



Development and validation of a prognostic predictive model of pulmonary spindle cell carcinoma from the surveillance, epidemiology and end results database

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Background: Pulmonary spindle cell carcinoma (PSCC) is a rare type of non-small cell lung cancer (NSCLC). The prognostic influential factors and therapeutic methods of PSCC are unclear, for there are only some case reports or small samples' analysis. This study aims to find prognosis related factors of PSCC, develop and validate a nomogram to predict their survival probability.

Methods: The Surveillance, Epidemiology, and End Results (SEER) 18 Registries database (2000–2018) was searched to study PSCC. According to diagnosed time, data was divided into primary cohort (2000–2015) and validation cohort (2016–2018), both followed until December 31 2018. Chosen by Least Absolute Shrinkage and Selection Operator (LASSO) regression, age, sex, stage, surgery, chemotherapy, N, size and history of malignancy were taken out as predictive variables. The primary cohort was used to develop a nomogram to predict 1-, 3- and 5-year overall survival (OS) probability, and be validated by the validation cohort using concordance index (C-index) and calibration curves. Both cohorts were used to conduct a Cox regression to find the influential factors on OS of PSCC.

Results: The nomogram shows a good concordance and discrimination on the prediction of OS, both internal (n=457 and C-index is 0.79) and external validation (n=100 and C-index is 0.76). The median survival time of PSCC is 4 months, with 20.1% OS possibility in 5 years. Multivariate analysis identified patients of older age [hazard ratio (HR), 1.02; 95% confidence interval (CI): 1.01–1.04], larger size of neoplasm (HR, 1.01; 95% CI: 1.01–1.01), M1 (HR, 2.96; 95% CI: 2.17–4.04), N2 (HR, 2.55; 95% CI: 1.81–3.59) or N3 (HR, 2.99; 95% CI: 1.58–5.66), regional stages (HR, 2.11; 95% CI: 1.29–3.44) and distant stages (HR, 6.17; 95% CI: 3.83–9.94) had a lower OS possibility, while surgery (HR, 0.39; 95% CI: 0.28–0.53) and history of malignancy (HR, 0.68; 95% CI: 0.48–0.98) was protective factors for PSCC. PSCC survived longer with surgery performed instead of chemotherapy or radiotherapy.

Conclusions: Patients of PSCC have a poor prognosis, and using the nomogram developed by this study can predict their 1-, 3- and 5-year OS probability. Surgery is a better choice for PSCC and more studies are necessary to find potential treatment like targeted therapy, programmed death-1 (PD-1) and programmed death ligand 1 (PD-L1).

Keywords: Pulmonary spindle cell carcinoma (PSCC); pulmonary sarcomatoid carcinoma (PSC); prognosis; Surveillance, Epidemiology, and End Results (SEER)

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Introduction

Pulmonary spindle cell carcinoma (PSCC) is a rare type of non-small cell lung cancer (NSCLC). According to the World Health Organization (WHO) classification of lung cancer, PSCC is a subtype of pulmonary sarcomatoid carcinoma (PSC). PSC usually has a poor prognosis and includes five subtypes: pleomorphic carcinoma, pulmonary blastoma, giant cell carcinoma, carcinosarcoma, and spindle cell carcinoma (1,2). Generally, PSC has similar imaging features to other lung cancers (3,4). Hence, the diagnosis of PSC relies on immunohistochemistry even molecular abnormality testing from resected specimen, and only a small number of cytological or biopsy specimens can fulfill the need of diagnosis (1,5,6).

PSCC consists of an almost pure population of epithelial spindle cells, with no differentiated carcinomatous elements, and the prevalence of PSCC is low, taking a count of about <1% in all kinds of lung cancer (1,2). The overall survival (OS) of PSC is very short [median OS: 9 months, 95% confidence interval (CI): 7–12 months], and the median survival time of PSCC has not been reported. According to case reports now available, PSCC is a highly malignant tumor with poor prognosis, even in early stage (3,7,8). Qi *et al* pointed out that most PSCC patients survived less than 24 months after diagnosed; Similarly, after summarizing previous reports, Kida *et al* mentioned gross PSCC patients had died or relapsed within 1 year, even they therapeutic (3,7-9). So, a study of enough samples, uncovering the prognostic factors of PSCC, is lacked but needed. And until now, there is not a predictive model reliable yet.

As existing studies have come to an agreement on the poor prognosis of PSCC, the choices of its cure are still unclear. Treatment of PSC is usually chosen from surgery, chemotherapy and radiotherapy, while some targeted drugs, programmed death-1 (PD-1) and programmed death ligand 1 (PD-L1) were potential therapies (5,10-14). And previous studies tended to use surgery or chemotherapy treating PSC but still with much dispute (4,15). Parallely, without enough studies on the PSCC, the therapy of it was decided often referring to PSC or a common lung cancer though its high malignance (16).

Due to the rarity of PSCC, there were few studies except some case reports, small samples' analysis or exploration on PSC (8,9,16-21). Retrospective or prospective studies with enough samples are necessary, applying survival analysis to reveal the prognostic factors and to provide treatment references of PSCC. And as we talked, there is

still much disagreement on if PSCC should be considered and treated as PSC (4,16). Therefore, to establish a retrospective cohort study on PSCC of huge samples, we searched the Surveillance, Epidemiology, and End Results (SEER) database of the National Cancer Institute (NCI) to conduct a survival analysis, aiming to develop and validate a prognostic model and explore the effective factors related to survival of PSCC. We present the following article in accordance with the TRIPOD reporting checklist (available at <https://tcr.amegroups.com/article/view/10.21037/tcr-22-427/rc>).

Methods

Data source and population

We browsed the NCI's SEER, using SEER*Stat (8.3.9.2). The SEER program registries routinely collect demographic and clinic data on patients, and the mortality data reported by SEER are provided by the National Center for Health Statistics. Using the 18 Registries database (2000–2018) which covers approximately 27.8% of the U.S. population, we set search option “*site and morphology site recode ICD-O-3/WHO2008*” as “*lung and bronchus*” and “*site and morphology ICD-O-3 Hist/behav*” as “*8032/3: spindle cell carcinoma*” to established a retrospective cohort. There are 833 patients diagnosed with PSCC in total. According to the diagnosed year, patients are allocated to the primary cohort (diagnosed in 2000–2015) and the validation cohort (diagnosed in 2016–2018). To compare the OS possibilities of PSC, we searched the same database changing “*site and morphology ICD-O-3 Hist/behav*” as “*8032/3: spindle cell carcinoma*”, “*8022/3: Pleomorphic carcinoma*”, “*8031/3: Giant cell carcinoma*”, “*8972/3: Pulmonary blastoma*” or “*8980/3: Carcinosarcoma, NOS*”. All 2,764 patients with PSC were included (Figure 1).

