The Independent Prognostic Effect of Marital Status On Non-Small Cell Lung Cancer Patients: A Population-Based Study

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Research

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Abstract

Background

Previous studies had demonstrated that marital status was an independent prognostic factor in multiple cancers. However, the impact of marital status on non-small cell lung cancer (NSCLC) patients was still highly controversial. In our research, we aimed to clarify the exact prognostic effect of marital status on NSCLC patients with a population-based database.

Method

: All NSCLC patients diagnosed between 2010–2016 were selected from the surveillance, epidemiology and end results (SEER) database. To control the confounding effect of related clinicopathological characteristics, propensity score matching (PSM) was conducted between married and unmarried groups. In addition, independent prognostic clinicopathological factors were evaluated via Cox proportional hazard regression. The survival curves of overall survival (OS) and cancer specific survival (CSS) were plotted and compared with Kaplan-Meier method and log-rank test.

Results

In total, 58424 NSCLC patients were enrolled according to the selection criteria. After PSM, 20148 patients were selected into each group for further analysis. The married group consistently demonstrated significantly better OS and CSS compared to unmarried group (OS median survival (95% CI): 25 (24–26) vs. 22 (21–23) months, $P < 0.001$; CSS median survival (95% CI): 31(30–32) vs. 27(26–28) months, $P < 0.001$). Moreover, single patients were associated with the worst OS (median survival (95% CI): 20 (19–22) months) and CSS (median survival (95%CI): 24(23–25) months) among unmarried subgroups. Besides, unmarried patients had a significantly worse prognosis compared to married patients in both univariate and multivariate Cox proportional hazard regressions. Furthermore, married group was associated with better survival in most subgroups.

Conclusion

This study demonstrated that unmarried NSCLC patients were associated with significantly worse OS and CSS compared to married NSCLC patients. Therefore, unmarried patients need not only closer surveillance, but also more social and family support, which may improve patients' adherence and compliance, and eventually improve the survival.

Introduction

Lung cancer is one of the most prevalent and deadly cancers in the world and causes more deaths than breast, prostate, colorectal, and brain cancers combined[1]. Non-small cell lung cancer (NSCLC) is a major histological type of lung cancer and accounts for approximately 85% of all lung cancer cases[2]. Currently, the AJCC TNM stage, which focuses on the anatomic extent of the tumour, is the most important prognostic factor for NSCLC[3]. Moreover, many prognostic factors, such as age, gender, histology and ethnicity, have been demonstrated in previous studies [3, 4].

The divorce rate has been increasing for the last 40 years, especially in the last 20 years. And more and more people marry at a later age or even do not marry at all. According to the study between 1960 and 2010, divorce got more and more common, and people started marrying later than before or not marrying at all [5]. Especially during 1990–2010, the divorce rate has doubled among the elderly, which attracted more and more researchers' attention[6]. Furthermore, marital status has been found to impact the physical condition of patients by influencing the adherence to treatments and the level of economic resources[7, 8]. In recent years, an increasing number of studies have demonstrated that marital status is an

independent prognostic factor in several cancers, such as breast cancer[9, 10], gastric adenocarcinoma[11], pancreatic cancer[12], and primary liver cancer[13]. However, studies from Jatoi et al., Siddiqui et al. and Saito-Nakaya et al. demonstrated that marital status was not prognostic of NSCLC survival[14–16].

The Surveillance, Epidemiology and End Results (SEER) cancer database, which is funded by the National Cancer Institute, provides demographic information and cancer characteristics of several cancers. Approximately 28% of the population in the USA is covered in the SEER database[17]. In this study, we aimed to perform a retrospective study on a large population to identify the prognostic influence of marital status on the survival of patients diagnosed with NSCLC. Meanwhile, propensity score matching methods were used to control confounding factors.

