years group), only a
few (0.2% in ≤80 years group; 0.1% in >80 years group) were living in the Northwest. Most patients did not receive surgical treatment (96.8% in ≤80 years group; 98.0% in >80 years group) or radiotherapy (51.1% in ≤80 years group; 74.4% in >80 years group). Patients in the early stage, married, treated with radiation but not surgery and had better education were more likely to receive chemotherapy. About 43% of the elderly patients in our study received chemotherapy. Most (73%) of the younger patients chose chemotherapy (Table 1). The proportion of SCLC patients choosing chemotherapy did not vary significantly with the year of diagnosis (Figure 2).

Comparison of survival curves between chemotherapy group and non-chemotherapy group

Enrolled in the study were 27,486 patients ≤80 years old and 4,550 patients >80 years old after propensity score matched analysis. KM analysis demonstrated improved OS and LCSS in patients of chemotherapy group compared to patients of non-chemotherapy group.

Figure 1. Study flow diagram. Abbreviations: SCLC: Small cell lung cancer; SEER: Surveillance, Epidemiology, and End Results registry.
| Variable                        | Age ≤ 80 year Chemotherapy | Age > 80 year Chemotherapy |
|--------------------------------|-----------------------------|-----------------------------|
|                                | Yes  n = 37136 (73)         |                             |
| Gender                         | Male                        | 18649 (50.2)                |
|                                | Female                      | 18487 (49.8)                |
| Race recode                    | White                       | 32288 (86.9)                |
|                                | Black                       | 3376 (9.1)                  |
|                                | Other                       | 1441 (3.9)                  |
|                                | Unknown                     | 31 (0.1)                    |
| CHSDA region                   | EAST                        | 19175 (51.6)                |
|                                | NORTHWEST                   | 81 (0.2)                    |
|                                | SOUTHWEST                   | 12904 (34.7)                |
|                                | NORTH                       | 4976 (13.4)                 |
| Year of diagnosis              | 2004–2007                   | 12499 (33.7)                |
|                                | 2008–2011                   | 12264 (33.0)                |
|                                | 2012–2017                   | 12373 (33.3)                |
| Primary Site                   | Upper lobe                  | 17512 (47.2)                |
|                                | Middle lobe                 | 1431 (3.9)                  |
|                                | Lower lobe                  | 6941 (18.7)                 |
|                                | NOS                         | 6301 (17.0)                 |
|                                | Overlapping lesion          | 559 (1.5)                   |
|                                | Main bronchus               | 4392 (11.8)                 |
| Grade                          | I                           | 53 (0.1)                    |
|                                | II                          | 116 (0.3)                   |
|                                | III                         | 3239 (8.7)                  |
|                                | IV                          | 6948 (18.7)                 |
|                                | Unknown                     | 26780 (72.1)                |
| Laterality                     | Right-origin of primary     | 20451 (55.1)                |
|                                | Left-origin of primary      | 14731 (39.7)                |
|                                | Paired sit                  | 1375 (3.7)                  |
|                                | Only one side - side        | 161 (0.4)                   |
|                                | unspecified                 | 79 (0.2)                    |
|                                | Not a paired sit            |                              |
|                                | Bilateral                   |                              |
|                                | single primary              |                              |
| Stage Group                    | I                           | 1416 (3.8)                  |
|                                | II                          | 842 (2.3)                   |
|                                | III                         | 11795 (31.8)                |
|                                | IV                          | 23083 (62.2)                |
| Radiation recode               | Yes                         | 22007 (59.3)                |
|                                | No                          | 15129 (40.7)                |
| Surgery                        | Yes                         | 1117 (3.0)                  |
|                                | No                          |                              |
|                                |                              |                              |
|                                |                              |                              |