Cut-off date of patients above was December 31 2018, according to the SEER's manual (submitted in November 2020).

Potential predictive variables

Age, sex, race, site, grade, stage, radiotherapy, surgery, chemotherapy, lymphatic metastasis, size, distant metastasis, and history of malignancy were the potential predictive variables. Age and tumor size were treated as categorical variables when presented in the baseline data (Table 1) but in subsequent statistical analysis, they were regarded as

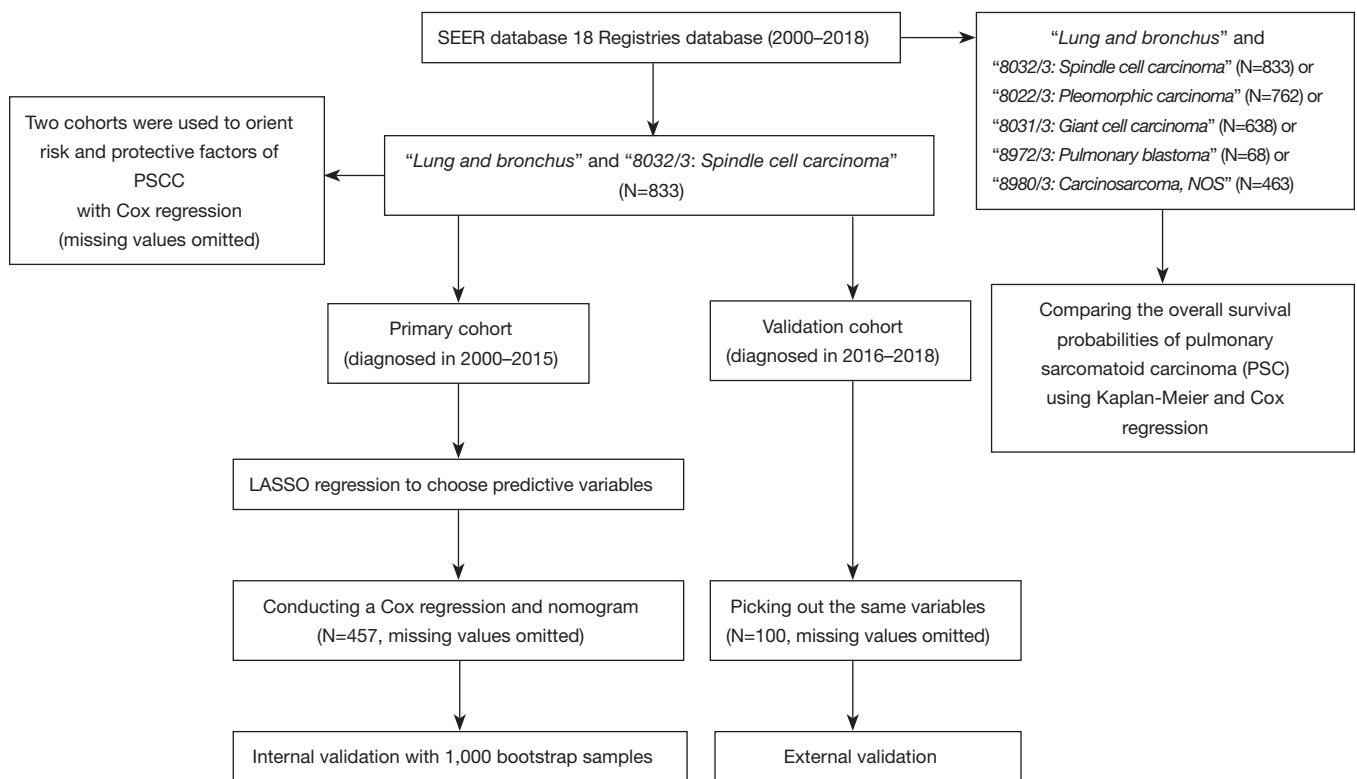


Figure 1 Flow chart of nomogram developed and comparing the overall survival probabilities of pulmonary sarcomatoid carcinoma. SEER, The Surveillance, Epidemiology, and End Results; PSCC, pulmonary spindle cell carcinoma; LASSO, Least Absolute Shrinkage and Selection Operator.

continuous variables.

Some variables mentioned above were not directly recorded in an univariable of SEER, so we have combined and adjusted them referring to the eighth edition American Joint Committee on Cancer (AJCC) stage. And considering the variance of 6th, 7th or 8th AJCC stage and lack of available data to adjust the TNM stage as accordant one, we chose the size of the tumor and stage by SEER (localized/regional/distant, Table S1) to act as potential predictive variables instead of T or stage by AJCC. The N and M by AJCC was reserved to describe a tumor’s lymph node and distant metastasis, which were regarded as potential predictive variables.

RX Summ—Surg/Rad Seq and *Radiation Recode* in SEER were used as references for radiotherapy. If either of the two variables recorded radiotherapy information or radiotherapy mode, it was defined as having received radiotherapy. Otherwise, it was considered as not receiving radiotherapy. *Reason no cancer-directed surgery* in SEER was used to judge if a patient acquired surgery. Tumor size referred to these

SEER variables: *CS tumor size (2004–2015)*, *tumor size Summary (2016+)*, and *EOD 10-size (1988–2003)*. If a record contained approximately data as reminding less than 3 cm (such as in *CS tumor Size 2004–2015* variable of SEER), the tumor size was still treated as 3 cm and other analogous size records were treated in the same way. Regional lymph nodes metastasis (N) referred to *Derived EOD 2018 N (2018+)*, *Derived AJCC N 6TH Ed (2004–2015)*, *EOD 10-Nodes (1988–2003)* and *Derived SEER Combined N (2016–2017)*. Distant metastasis (M) was judged referring to *Derived EOD 2018 M (2018+)*, *Derived AJCC M 7th Ed (2010–2015)*, *Derived SEER Combined M (2016–2017)*, *Derived AJCC M 6th Ed (2004–2015)* and *EOD 10-extent (1988–2003)* variables. Stage was derived from the *Summary stage 2000 (1998–2017)* and *Combined Summary Stage (2004+)* variables, which was divided into three categories: localized, regional and distant by SEER (the definition of the three categories shown in Table S1).