Method

Patient selection

All NSCLC patients diagnosed between 2010-2016 were selected from the SEER database. The specific inclusion criteria were as follows: (1) patients older than 17 years; (2) patients diagnosed between 2010-2016; (3) patients diagnosed with only one primary lung cancer (ICD-O-3 primary site codes: C340-343 and C348-349); (4) patients diagnosed with NSCLC (ICD-O-3 histology code: large cell carcinoma 8012, 8013, and 8014; adenocarcinoma 8140–8147, 8250–8255, 8310, 8333, 8470, 8480, 8481, 8490, 8550, and 8551; squamous cell carcinoma 8052, 8070–8078, and 8083; and adenosquamous cell carcinoma 8560)

The exclusion criteria were as follows: (1) patients diagnosed with autopsy; (2) patients without complete demographic and cancer characteristic information; (3) patients without positive histological or immunophenotyping diagnosis; (4) patients without complete information about therapy; (5) patients without complete survival states and time; and (6) patients with a time of follow-up less than 1 month.

Finally, 58424 patients were selected for our study based on the above selection criteria, and related clinicopathological characteristics including age, gender, race, marital status, histology, grade, TNM stage, therapy, survival state, and survival time were extracted. In addition, overall survival (OS) and cancer-specific survival (CSS) were used as the primary outcomes.

According to the regulation of the SEER database, we obtained permission to access the research data, and the reference number was 14,683-Nov2019. Since the SEER database is publicly available and all patients were deidentified, ethical approval was waived by the ethical committee of our hospital.

Propensity score matching

The marital status of all the patients was dichotomized as married and unmarried, and the latter was further specified into single, separated, divorced, and widowed statuses. To accurately identify the difference of marital status in NSCLC patients, 1:1 propensity score matching (PSM) was conducted to control confounding clinicopathological characteristics between the two groups by using the nearest-neighbour algorithm with a calliper of 0.0001.

Statistics analysis

In our study, the National Cancer Institute's SEER*Stat software (version 8.3.6; SEER 18 Regs Custom Data (with additional treatment fields), November 2018 Sub (1975–2016 varying) database) was used in this study. All related clinicopathological characteristics were presented with descriptive statistics, including number and percentage. Pearson's chi-square tests were used to examine the difference between marital status and other variables. The survival curves of OS and CSS were performed by using the Kaplan-Meier method, and the difference between survival curves was assessed by using log-rank tests. Additionally, we assessed the hazard ratios (HRs) and 95% confidence intervals (CIs) of all the variables of the PS-

matched cohort over OS and CSS via univariable and multivariable Cox proportional hazards regression models with the Enter method.

All statistical tests were 2-sided, and a value of $P < 0.05$ was regarded as a statistically significant difference. Statistical analyses were performed using Statistical Product and Service Solutions (SPSS version 26.0; IBM Corporation, Armonk, NY, USA) and R (version 3.6.3; R Development Core Team, <http://www.r-project.org>).

Results

Clinicopathological characteristics of patients

A total of 58424 patients were enrolled in this study, among which 32025 (54.8%) were married and 26399 (45.2%) were unmarried. Detailed demographic and clinicopathological characteristics are shown in Table 1, and these characteristics are stratified by marital status. Chi-square tests demonstrated significant differences in most of the other variables between different marital status, including gender ($P < 0.001$), race ($P < 0.001$), histology ($P < 0.001$), grade ($P < 0.001$), stage ($P = 0.016$), surgery of primary site ($P < 0.001$), intraoperative lymph node evaluation ($P < 0.001$), and chemotherapy ($P < 0.001$). Additionally, clinicopathological characteristics comparison by the single, separated, divorced and widowed patients within unmarried group were shown in Supplementary Table 1.

Table 1
Clinicopathological characteristics of NSCLC patients in SEER database before propensity score matching