|                                | Median age at diagnosis     | 64 (58–71)                  |
|                                |                             | 68 (61–74)                  |
|                                |                             | 65 (59–72)                  |
|                                |                             |                              |
|                                | Male                        | 18649 (50.2)                |
|                                | Female                      | 18487 (49.8)                |
|                                | White                       | 32288 (86.9)                |
|                                | Black                       | 3376 (9.1)                  |
|                                | Other                       | 1441 (3.9)                  |
|                                | Unknown                     | 31 (0.1)                    |
|                                | EAST                        | 19175 (51.6)                |
|                                | NORTHWEST                   | 81 (0.2)                    |
|                                | SOUTHWEST                   | 12904 (34.7)                |
|                                | NORTH                       | 4976 (13.4)                 |
|                                | 2004–2007                   | 12499 (33.7)                |
|                                | 2008–2011                   | 12264 (33.0)                |
|                                | 2012–2017                   | 12373 (33.3)                |
|                                | Upper lobe                  | 17512 (47.2)                |
|                                | Middle lobe                 | 1431 (3.9)                  |
|                                | Lower lobe                  | 6941 (18.7)                 |
|                                | NOS                         | 6301 (17.0)                 |
|                                | Overlapping lesion          | 559 (1.5)                   |
|                                | Main bronchus               | 4392 (11.8)                 |
|                                | I                           | 53 (0.1)                    |
|                                | II                          | 116 (0.3)                   |
|                                | III                         | 3239 (8.7)                  |
|                                | IV                          | 6948 (18.7)                 |
|                                | Unknown                     | 26780 (72.1)                |
|                                | Right-origin of primary     | 20451 (55.1)                |
|                                | Left-origin of primary      | 14731 (39.7)                |
|                                | Paired sit                  | 1375 (3.7)                  |
|                                | Only one side - side        | 161 (0.4)                   |
|                                | Not a paired sit            | 79 (0.2)                    |
|                                | Bilateral                   |                              |
|                                | single primary              |                              |
|                                | I                           | 1416 (3.8)                  |
|                                | II                          | 842 (2.3)                   |
|                                | III                         | 11795 (31.8)                |
|                                | IV                          | 23083 (62.2)                |
|                                | Yes                         | 22007 (59.3)                |
|                                | No                          | 15129 (40.7)                |
|                                | Yes                         | 1117 (3.0)                  |

Note: P values are indicated for each comparison.
with the survival curves showing statistically significant differences (log rank $P < 0.0001$) in both $\leq 80$ years group and $> 80$ years group (Figure 3).

The effects of chemotherapy on the survival of patients with SCLC

Cox analysis demonstrated the survival benefit of chemotherapy in both $\leq 80$ years group (OS: HR 0.435; 95% CI 0.424–0.447; $P < 0.001$; LCSS: HR 0.436; 95% CI 0.424–0.448; $P < 0.001$) and $> 80$ years group (OS: HR 0.424; 95% CI 0.397–0.451; $P < 0.001$; CSS: HR 0.415; 95% CI 0.389–0.444; $P < 0.001$). Also, survival varied with the change of other variables including sex, primary site, laterality, stage, surgery, radiation and household income. Additionally, variables like race, year of diagnosis, region, age, marital status, and education status also affected survival in in $\leq 80$ years group (Tables 2 and 3; Figure 4). The following parameters had a negative impact on survival of patients in $\leq 80$ years group: Caucasian, male sex, later year of diagnosis, older age, north region, tumor location in main bronchus, increased stage and grade, bilateral tumor, no surgery or radiation, separation, lower median household income and poorer educated, while the following parameters had a negative impact on survival of patients in $> 80$ years group: male...
### Table 2. Multivariate analysis using a Cox proportional hazards model in SCLC patients ≤ 80.