In the data, we noticed an extreme value of tumor size 88 cm (a 69-year-old male diagnosed in 2014), which may

Table 1 Demographics and clinical characteristic of 833 patients

Variables	Primary cohort [2000–2015] (N=693), N (%)	Validation cohort [2016–2018] (N=140), N (%)
Age, years		
20–24	3 (0.43)	1 (0.71)
25–29	1 (0.14)	1 (0.71)
35–39	4 (0.58)	0 (0)
40–44	5 (0.72)	0 (0)
45–49	16 (2.31)	1 (0.71)
50–54	21 (3.03)	5 (3.57)
55–59	42 (6.06)	12 (8.57)
60–64	82 (11.83)	14 (10.00)
65–69	81 (11.69)	18 (12.86)
70–74	126 (18.18)	24 (17.14)
75–79	123 (17.75)	19 (13.57)
80–84	113 (16.31)	22 (15.71)
85+	76 (10.97)	23 (16.43)
Sex		
Female	302 (43.58)	52 (37.14)
Male	391 (56.42)	88 (62.86)
Race		
White	603 (87.01)	112 (80.00)
Black	53 (7.65)	12 (8.57)
Other	34 (4.91)	15 (10.71)
Unknown	3 (0.43)	1 (0.71)
Marital status		
Single (never married)	71 (10.25)	20 (14.29)
Married (including common law)	356 (51.37)	74 (52.86)
Separated	7 (1.01)	0 (0)
Divorced	77 (11.11)	11 (7.86)
Widowed	142 (20.49)	31 (22.14)
Unknown	40 (5.77)	4 (2.86)

Table 1 (continued)**Table 1** (continued)

Variables	Primary cohort [2000–2015] (N=693), N (%)	Validation cohort [2016–2018] (N=140), N (%)
Site		
Upper lobe	308 (44.44)	57 (40.71)
Middle lobe	42 (6.06)	10 (7.14)
Lower lobe	197 (28.43)	41 (29.29)
Main bronchus	20 (2.89)	3 (2.14)
Overlapping lesion of lung	10 (1.44)	2 (1.43)
Unknown	116 (16.74)	27 (19.29)
Size, mm		
≤10	15 (2.16)	4 (2.86)
≤20	52 (7.50)	11 (7.86)
≤30	56 (8.08)	9 (6.43)
≤40	56 (8.08)	17 (12.14)
≤50	74 (10.68)	12 (8.57)
≤60	61 (8.80)	11 (7.86)
≤70	49 (7.07)	11 (7.86)
>70	150 (21.65)	34 (24.29)
Unknown	180 (25.97)	31 (22.14)
History of malignancy		
No	512 (73.88)	95 (67.86)
Yes	181 (26.12)	45 (32.14)
N		
N0	314 (45.31)	73 (52.14)
N1	48 (6.93)	8 (5.71)
N2	185 (26.70)	32 (22.86)
N3	38 (5.48)	9 (6.43)
Unknown	108 (15.58)	18 (12.86)
M		
M0	328 (47.33)	55 (39.29)
M1	339 (48.92)	83 (59.29)
Unknown	26 (3.75)	2 (1.43)

Table 1 (continued)

Table 1 (continued)

Variables	Primary cohort [2000–2015] (N=693), N (%)	Validation cohort [2016–2018] (N=140), N (%)
Grade		
Well differentiated; grade I	9 (1.30)	3 (2.14)
Moderately differentiated; grade II	5 (0.72)	0 (0)
Poorly differentiated; grade III	252 (36.36)	27 (19.29)
Undifferentiated; anaplastic; grade IV	61 (8.80)	7 (5.00)
Unknown	366 (52.81)	103 (73.57)
Stage		
Localized	119 (17.17)	26 (18.57)
Regional	154 (22.22)	23 (16.43)
Distant	394 (56.85)	86 (61.43)
Unknown	26 (3.75)	5 (3.57)
Radiotherapy		
No	471 (67.97)	102 (72.86)
Yes	222 (32.03)	38 (27.14)
Surgery		
No	493 (71.14)	116 (82.86)
Yes	193 (27.85)	23 (16.43)
Unknown	7 (1.01)	1 (0.71)
Chemotherapy		
No	476 (68.69)	101 (72.14)
Yes	217 (31.31)	39 (27.86)
Survival time		
Median [IQR]	4 [1, 16]	3 [1, 10]
Range	1–218	1–32

Follow-up cut-off date above was December 31 2018. IQR, interquartile range.

have been misremembered, so its diameter was regarded as a missing value. Survival time less than a month was still counted as 1 month.

The adjusted variables and patients' demographics and clinical characteristics are shown in *Table 1*.

Variable selection

We used the Least Absolute Shrinkage and Selection Operator (LASSO) regression to minimize the potential collinearity of variables and select the final predictive variables. The crucial point of LASSO regression is to designate the appropriate λ value. Using data from primary cohort, we made 5-fold cross validation to determine λ value (the minimum one *Figure S1*). Based on the λ value, we established a Cox regression and chose variables with non-zero coefficients as the predictive variables. In this way, age, sex, stage, surgery, chemotherapy, N, size and history of malignancy were finally chosen to be predictive variables. All above data were only used from the primary cohort (diagnosed in 2000–2015).