Variable	Total	Married	Unmarried	P value
	(n = 58424)	(n = 32025,54.8%)	(n = 26399,45.2%)	
Gender				P<0.001
Male	30296(51.9%)	19319(60.3%)	10977(41.6%)	
Female	28128(48.1%)	12706(39.7%)	15422(58.4%)	
Age				P = 0.386
≤ 65	23146(39.6%)	12636(39.5%)	10510(39.8%)	
>65	35278(60.4%)	19389(60.5%)	15889(60.2%)	
Race				P<0.001
White	47010(80.5%)	26470(82.7%)	20540(77.8%)	
Black	6710(11.5%)	2372(7.4%)	4338(16.4%)	
Other	4707(8.1%)	3183(9.9%)	1521(5.8%)	
Histology				P<0.001
ADC	35374(60.5%)	19863(62.0%)	15511(58.8%)	
SCC	20585(35.2%)	10821(33.8%)	9764(37.0%)	
LCC	1215(2.1%)	628(2.0%)	587(2.2%)	
ASC	1250(2.1%)	713(2.2%)	537(2.0%)	
Grade				P<0.001
Well differentiated	6572(11.2%)	3770(11.8%)	2802(10.6%)	
Moderately differentiated	23324(39.9%)	12918(40.3%)	10406(39.4%)	
Poorly differentiated	27581(47.2%)	14849(46.4%)	12732(48.2%)	
Undifferentiated	947(1.6%)	488(1.5%)	459(1.7%)	
Stage				P = 0.016
I	19051(32.6%)	10586(33.0%)	8483(32.1%)	
II	7817(13.4%)	4339(13.5%)	3478(13.2%)	
III	12899(22.1%)	7047(22.0%)	5852(22.2%)	
IV	18657(31.9%)	10071(31.4%)	8586(32.5%)	
Surgery of primary site				P<0.001
No	31304(53.6%)	16096(50.3%)	15208(57.6%)	
Yes	27120(46.4%)	15929(49.7%)	11191(42.4%)	
Intraoperative lymph node evaluation				P<0.001

ADC Adenocarcinoma, SCC Squamous cell carcinoma, LCC Large Cell Carcinoma, ASC Adenosquamous carcinoma

Variable	Total	Married	Unmarried	P value
No	30865(52.8%)	15809(49.4%)	15056(57.0%)	
Yes	27559(47.2%)	16216(50.6%)	11343(43.0%)	
Chemotherapy				P<0.001
No	32318(55.3%)	16696(52.1%)	15622(59.2%)	
Yes	26106(44.7%)	15329(47.9%)	10777(40.8%)	
Radiotherapy				P = 0.198
No	35966(61.6%)	19790(61.8%)	16176(61.3%)	
Yes	22458(38.4%)	12235(38.2%)	10223(38.7%)	
ADC Adenocarcinoma, SCC Squamous cell carcinoma, LCC Large Cell Carcinoma, ASC Adenosquamous carcinoma				

Survival Analysis

Before PSM, the married group had significantly better OS and CSS outcomes than the unmarried group (OS median survival (95% CI): 26 (26–27) vs. 20 (19–20) months, $P < 0.001$; CSS median survival (95% CI): 32 (31–34) vs. 24 (24–25) months, $P < 0.001$). Within the unmarried group, patients who were divorced had better OS (median survival (95% CI): 21 (20–23) months) compared to those who were single (median survival (95% CI): 19 (18–20) months, $p < 0.001$) or widowed (median survival (95% CI): 20 (19–20) months, $p < 0.001$). In addition, single patients had worse CSS (median survival (95% CI): 22 (21–24) months) than divorced patients (median survival (95% CI): 26 (25–28) months, $p < 0.001$) or widowed patients (median survival (95% CI): 25 (24–26) months, $p = 0.016$) (Fig. 1).

Since most clinicopathological characteristics between married and unmarried groups were significantly different, PSM was performed to balance potentially confounding factors. The married group was matched at a 1:1 ratio with the unmarried group. After matching, 20148 pairs were selected into further analysis, and all clinicopathological characteristics between the married and unmarried groups were well balanced without significant difference, as examined by chi-square tests (Table 2 and Supplementary Fig. 1).

Table 2
Clinicopathological characteristics of NSCLC patients in SEER database after propensity score matching