| Variable                        | Multivariate analysis | OS          | CSS        |
|---------------------------------|-----------------------|-------------|------------|
|                                 |                       | HR 95% CI   | P          | HR 95% CI   | P          |
| Race recode                     |                       |             |            |             | <0.001     | <0.001     |
| White                           | Reference             |             |            |             |            |            |
| Black                           | 0.909                 | 0.870 to 0.949 | <0.001 | 0.896 | 0.856 to 0.938 | <0.001     |
| Other                           | 0.909                 | 0.849 to 0.974 | 0.007 | 0.884 | 0.822 to 0.951 | 0.001     |
| Unknown                         | 0.572                 | 0.365 to 0.898 | 0.015 | 0.395 | 0.224 to 0.696 | 0.001     |
| Sex                             |                       | <0.001      |            |             |            |            |
| Male                            | Reference             |             |            |             |            |            |
| Female                          | 0.885                 | 0.863 to 0.908 | <0.001 | 0.896 | 0.872 to 0.920 | <0.001     |
| Year of diagnosis               |                       | <0.001      |            |             |            |            |
| 2012-2015                       | Reference             |             |            |             | <0.001     | <0.001     |
| 2008-2011                       | 0.922                 | 0.894 to 0.951 | <0.001 | 0.924 | 0.894 to 0.955 | <0.001     |
| 2004-2007                       | 0.920                 | 0.891 to 0.950 | <0.001 | 0.933 | 0.903 to 0.965 | <0.001     |
| CHSDA Region                    |                       | 0.001       |            |             |            | <0.001     |
| NORTH                           | Reference             |             |            |             | <0.001     | <0.001     |
| SOUTHWEST                       | 0.946                 | 0.902 to 0.992 | 0.023 | 0.946 | 0.900 to 0.993 | <0.001     |
| EAST                            | 0.919                 | 0.879 to 0.960 | <0.001 | 0.907 | 0.866 to 0.949 | <0.001     |
| Primary Site                    |                       | <0.001      |            |             | <0.001     |            |
| Main bronchus                   | Reference             |             |            |             | <0.001     | <0.001     |
| Upper lobe                      | 0.918                 | 0.881 to 0.957 | <0.001 | 0.913 | 0.874 to 0.953 | <0.001     |
| Middle lobe                     | 0.899                 | 0.834 to 0.969 | 0.005 | 0.880 | 0.814 to 0.952 | 0.001     |
| Lower lobe                      | 0.931                 | 0.888 to 0.975 | 0.003 | 0.923 | 0.879 to 0.969 | 0.001     |
| NOS                             | 1.029                 | 0.980 to 1.081 | 0.253 | 1.019 | 0.968 to 1.072 | 0.476     |
| Overlapping lesion              | 1.011                 | 0.913 to 1.120 | 0.836 | 0.996 | 0.896 to 1.108 | 0.941     |
| Grade                           |                       | <0.001      |            |             | <0.001     | <0.001     |
| Unknown                         | Reference             |             |            |             |            |            |
| I                               | 0.497                 | 0.353 to 0.700 | <0.001 | 0.491 | 0.341 to 0.708 | <0.001     |
| II                              | 0.876                 | 0.708 to 1.083 | 0.222 | 0.935 | 0.752 to 1.163 | 0.545     |