Study design and statistical analysis

In this retrospective cohort study, Kaplan-Meier curve was used to compare the survival probabilities, with log-rank test calculating P value. And Cox proportional hazard regression was applied to count the hazard ratio (HR). Chosen by LASSO regression, age, sex, stage, surgery, chemotherapy, N, size and history of malignancy were the predictive variables. These above variables were taken out from the primary cohort and the validation cohort respectively, with missing values omitted. Finally, 457 samples were collected from the primary cohort and 100 samples from the validation cohort (*Figure 1*). We used the data from the primary cohort to perform a Cox proportional hazard regression and establish a nomogram to predict the OS probability of a PSCC patient in 1-, 3- and 5-year. To measure the nomogram's performance, we implemented internal and external validation. For internal validation, we used 1,000 bootstrap samples to estimate the concordance index (C-index) and plotted calibration curves to evaluate the deviation between predicted probability and actual probability. The C-index close to 1.0 indicates a perfect prediction, with bigger than 0.7 or 0.8 thought to be a potentially good one, while a 0.5 or smaller one tends to randomly guess. To avoid overfitting, the validation cohort was used to conduct external validation by calculating C-index and plot a 1-year calibration curve. As the cut-off date was December 31 2018, we validated the nomogram just in 1 year with the validation cohort. All potential variables were finally employed to draw Kaplan-Meier curve and to conduct a Cox proportional hazard regression to find

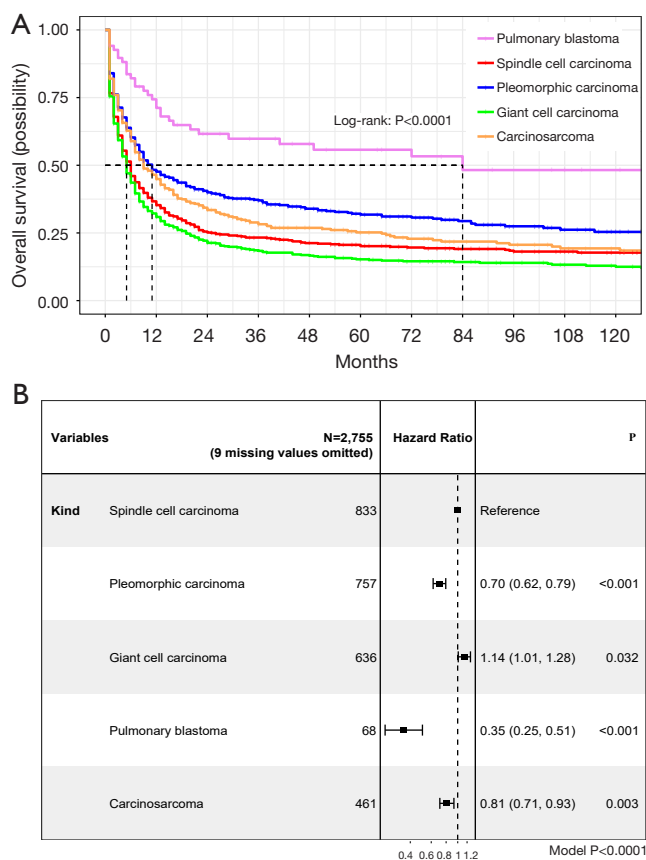


Figure 2 The survival analysis of PSC. (A) The Kaplan-Meier plot shows different OS of PSC, $P < 0.0001$. (B) The forest plot shows hazard ratio among PSC. OS, overall survival; PSC, pulmonary sarcomatoid carcinoma.

Table 2 The OS time of PSCC patients from both cohorts

Variables	Median [IQR] (months)	Range (months)
All (N=833)	4 [1, 14]	1–218
Surgery (N=216)	18 [5, 72]	1–218
Chemotherapy (N=256)	7 [3, 17]	1–218
Radiotherapy (N=260)	5 [2, 14]	1–218

OS, overall survival; PSCC, pulmonary spindle cell carcinoma; IQR, interquartile range.

the risk and protective factors of PSCC. $P < 0.05$ of two-sided was considered statistically significant and the analysis was performed in R software (4.1.2, <https://www.r-project.org/>) using these packages: *epiDisplay*, *glmnet*, *rms*, *survival*, *pec* and *ezcox*.

Ethical consideration

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The authors signed the Data-Use Agreement for the 1975–2018 SEER Research Data File. This study has been approved by the Ethics Committee of Beijing Chest Hospital affiliated to Capital Medical University (No. LW-2022-001) and individual consent for this retrospective analysis was waived.

Results

Different OS possibilities among PSC

The Kaplan-Meier plot using data from 2,764 patients showed five subtypes of PSC owned different OS ($P < 0.0001$, *Figure 2*). The median OS time of pleomorphic carcinoma patients was 7 months [interquartile range (IQR), 2–27 months; range, 1–203 months]; the median OS time of giant cell carcinoma patients was 4 months (IQR, 1–13 months; range, 1–227 months); the median OS time of pulmonary blastoma patients was 28 months (IQR, 8–106 months; range, 1–226 months); the median OS time of carcinosarcoma patients was 7 months (IQR, 2–24 months; range, 1–219 months); and the median OS of PSCC patients was 4 months (IQR, 1–14 months; range, 1–218 months; *Table 2*, *Table S2*). Cox regression indicated compared to PSCC, giant cell carcinoma patients had shorter OS (HR, 1.14; 95% CI: 1.01–1.28) while pleomorphic carcinoma (HR, 0.70; 95% CI: 0.62–0.79), pulmonary blastoma (HR, 0.35; 95% CI: 0.25–0.51) and carcinosarcoma (HR, 0.81; 95% CI: 0.71–0.93) patients had longer OS (*Figure 2*).

Development and validation of nomogram

Using the primary cohort, we established a nomogram to predict PSCC patients OS probability in 1-, 3- and 5-year (*Figure 3*). The C-index of nomogram in the primary cohort was 0.79 (95% CI: 0.76–0.82). With 1,000 bootstrap samples, the C-index in 1-, 2-, 3-, 4- and 5-year were 0.77, 0.76, 0.76, 0.76, 0.76, whose trend was plotted in *Figure 4*. Three calibration curves (*Figure 5A–5C*) for predicting the 1-, 3- and 5-year OS probability were plotted, indicating a good discrimination of the nomogram in internal validation. The C-index in the validation cohort was 0.76 (1 year OS probability) and the calibration curve showed a good discrimination (*Figure 5D*).