Variable	Total	Married	Unmarried	P value
	(n = 40296)	(n = 20148,50.0%)	(n = 20148,50%)	
Gender				P = 0.952
Male	19210(47.7%)	9608(47.7%)	9602(47.7%)	
Female	21086(52.3%)	10540(52.3%)	10546(52.3%)	
Age				P = 0.871
≤ 65	16622(41.2%)	8303(41.2%)	8319(41.3%)	
>65	40296(58.8%)	11845(58.8%)	11829(58.7%)	
Race				P = 0.721
White	33888(84.1%)	16954(84.1%)	16934(84.0%)	
Black	4010(10.0%)	1984(9.8%)	2026(10.1%)	
Other	2398(6.0%)	1210(6.0%)	1188(5.9%)	
Histology				P = 0.966
ADC	24913(61.8%)	12444(61.8%)	12469(61.9%)	
SCC	14131(35.1%)	7070(35.1%)	7061(35.0%)	
LCC	635(1.6%)	320(1.6%)	315(1.6%)	
ASC	617(1.5%)	314(1.6%)	303(1.5%)	
Grade				P = 0.986
Well differentiated	4309(10.7%)	2143(10.6%)	2166(10.8%)	
Moderately differentiated	16234(40.3%)	8119(40.3%)	8115(40.3%)	
Poorly differentiated	19302(47.9%)	9661(48.0%)	9641(47.9%)	
Undifferentiated	451(1.1%)	225(1.1%)	226(1.1%)	
Stage				P = 0.993
I	13348(33.1%)	6665(33.1%)	6683(33.2%)	
II	5191(12.9%)	2591(12.9%)	2600(12.9%)	
III	8569(21.3%)	4285(21.3%)	4248(21.3%)	
IV	13188(32.7%)	6607(32.8%)	6581(32.7%)	
Surgery of primary site				P = 0.811
No	21576(53.5%)	10776(53.5%)	10800(53.6%)	
Yes	18720(46.5%)	9372(46.5%)	9348(46.4%)	
Intraoperative lymph node evaluation				P = 0.992

ADC Adenocarcinoma; SCC Squamous cell carcinoma; LCC Large Cell Carcinoma; ASC Adenosquamous carcinoma

Variable	Total	Married	Unmarried	P value
No	21309(52.9%)	10655(52.9%)	10654(52.9%)	
Yes	18987(47.1%)	9493(47.1%)	9494(47.1%)	
Chemotherapy				P = 0.904
No	22420(55.6%)	11216(55.7%)	11204(55.5%)	
Yes	17876(44.4%)	8932(44.3%)	8944(44.4%)	
Radiotherapy				P = 0.821
No	25162(62.4%)	12592(62.5%)	12570(62.4%)	
Yes	15134(37.6%)	7556(37.5%)	7578(37.6%)	
ADC Adenocarcinoma; SCC Squamous cell carcinoma; LCC Large Cell Carcinoma; ASC Adenosquamous carcinoma				

After PSM, the married group consistently demonstrated better OS and CSS outcomes than unmarried group (OS median survival (95% CI): 25 (24–26) vs. 22 (21–23) months, $P < 0.001$; CSS median survival (95% CI): 31 (30–32) vs. 27 (26–28) months, $P < 0.001$). Similarly, within the unmarried group, the divorced patients had better OS (median survival (95% CI): 23 (22–24) months) than single patients (median survival (95% CI): 20 (19–22) months, $P = 0.006$). Additionally, single patients had worse CSS (median survival (95% CI): 24 (23–25) months) than divorced patients (median survival (95% CI): 28 (26–30) months, $p = 0.003$) or widowed patients (median survival (95% CI): 30 (28–33) months, $p < 0.001$) (Fig. 2).

Cox Proportional Hazards Regression Model

To further explore whether different marital statuses had different impact on OS and CSS, we analysed all related variables, including marital status, with a Cox proportional hazards regression model. In univariable analysis, single patients had significantly worse OS (HR (95% CI): 1.047 (1.009–1.087), $P = 0.015$) and CSS (HR (95% CI): 1.045 (1.004–1.087), $P = 0.031$) than married patients, and so did the divorced patients compared to married patients (OS: HR (95% CI): 1.125 (1.085–1.166), $P < 0.001$; CSS: HR (95% CI): 1.131 (1.089–1.175), $P < 0.001$). In addition, the widowed patients were associated with worse OS compared to married patients (HR (95% CI): 1.093 (1.056–1.132), $P < 0.001$). We also performed multivariable Cox proportional hazards regression analysis. And all subgroups but separated patients within unmarried group had significantly worse survival compared to married group (OS: single (HR (95% CI): 1.085 (1.046–1.126), $P < 0.001$), separated (HR (95% CI): 1.137 (1.019–1.270), $P = 0.022$), divorced (HR (95% CI): 1.148 (1.106–1.192), $P < 0.001$) and widowed (HR (95% CI): 1.139 (1.099–1.181), $P < 0.001$); CSS: single (HR (95% CI): 1.073 (1.032–1.116), $P < 0.001$), separated (HR (95% CI): 1.074 (0.953–1.211), $P = 0.240$), divorced (HR (95% CI): 1.144 (1.099–1.190), $P < 0.001$) and widowed (HR (95% CI): 1.100 (1.058–1.144), $P < 0.001$) (Table 3).