| III                             | 0.963                 | 0.920 to 1.007 | 0.101 | 0.966 | 0.922 to 1.013 | 0.156     |
| IV                              | 0.982                 | 0.950 to 1.014 | 0.265 | 0.986 | 0.953 to 1.020 | 0.43      |
| Laterality                      |                       | <0.001      |            |             | <0.001     | <0.001     |
| Bilateral, single primary       | Reference             |             |            |             | <0.001     | <0.001     |
| Right-origin of primary         | 1.092                 | 0.985 to 1.211 | 0.096 | 1.058 | 0.952 to 1.175 | 0.297     |
| Left-origin of primary          | 1.101                 | 0.993 to 1.222 | 0.069 | 1.068 | 0.960 to 1.187 | 0.224     |
| Paired sit                      | 0.922                 | 0.825 to 1.030 | 0.152 | 0.886 | 0.791 to 0.992 | 0.036     |
| Only one side - side unspecified| 0.827                 | 0.691 to 0.991 | 0.04  | 0.779 | 0.645 to 0.941 | 0.010     |
| Not a paired site               | 1.044                 | 0.797 to 1.368 | 0.755 | 0.995 | 0.751 to 1.317 | 0.970     |
| Stage Group                     |                       | <0.001      |            |             | <0.001     | <0.001     |
| IV                              | Reference             |             |            |             |            |            |
| III                             | 0.653                 | 0.633 to 0.673 | <0.001 | 0.623 | 0.603 to 0.644 | <0.001     |
| II                              | 0.521                 | 0.465 to 0.583 | <0.001 | 0.477 | 0.422 to 0.539 | <0.001     |
| I                               | 0.307                 | 0.283 to 0.333 | <0.001 | 0.255 | 0.233 to 0.279 | <0.001     |
| Surgery                         |                       | <0.001      |            |             | <0.001     | <0.001     |
| Yes                             | Reference             |             |            |             | <0.001     | <0.001     |
| Radiation recode               |                       | <0.001      |            |             | <0.001     | <0.001     |
| No                              | Reference             |             |            |             | <0.001     | <0.001     |
| Yes                             | 0.685                 | 0.664 to 0.706 | <0.001 | 0.695 | 0.673 to 0.718 | <0.001     |
| Age at diagnosis                | 1.013                 | 1.011 to 1.015 | <0.001 | 1.012 | 1.010 to 1.013 | <0.001     |
| Marital status                  |                       | <0.001      |            |             | <0.001     | <0.001     |
| Separated                       | Reference             |             |            |             | <0.001     | <0.001     |
| Divorced                        | 1.023                 | 0.917 to 1.142 | 0.681 | 1.021 | 0.911 to 1.144 | 0.721     |
| Single                          | 1.011                 | 0.906 to 1.128 | 0.839 | 0.997 | 0.890 to 1.117 | 0.956     |
| Windowed                        | 0.980                 | 0.878 to 1.094 | 0.717 | 0.984 | 0.878 to 1.103 | 0.780     |
| Unknown                         | 0.912                 | 0.807 to 1.030 | 0.137 | 0.918 | 0.808 to 1.041 | 0.182     |
| Married                         | 0.907                 | 0.815 to 1.010 | 0.075 | 0.918 | 0.822 to 1.026 | 0.132     |
| Unmarried or domestic partner   | 0.825                 | 0.564 to 1.205 | 0.319 | 0.830 | 0.560 to 1.230 | 0.354     |
sex, tumor location in main bronchus, increased stage, bilateral tumor, no surgery or radiation, and lower median household income.