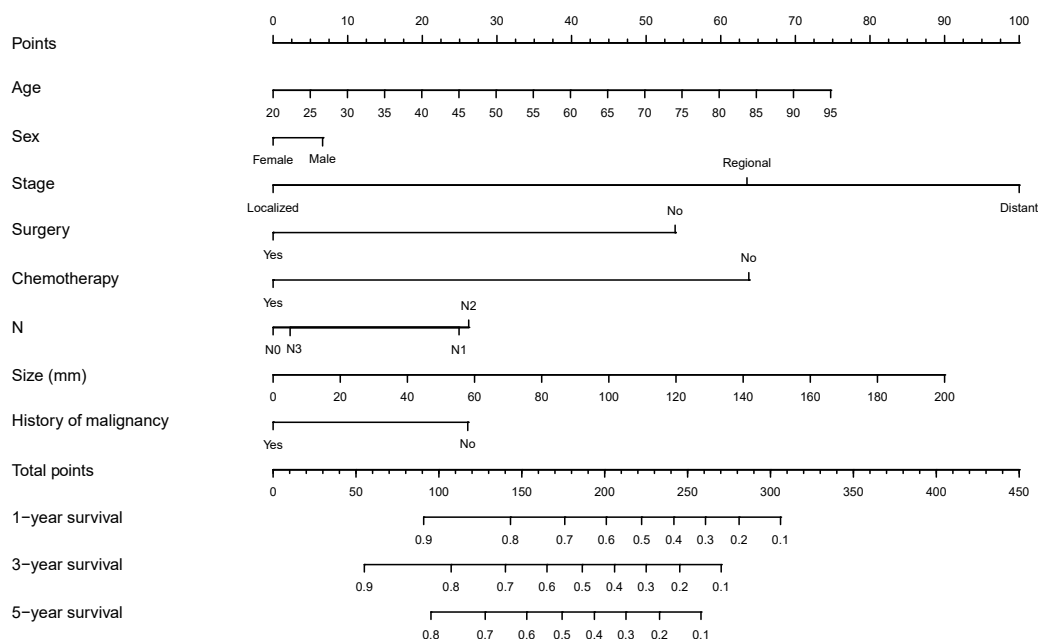


Figure 3 Nomogram to predict the 1-, 3- and 5-year OS of patients with PSCC. OS, overall survival; PSCC, pulmonary spindle cell carcinoma.

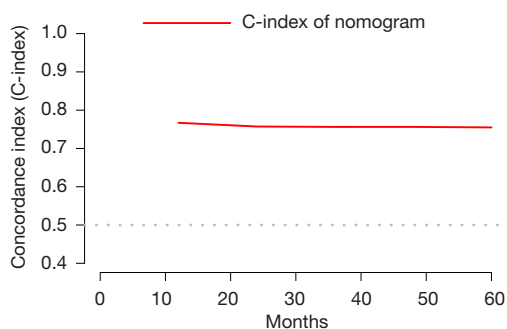


Figure 4 C-index trend of nomogram with 1,000 bootstrap samples from primary cohort. C-index, concordance index.

Survival analysis

Age, sex, race, site, grade, stage, radiotherapy, surgery, chemotherapy, lymphatic metastasis, size, distant metastasis, and history of malignancy were used to conduct a multivariate Cox proportional hazard regression using all primary and validation cohort data (N=247, with missing values of above variables omitted). Patients of older age (HR, 1.02; 95% CI: 1.01–1.04), larger size of neoplasm (HR, 1.01; 95% CI: 1.01–1.01), M1 distant metastasis (HR, 2.96; 95% CI: 2.17–4.04), N2 (HR, 2.55; 95% CI: 1.81–3.59) or N3 (HR, 2.99; 95% CI: 1.58–5.66), regional stages (HR,

2.11; 95% CI: 1.29–3.44) and distant stages (HR, 6.17; 95% CI: 3.83–9.94) had a lower OS possibility, while surgery (HR, 0.39; 95% CI: 0.28–0.53) and history of malignancy (HR, 0.68; 95% CI: 0.48–0.98) were protective factors for PSCC (Figure 6). The median OS of PSCC patients was 4 months (IQR, 1–14 months; range, 1–218 months, Table 2), and the Kaplan-Meier cure was plotted in Figure 7A. Different treatments might produce different therapeutic effects, surgery indicating a longer OS (Figure 7B–7D). The median OS of received surgery patients was 18 (IQR, 5–72 months; range, 1–218 months). The median OS of received chemotherapy patients was 7 (IQR, 3–17 months; range, 1–218 months). And the median OS of received radiotherapy patients was 5 (IQR, 2–14 months; range, 1–218 months) (Table 2). The OS probability of 1-, 2-, 3-, 4- and 5-year was 35.3% (95% CI: 32.0–38.9%), 25.2% (95% CI: 22.1–28.7%), 23.0% (estimated by life table, Table S3), 21.0% (estimated by life table), 20.1% (95% CI: 17.2–23.6%) (Table 3).

Discussion

We first discuss the OS time, influential factors, develop and validate a predictive nomogram of PSCC patients using large samples’ data. By contrasting five subtypes from