Table 3

Univariate and multivariate analysis of overall survival and cancer specific survival after propensity score matching

Univariate			multivariate					
Variable	Overall survival		Cancer specific survival		Overall survival		Cancer specific survival	
	Hazard ratio(95%CI)	P value	Hazard ratio(95%CI)	P value	Hazard ratio(95%CI)	P value	Hazard ratio(95%CI)	P value
Gender								
Male	Reference		Reference		Reference		Reference	
Female	0.618(0.602–0.634)	< 0.001	0.618(0.602–0.634)	< 0.001	0.772(0.752–0.793)	< 0.001	0.791(0.769–0.814)	< 0.001
Age								
≤ 65	Reference		Reference		Reference		Reference	
> 65	1.130(1.101–1.160)	< 0.001	1.130(1.101–1.160)	< 0.001	1.188(1.156–1.222)	< 0.001	1.129(1.095–1.163)	< 0.001
Race								
White	Reference		Reference		Reference		Reference	
Black	1.152(1.106–1.200)	< 0.001	1.152(1.106–1.200)	< 0.001	0.945(0.906–0.985)	0.007	0.936(0.895–0.978)	0.003
Other	0.836(0.790–0.885)	< 0.001	0.836(0.790–0.885)	< 0.001	0.749(0.707–0.794)	< 0.001	0.781(0.736–0.830)	< 0.001
Histology								
ADC	Reference		Reference		Reference		Reference	
SCC	1.480(1.442–1.520)	< 0.001	1.480(1.442–1.520)	< 0.001	1.184(1.151–1.218)	< 0.001	1.137(1.103–1.173)	< 0.001
LCC	1.651(1.504–1.812)	< 0.001	1.651(1.504–1.812)	< 0.001	1.381(1.246–1.530)	< 0.001	1.405(1.262–1.565)	< 0.001
ASC	1.114(1.003–1.236)	0.043	1.114(1.003–1.236)	0.043	1.204(1.084–1.337)	0.001	1.181(1.053–1.324)	0.004
Marital status								
Married	Reference		Reference		Reference		Reference	
Single	1.047(1.009–1.087)	0.015	1.047(1.009–1.087)	0.015	1.085(1.046–1.126)	< 0.001	1.073(1.032–1.116)	< 0.001
Separated	1.059(0.949–1.182)	0.305	1.059(0.949–1.182)	0.305	1.137(1.019–1.270)	0.022	1.074(0.953–1.211)	0.24
Divorced	1.125(1.085–1.166)	< 0.001	1.125(1.085–1.166)	< 0.001	1.148(1.106–1.192)	< 0.001	1.144(1.099–1.190)	< 0.001
Widowed	1.093(1.056–1.132)	< 0.001	1.093(1.056–1.132)	< 0.001	1.139(1.099–1.181)	< 0.001	1.100(1.058–1.144)	< 0.001
Grade								

ADC Adenocarcinoma, SCC Squamous cell carcinoma, LCC Large Cell Carcinoma, ASC Adenosquamous carcinoma,