**DISCUSSION**

The results of our study demonstrated the benefit of chemotherapy in both young and elderly SCLC patients. Although chemotherapy could benefit OS and LCSS regardless of age, patients older than 80 years tended to reject chemotherapy compared with patients younger than 80 years. Besides, the results of our COX analysis showed that male sex, an increased stage and grade, and no surgery or radiation were associated with worse prognoses. In < 80 years group, Caucasian patients who were diagnosed late or at an older age tended to have worse prognoses.

More studies have paid increasing attention to the relationship between chemotherapy and survival of patients with SCLC.

**Figure 3. Comparison of survival curves between chemotherapy group and group without chemotherapy.** (A) Comparison of OS in patients ≤ 80 years old; (B) Comparison of LCSS in patients ≤ 80 years old; (C) Comparison of OS in patients > 80 years old; (D) Comparison of LCSS in patients > 80 years old. Abbreviations: OS: Overall survival; LCSS: Lung cancer-specific survival; Cum: Cumulative.
Table 3. Multivariate analysis using a Cox proportional hazards model in SCLC patients >80.

| Variable                      | Multivariate analysis |       |       |
|-------------------------------|-----------------------|-------|-------|
|                               | OS                    |       | CSS   |       |
|                               | HR  | 95% CI | P    | HR   | 95% CI | P   |
| Sex                           |     |        |      |      |        |     |
| Male                          | Reference             | 1.000 | <0.001| 1.000 | <0.001|
| Female                        | 0.883                    | 0.831 to 0.939 | <0.001 | 0.896                    | 0.841 to 0.955 | <0.001|
| Primary Site                  |     |        |      |      |        |     |
| Main bronchus                 | Reference             | 0.002 |        | 0.003|
| Upper lobe                    | 0.828                  | 0.739 to 0.927 | 0.001 | 0.812                  | 0.722 to 0.913 | 0.001|
| Middle lobe                   | 0.820                  | 0.683 to 0.985 | 0.033 | 0.819                  | 0.677 to 0.991 | 0.040|
| Lower lobe                    | 0.872                  | 0.774 to 0.983 | 0.024 | 0.858                  | 0.757 to 0.972 | 0.016|
| NOS                           | 0.936                  | 0.824 to 1.063 | 0.308 | 0.925                  | 0.810 to 1.056 | 0.248|
| Overlapping lesion            | 1.080                  | 0.846 to 1.378 | 0.536 | 1.025                  | 0.792 to 1.326 | 0.852|
| Laterality                    |     |        |      |      |        |     |
| Bilateral, single primary     | Reference             | 0.001 | <0.001|      |
| Right-origin of primary       | 0.912                  | 0.681 to 1.220 | 0.533 | 0.926                  | 0.683 to 1.254 | 0.618|
| Left-origin of primary        | 0.987                  | 0.737 to 1.323 | 0.932 | 1.009                  | 0.744 to 1.369 | 0.956|
| Paired sit                    | 0.716                  | 0.524 to 0.977 | 0.035 | 0.704                  | 0.508 to 0.975 | 0.035|
| Only one side - side         |                      |        |      |      |        |     |
| unspecified                  | 0.636                  | 0.380 to 1.064 | 0.085 | 0.660                  | 0.388 to 1.122 | 0.124|
| Not a paired site             | 0.917                  | 0.458 to 1.833 | 0.805 | 0.890                  | 0.429 to 1.844 | 0.753|
| Stage Group                   |     |        |      |      |        |     |
| IV                            | Reference             | <0.001 | <0.001|      |
| III                           | 0.739                  | 0.689 to 0.792 | <0.001 | 0.717                  | 0.667 to 0.771 | <0.001|
| II                            | 0.539                  | 0.428 to 0.679 | <0.001 | 0.480                  | 0.373 to 0.618 | <0.001|
| I                             | 0.369                  | 0.318 to 0.429 | <0.001 | 0.326                  | 0.277 to 0.384 | <0.001|
| Surgery                       |     |        |      |      |        |     |
| No                            | Reference             | <0.001 | <0.001|      |
| Yes                           | 0.536                  | 0.406 to 0.709 | <0.001 | 0.596                  | 0.446 to 0.796 | <0.001|
| Radiation recode              |     |        |      |      |        |     |
| No                            | Reference             | <0.001 | <0.001|      |
| Yes                           | 0.678                  | 0.631 to 0.728 | <0.001 | 0.680                  | 0.630 to 0.733 | <0.001|
| Median household income       |     |        |      |      |        |     |
| >63000                        | Reference             | <0.001 | 0.014 |
| 48000–62999                   | 1.050                  | 0.981 to 1.123 | 0.162 | 1.047                  | 0.976 to 1.125 | 0.201|
| 38000–47999                   | 1.159                  | 1.061 to 1.266 | 0.001 | 1.157                  | 1.055 to 1.269 | 0.002|
| <38000                        | 0.994                  | 0.867 to 1.139 | 0.929 | 0.967                  | 0.837 to 1.116 | 0.643|
| Chemotherapy recode           |     |        |      |      |        |     |
| No                            | Reference             | <0.001 | <0.001|      |
| Yes                           | 0.424                  | 0.397 to 0.451 | <0.001 | 0.415                  | 0.389 to 0.444 | <0.001|

Abbreviations: SCLC: Small cell lung cancer; NOS: Not otherwise specified; HR: hazard ratio; CI: Confidence interval.