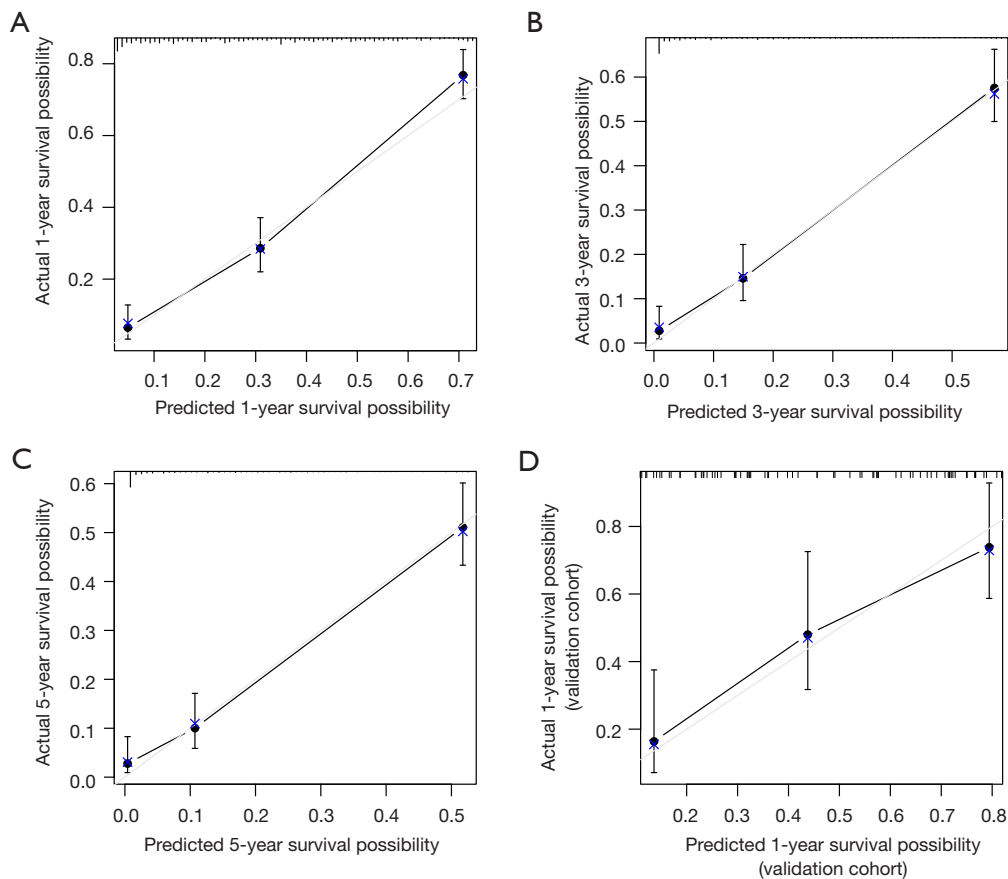


Figure 5 Calibration curves both primary cohort and validation cohorts. (A) Calibration curve of nomogram of 1-year OS in PSCC primary cohort. (B) Calibration curve of nomogram of 3-year OS in PSCC primary cohort. (C) Calibration curve of nomogram of 5-year OS in PSCC primary cohort. (D) Calibration curve of nomogram of 1-year OS in PSCC validation cohort. OS, overall survival; PSCC, pulmonary spindle cell carcinoma.

2,764 patients' data, we found the OS differed in PSC. Then we analyzed 833 PSCC patients and found older age, larger size, M1, N2, N3, regional stages, and distant stages meant a short OS time. Surgery was an effective treatment of PSCC instead of chemotherapy or radiotherapy. Radiotherapy had no effect on PSCC while patients treated with chemotherapy underwent a shorter OS in the long terms. The nomogram developed by us can offer an OS prediction of PSCC patients.

WHO classified PSC into five subtypes: pleomorphic carcinoma, pulmonary blastoma, giant cell carcinoma, carcinosarcoma, and spindle cell carcinoma (1). As a rare NSCLC, there were few studies on PSC and much fewer on PSCC. For there are few papers discussing the prognosis and treatment of PSCC, we compared our study with some PSCs.

Ung *et al.* reported the median size of PSC was about 6 cm, which is similar to our observation (the median of size 52.50 mm) (22). The 5-year OS in our observation is 20.1% (95% CI: 17.2–23.6%), which is similar to other reports (4,23,24). But there are studies reporting different OS, the deviation might result from the difference between PSCC and PSC (2,25). For PSC, smoking, N3, T3 and T4 is dangerous factors and surgery (median OS time 16.4 months; our observation was 18 months) has significant impact on survival (2,22,24), and the similar consequence was revealed by our study. But Ung *et al.* considered age was not a significant factor, which is different from our analysis. The imparity might result from the age range and the number of samples: they analyzed 93 patients whose ages' median is 63 years (range, 40–85 years), and we observed 833 patients whose ages median is 73 years

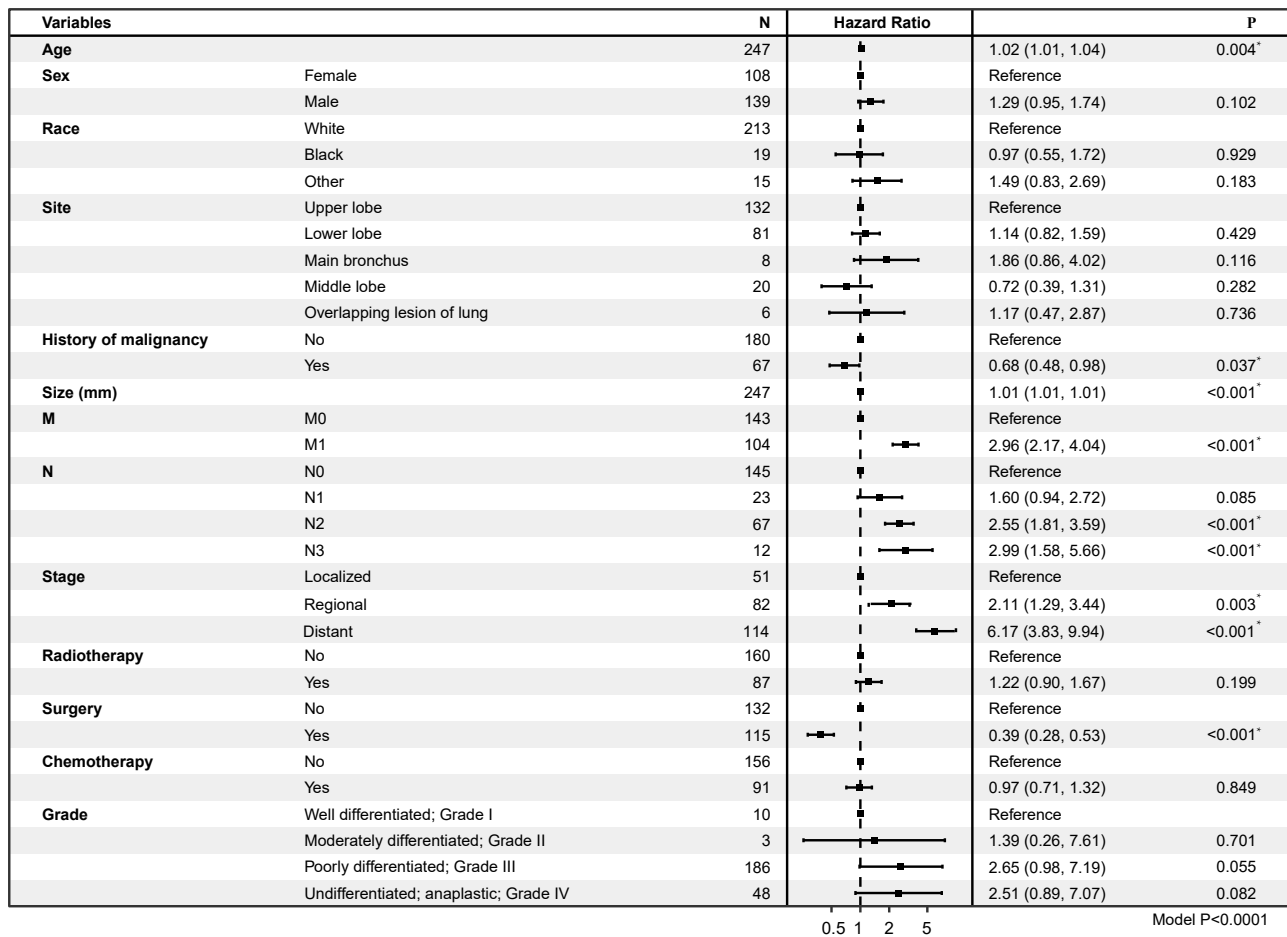


Figure 6 Multivariate analysis of pulmonary spindle cell carcinoma with Cox regression. *, P<0.05.