	Univariate			multivariate				
Well differentiated	Reference		Reference		Reference		Reference	
Moderately differentiated	1.919(1.815–2.028)	< 0.001	1.919(1.815–2.028)	< 0.001	1.382(1.306–1.462)	< 0.001	1.399(1.313–1.491)	< 0.001
Poorly differentiated	2.981(2.824–3.147)	< 0.001	2.981(2.824–3.147)	< 0.001	1.642(1.553–1.737)	< 0.001	1.690(1.587–1.799)	< 0.001
Undifferentiated	3.073(2.719–3.472)	< 0.001	3.073(2.719–3.472)	< 0.001	1.546(1.352–1.768)	< 0.001	1.597(1.369–1.821)	< 0.001
Stage								
I	Reference		Reference		Reference		Reference	
II	2.058(1.975–2.164)	< 0.001	2.058(1.975–2.164)	< 0.001	2.230(2.118–2.349)	< 0.001	2.974(2.772–3.133)	< 0.001
III	3.779(3.627–3.937)	< 0.001	3.779(3.627–3.937)	< 0.001	3.181(3.030–3.399)	< 0.001	4.553(4.302–4.819)	< 0.001
IV	7.952(7.657–8.258)	< 0.001	7.952(7.657–8.258)	< 0.001	5.435(5.178–5.704)	< 0.001	7.974(7.535–8.439)	< 0.001
Surgery of primary site								
No	Reference		Reference		Reference		Reference	
Yes	0.185(0.180–0.191)	< 0.001	0.185(0.180–0.191)	< 0.001	0.460(0.434–0.487)	< 0.001	0.442(0.416–0.470)	< 0.001
Intraoperative lymph node evaluation								
No	Reference		Reference		Reference		Reference	
Yes	0.223(0.216–0.229)	< 0.001	0.223(0.216–0.229)	< 0.001	0.725(0.690–0.763)	< 0.001	0.735(0.697–0.776)	< 0.001
Chemotherapy								
No	Reference		Reference		Reference		Reference	
Yes	1.559(1.520–1.599)	< 0.001	1.559(1.520–1.599)	< 0.001	0.555(0.539–0.572)	< 0.001	0.561(0.544–0.579)	< 0.001
Radiotherapy								
No	Reference		Reference		Reference		Reference	
Yes	2.090(2.037–2.144)	< 0.001	2.090(2.037–2.144)	< 0.001	0.987(0.950–1.007)	0.142	0.984(0.955–1.015)	0.307
ADC Adenocarcinoma, SCC Squamous cell carcinoma, LCC Large Cell Carcinoma, ASC Adenosquamous carcinoma,								

In further subgroup analysis, all subgroups of age, gender, stage, surgery of primary site, intraoperative lymph node evaluation, chemotherapy and radiotherapy, unmarried patients had significantly worse OS compared to married patients. Similarly, we demonstrated that unmarried patients also had significantly worse CSS in the above subgroups compared to married patients, except in the well differentiated and stage II subgroups with higher risks in the OS (Fig. 3).

Discussion

In the present study, we demonstrated that married patients had a significantly better prognosis than unmarried patients with a population-based database. Moreover, after adjusting for confounding clinicopathological characteristics by PSM, married group was still associated with better survival outcomes. Within unmarried patients, single patients always had a shorter median survival time in terms of OS and CSS than that in other unmarried patients. Additionally, when confounding factors were controlled by the Cox proportional hazards regression, we still found that unmarried patients had a higher risk than married patients. In the subgroup analysis, married patients were consistently associated with better survival in most subgroups.

The conclusions of this study are consistent with previous studies conducted in other cancers[9–13] that married patients had significantly better prognosis than unmarried patients. However, few studies had investigated the impact of marital status on NSCLC survival. In a previous study by Jatoi A et al.[14], with 5,898 NSCLC patients diagnosed in 1999–2006, no significant differences in survival or quality of life was found by different marital status. In addition, Siddiqui et al.[15] and Saito-Nakaya et al.[16] enrolled 1365 and 238 NSCLC patients diagnosed during 1990s, respectively, and showed that marital status was not an independent prognostic factor. We believe our results contradicted to theirs were mainly due to the following reasons: firstly, a total of 58424 patients were enrolled in this study, which was significantly larger sample size than previous studies; secondly, the SEER database covered as much as 28% population from the USA diagnosed between 2010 and 2016, which is more representative to the latest trend of marital status in modern society.

Multiple reasons account for the impact of marital status on NSCLC survival. Marital psychological effect is found to be one of the most important ones. Holt-Lunstad et al.[18] found that familial support from a marriage had a significant positive influence on long-term health. In contrast, loneliness and isolation associated with unmarried status may lead to unhealthy life style, including smoking and low physical activity[19]. Moreover, Steptoe et al.[20] observed that married participants had lower loneliness scores than single and divorced participants, which might significantly improve their health. And a prospective study further suggested that a higher degree of optimism was associated with a lower mortality risk[21]. Furthermore, psychological factors were found to have a strong impact on tumour immune microenvironment. [22]. The study of Reiche et al.[23] demonstrated that depression and stress decreased cytotoxic T-cell and natural killer cell activities, which might decrease the immune surveillance capability and promote tumoral growth.