SCLC patients, especially in elderly SCLC patients. Elegbede et al. reviewed 404 SCLC patients managed at a tertiary cancer center in Canada from 2010 to 2016 and found that chemotherapy benefited survival of SCLC patients, especially those in extensive stages (HR 0.33; 95% CI 0.22–0.48; P < 0.01) [19]. Another study developed a nomogram prognostic model based on a large cohort of 24,680 SCLC patients from the National Cancer Database (NCDB), and their result showed that chemotherapy was beneficial to improving prognosis (HR 0.35; 95% CI 0.33–0.36; P < 0.001) [20]. A study from the Japanese Joint Committee of Lung Cancer Registry [21] reported that OS of their 228 SCLC patients aged > 75 years who received second-line chemotherapy was 13.9 weeks, which was significantly higher than 7.5 months in those who received supportive care alone in a previous randomized controlled study [22]. A meta-analysis recruiting 14 relevant randomized clinical trials from the Medline and Cochrane databases reported that the 1-year OS improved from 30% to 39% and the 2-year OS improved from 10% to 14% in SCLC patients who received maintenance chemotherapy [23]. Several previous studies concluded that patients of advanced
age tended to reject chemotherapy, which is consistent with our study. By reviewing a number of retrospective studies, Deppermann et al. [24] concluded that elderly patients were often offered only suboptimal or no treatment. Researchers from the British Columbia Cancer Agency carried out a retrospective review on 174 patients with SCLC between 1991 and 1999, and categorized them into three age groups: < 65 years (\(n = 55\)), 65–74 years (\(n = 76\)), and ≥ 75 years (\(n = 43\)). The results displayed that elder patients tended to fail to complete an “optimal” course (intravenous regimens, more than 85% total doses, 4+ cycles, and less than 2 weeks total treatment delays) of first-line chemotherapy (\(P < 0.05\)), and patients >65 years were less likely to administer second-line chemotherapy (\(P < 0.05\)) [16]. In the light of a recently published retrospective analysis of SCLC patients at IPO-Porto, Portugal’s largest oncology hospital, the median age of patients who received platinum doublet chemotherapy was lower than the respective full populations (LS-SCLC: 64 years

![Figure 4. Forest plot of HRs of factors that can influence OS or LCSS in patients ≤ or >80. (A) HRs of factors influencing OS in patients ≤80 years old; (B) HRs of factors influencing LCSS in patients ≤80 years old; (C) HRs of factors influencing OS in patients >80 years old; (D) HRs of factors influencing LCSS in patients >80 years old. Abbreviations: HRs: Hazard ratios; OS: Overall survival; LCSS: Lung cancer-specific survival.]
Our study investigated a large cohort of 57,460 SCLC patients from real world data. Although many other studies have also addressed the effect of chemotherapy on the survival prognosis of SCLC patients [16, 17, 19, 20, 22], they were mostly based on limited sample sizes, and there have been few investigations on the prognosis of different age subgroups. Given aging of the population, patients older than 80 years will account for a greater proportion. Therefore, the results of our study may provide useful information for clinical oncologists and elderly patients in choosing treatment options. Additionally, we also analyzed the impact of other factors on patient survival, which may also guide patient management. However, several deficiencies in our research need to be mentioned. Despite the large sample size of the SEER, the smoking status and PS are not available in the database, knowing that the former is strongly associated to SCLC [30, 31], and the latter has also proved to be related to the prognosis of SCLC patients [32]. It is possible that patients who smoke or have a low PS score were included in the non-chemotherapy group, which may induce biases in the results. Concurrently, reasons for not choosing chemotherapy, or potential factors affecting the receipt of chemotherapy, such as the nutritional status, cognitive function and geriatric syndrome, are not included in the SEER, either. These limitations need to be refined in future validation using data from hospitals, or randomized controlled trials.

CONCLUSIONS

To conclude, chemotherapy is a beneficial choice for patients with SCLC over 80 years old, although elderly patients are less likely to receive chemotherapy. Age should not be the main basis for deciding whether to receive chemotherapy or not.

Abbreviations

SCLC: Small cell cancer; NSCLC: Non-small cell cancer; SEER: Surveillance, Epidemiology, and End Results registry; OS: Overall survival; LCSS: Lung cancer-specific survival; HRs: Hazard ratios; CI: Confidence interval; PS: Performance status.

AUTHOR CONTRIBUTIONS

H.R., A.M., and S.Z. designed the study; H.R. and S.X. were responsible for collection and assembly of data; S.X. revised it critically for important intellectual content. All authors contributed to data analysis and interpretation have reviewed the final version.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest related to this study.

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