(range, 21–96 years) (22). But they did agree chemotherapy has no effective influence on survival either. Usually, PSC have a high resistance to chemotherapy whose stand point is the same with ours, but others reported a platinum-based combination chemotherapy might have influence on OS (4,15,22).

Domblides *et al.* indicated after treated with immune checkpoint inhibitors (ICIs) such like nivolumab (86.5% of cases), the objective response rate of 37 sarcomatoid carcinoma patients was 40.5% and disease control rate was 64.8% regardless of PD-L1 status, while the objective response rate of patients with PD-L1⁺ was 58.8% (26). Jiao *et al.* found received treatment with PD-1 inhibitor toripalimab, the tumor of an advanced PSC patient shrank and the response evaluation was partial response (PR) (27). As PSCs and pleomorphic carcinoma patients usually highly expressed PD-L1 (53–90%), immunotherapy might release huge potential in the therapy of PSC (11,28,29).

Above all, PSC patients have a poor prognosis and there are only limited therapy options. Surgery might be the better one on the OS time instead of chemotherapy or radiotherapy. Some studies argued C-MET inhibitor, targeted drugs, PD-1 or PD-L1 might be the potential therapy of PSC (5,10-14,30,31), but more studies related still needed.

This retrospective study is conducted using data from SEER database, which might bring out some selection bias and information bias. Patients of PSC are usually smoking but there is no more information about smoke status in SEER database (4,22,23). The sample size of this study is modest.

Conclusions

PSCC patients have a poor prognosis, using the nomogram developed by this study can predict their 1-, 3- and 5-year

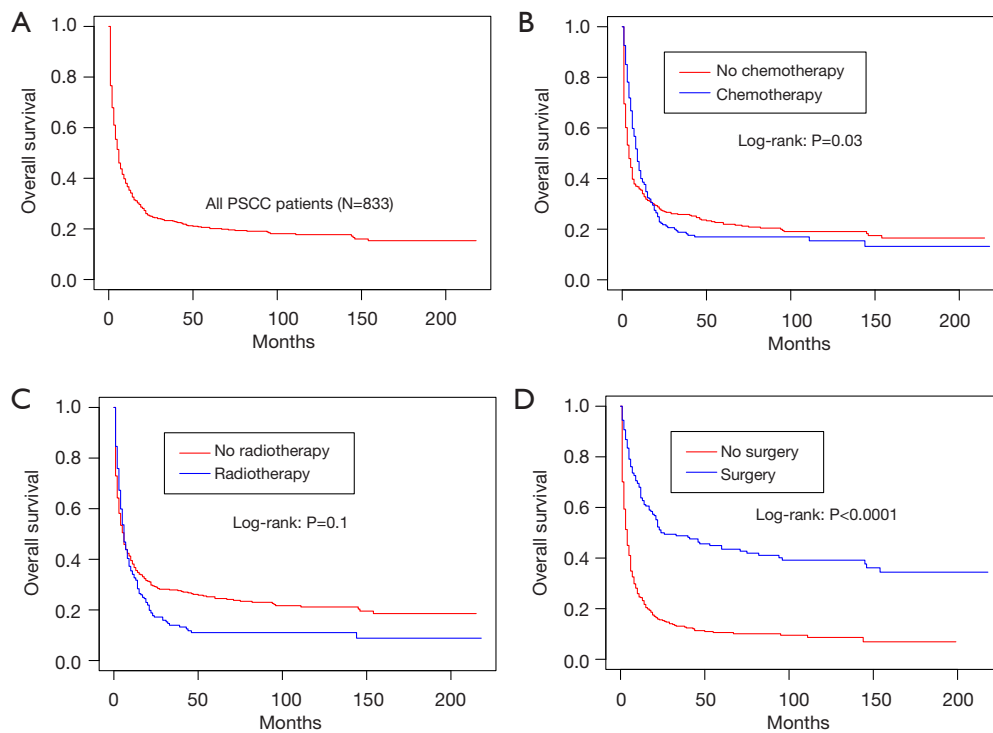


Figure 7 K-M curves of PSCC with or without therapies. (A) K-M curve of all PSCC patients. (B) K-M curve of PSCC patients based on whether received chemotherapy or not. (C) K-M curve of PSCC patients based on whether received radiotherapy or not. (D) K-M curve of PSCC patients based on whether received surgery or not. K-M curve, Kaplan-Meier curve; PSCC, pulmonary spindle cell carcinoma.

Table 3 The OS probability of PSCC patients from both cohorts

Time	Probability (%)	95% CI (%)
1-year	35.3	32.0–38.9
2-year	25.2	22.1–28.7
3-year	23.0	Estimated by life table, Table S3
4-year	21.0	Estimated by life table, Table S3
5-year	20.1	17.2–23.6

OS, overall survival; PSCC, pulmonary spindle cell carcinoma; CI, confidence interval.

OS probability. The nomogram shows a good concordance and discrimination on both the primary and validation cohorts. Surgery is a better option for PSCC and more studies are necessary to find potential treatments like targeted therapy, PD-1 or PD-L1.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The authors signed the Data-Use

Agreement for the 1975–2018 SEER Research Data File. This study has been approved by the Ethics Committee of Beijing Chest Hospital affiliated to Capital Medical University (No. LW-2022-001) and individual consent for this retrospective analysis was waived.