Furthermore, A meta-analysis including 122 studies demonstrated that marriage and living with another person could increase adherence modestly, and patients from cohesive families had higher adherence than those from families in conflict[24]. And many previous studies demonstrated higher compliance and adherence to the treatment was also associated with better survival outcomes[25, 26]. In addition, the study from Makubate et al.[27] demonstrated that low adherence to tamoxifen or aromatase inhibitors for women with breast cancer increased the risk of death. And McCowan et al.[28] observed that women who had low adherence to tamoxifen were significantly at increased risk of death. In addition, it was demonstrated by Langenbach et al.[29] that marital status had a significant influence on the treatment delay of colorectal cancer, which influenced the survival of patients. Last but not least, Ou et al.[30] found that unmarried status was associated with low socioeconomic status, which was an independent poor prognostic factor for NSCLC survival.

Several limitations are worth mentioning in this study. First, the quality of marriage was not recorded in the SEER database, and therefore we can't further evaluate its impact on NSCLC survival. Manne et al.[31] found that the closeness of the marital relationship had an influence on psychological adaptation to cancer. Second, changes in marital status after diagnosis were also unavailable in the SEER database. Third, other therapeutic details, including the specific dosage of chemotherapy and radiotherapy were not recorded, which might confound the final results. Forth, other socioeconomic factors, including family income levels and medical insurance status, need further investigation.

Conclusion

In conclusion, our study still fully indicates that married patients with NSCLC have better survival outcomes than unmarried patients with NSCLC. Therefore, enhanced surveillance with a more intense follow-up regimen should be implemented for unmarried patients to decrease the survival risk caused by marital status. In addition, efforts to provide unmarried patients with social and psychological support will increase positive emotions, which are associated with better survival in cancer by influencing the immune system. Furthermore, closer surveillance and more social and family support simultaneously improve patients' adherence and compliance to the treatments, which eventually improve survival. This study demonstrated that unmarried NSCLC patients was associated with significantly worse OS and CSS compared to married NSCLC patients. Therefore, unmarried patients need not only closer surveillance, but also more social and family support, which may improve patients' adherence and compliance, and eventually improve the survival.

Declarations

Ethics approval and consent to participate: Since the SEER database is publicly available and all patients were deidentified, ethical approval was waived by the ethical committee of our hospital.

Consent for publication: Not applicable.

Availability of data and materials: The data that support the findings of this study are available from SEER database but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of SEER database, and the reference number was 14,683-Nov2019.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: Lanjun Zhang, Dechang Zhao and Rusi Zhang conceived the idea and designed the research. Dechang Zhao contributed to data collection and analysis. And all authors interpreted the outcomes and wrote the paper together. Besides, the submission to the Global Health Research and Policy was agreed by all authors.

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Figures

Figure 1

Kaplan-Meier survival curves of non-small cell lung cancer patients according to marital status before propensity score matching. A. Overall survival comparison between married and unmarried patients; B. Overall survival comparison among married, single, separated, divorced and widowed patients; C. Cancer specific survival comparison between married and unmarried patients; D. Cancer specific survival comparison among married, single, separated, divorced and widowed patients. The color band represents the 95% confidence interval of survival curves.

Figure 2

Kaplan-Meier survival curves of non-small cell lung cancer patients according to marital status after propensity score matching. A. Overall survival comparison between married and unmarried patients; B. Overall survival comparison among married, single, separated, divorced and widowed patients; C. Cancer specific survival comparison between married and unmarried patients; D. Cancer specific survival comparison among married, single, separated, divorced and widowed patients. The color band represents the 95% confidence interval of survival curves.

Figure 3

Survival comparison between married non-small cell lung cancer (NSCLC) patients and unmarried NSCLC patients in different clinicopathological subgroups analysis. Red and blue boxes represent the hazard ratios (HRs) of overall survival and cancer specific survival respectively. The lines represent the 95% confidence interval of hazard ratio (HR).

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