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Table S1 The definition of tumors' stage by SEER

Stage	Invasion area
Localized	Adjacent ipsilateral lobe
	Confined to hilus
	Main stem bronchus (without involvement of the carina), including extension from other part of lung
	Minimally invasive adenocarcinoma
	Superficial tumor with invasive component limited to bronchial wall, with or without proximal extension to main stem bronchus
Regional	Atelectasis/obstructive pneumonitis
	Blood vessel(s): aorta, azygos vein, pulmonary artery or vein superior vena cava
	Brachial plexus
	Carina from lung
	Chest wall (thoracic wall)
	Compression of esophagus or trachea not specified as direct extension
	Diaphragm
	Esophagus
	Mediastinum
	Nerve(s): cervical sympathetic (Horner's syndrome), recurrent laryngeal (vocal cord paralysis), vagus, phrenic nerve
	Pancoast tumor (superior sulcus syndrome)
	Visceral pleura invasion (PL1, PL2 or PL3)
	Pericardium
	Pulmonary ligament
	Separate tumor nodule(s) in the same lobe as the primary
	Trachea
	Lymph node(s): N1 or N2
Distant	Adjacent rib
	Contralateral lung
	Contralateral main stem bronchus
	Heart
	Inferior vena cava
	Neural foramina
	Pericardial nodules or pleural effusion (malignant) (ipsilateral, contralateral, bilateral)
	Pleural tumor foci or nodules on ipsilateral lung (separate from direct extension) or contralateral lung
	Skeletal muscle, skin of chest, sternum, vertebra(e) (vertebral body) or another distant metastasis
	Lymph node: N3

SEER, The Surveillance, Epidemiology, and End Results database.

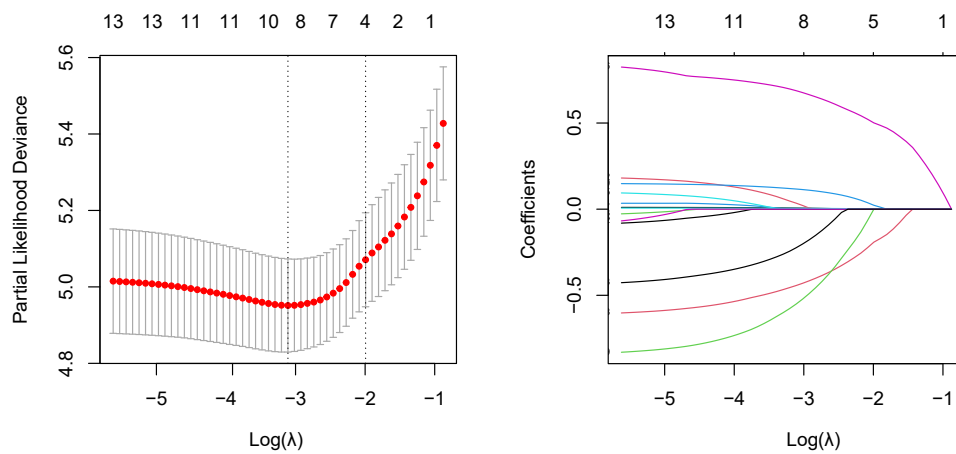


Figure S1 The LASSO regression result used to decide λ value. LASSO, Least Absolute Shrinkage and Selection Operator.

Table S2 The OS time of the other four subtypes of PSC patients

Subtypes	Median [IQR] (months)	Range (months)
Pleomorphic carcinoma (N=757)	7 [2, 27]	1–203
Giant cell carcinoma (N=636)	4 [1, 13]	1–227
Pulmonary blastoma (N=68)	28 [8, 106]	1–226
Carcinosarcoma (N=461)	7 [2, 24]	1–219

OS, overall survival; PSC, pulmonary sarcomatoid carcinoma; IQR, interquartile range.

Table S3 Life table of pulmonary spindle cell carcinoma (n=833)

Time (months)	N.Risk	N.Event	Survival probability	Lower 95% CI	Upper 95% CI
1	833	195	76.6%	73.8%	79.5%
2	598	68	67.9%	64.7%	71.2%
3	512	52	61.0%	57.7%	64.5%
4	447	41	55.4%	52.0%	59.0%
5	401	29	51.4%	48.0%	55.0%
6	364	38	46.0%	42.6%	49.7%
7	322	16	43.7%	40.3%	47.4%
8	301	15	41.6%	38.2%	45.2%
9	283	12	39.8%	36.4%	43.5%
10	269	12	38.0%	34.7%	41.7%
11	253	9	36.7%	33.3%	40.3%
12	237	9	35.3%	32.0%	38.9%
13	226	7	34.2%	30.9%	37.8%
14	212	10	32.6%	29.3%	36.2%
15	200	7	31.4%	28.2%	35.0%
16	193	2	31.1%	27.9%	34.7%
17	190	5	30.3%	27.1%	33.9%
18	182	4	29.6%	26.4%	33.2%
19	176	6	28.6%	25.4%	32.2%
20	170	3	28.1%	24.9%	31.7%
21	166	5	27.3%	24.1%	30.8%
22	157	7	26.0%	22.9%	29.6%
23	146	3	25.5%	22.4%	29.0%
24	143	2	25.2%	22.1%	28.7%
25	141	1	25.0%	21.9%	28.5%
26	138	2	24.6%	21.6%	28.1%
27	134	1	24.4%	21.4%	27.9%
29	130	2	24.1%	21.0%	27.5%
31	128	1	23.9%	20.8%	27.3%
32	127	1	23.7%	20.6%	27.2%
33	123	2	23.3%	20.3%	26.8%
38	118	1	23.1%	20.1%	26.6%
39	116	1	22.9%	19.9%	26.4%
40	114	1	22.7%	19.7%	26.2%
41	112	1	22.5%	19.5%	26.0%
43	109	1	22.3%	19.3%	25.7%
44	108	2	21.9%	18.9%	25.3%
46	106	2	21.5%	18.5%	24.9%
47	102	1	21.2%	18.3%	24.7%
50	99	1	21.0%	18.1%	24.5%
53	98	1	20.8%	17.9%	24.3%
55	93	1	20.6%	17.7%	24.0%
60	87	2	20.1%	17.2%	23.6%
67	80	1	19.9%	16.9%	23.3%
71	77	1	19.6%	16.7%	23.1%
75	75	1	19.4%	16.4%	22.8%
82	69	1	19.1%	16.2%	22.5%
94	60	1	18.8%	15.8%	22.2%
95	59	1	18.4%	15.5%	21.9%
96	58	1	18.1%	15.2%	21.6%
111	47	1	17.7%	14.8%	21.2%
144	31	1	17.2%	14.2%	20.8%
145	30	1	16.6%	13.5%	20.3%
146	29	1	16.0%	12.9%	19.8%
154	24	1	15.3%	12.2%	19.3%

CI, confidence interval; N.Risk, the number of people at risk; N.Event, the number of observed events.