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Association of marital status with cardiovascular death risk in patients with lung cancer: A population-based study

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ABSTRACT

Background: To investigate the association of marital status on cardiovascular death risk in lung cancer patients.
Methods: Using data from the Surveillance, Epidemiology, and End Results (SEER) database in the United States from 2011 to 2015 (N = 118,293), the association between marital status and cardiovascular death (CVD) risk in patients with lung cancer was assessed by competing-risks regression models.
Results: Unmarried status was associated with increased risk of cardiovascular death in lung cancer patients [hazard ratio (HR) = 1.398, 95 % confidence interval (CI): 1.268–1.542], which remained significant even after adjusting for potential covariates (HR = 1.407, 95 % CI: 1.276–1.551). Further unmarried subgroups analysis showed that the different unmarried status were associated with increased cardiovascular death risk as follows: single (HR = 1.397, 95 % CI: 1.236–1.1.580), separated (HR = 1.630, 95 % CI: 1.153–2.305), divorced (HR = 1.318, 95 % CI: 1.158–1.500), and widowed (HR = 1.561, 95 % CI: 1.393–1.749). Further subgroup analysis by sex revealed that compared to male lung cancer patients with married, CVD risk was significant increased in their counterparts with widowed (adjusted HR = 1.509, 95 % CI: 1.291–1.764, $P<0.001$), single (adjusted HR = 1.361, 95 % CI: 1.168–1.585, $P<0.001$) and divorced (adjusted HR = 1.353, 95 % CI: 1.177–1.555, $P<0.001$) rather than those with separated. However, similar phenomena was only observed in female lung cancer patients with widowed (adjusted HR = 1.414, 95 % CI: 1.220–1.640, $P<0.001$) and single (adjusted HR = 1.438, 95 % CI: 1.195–1.730, $P<0.001$).
Conclusion: Unmarried status was associated with increased cardiovascular death risk in patients with lung cancer, which highlighted that more attention and humanistic/supportive care should be offered to unmarried lung cancer patients for improving the prognosis.

1. Introduction

Lung cancer remains one of the most common cancers in the world, accounting for about 18 % of newly diagnosed cancers in Bary et al. (2020). Lung cancer is also the leading cause of cancer deaths worldwide (Torre et al., 2015), making up almost 25 % of all cancer deaths. Death in patients with lung cancer includes cancer-related and non-cancer-related mortality. The most common cause of non-cancer mortality was cardiovascular death (CVD) (Abdel-Rahman, 2017; Sung et al., 2021). The CVD risk in lung cancer patients was not only associated with cardiovascular toxicity related (Gilchrist et al., 2019; Zamorano et al., 2016) to cancer treatment and monitoring of cardiac dysfunction, but

Abbreviations: AJCC, The American Joint Committee on Cancer; CI, Confidence interval; CVD, Cardiovascular death; HR, Hazard ratio; ICD-10, International Classification of Diseases-10; PSM, Propensity-score matching; SEER, Surveillance, Epidemiology, and End Results.

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also associated with the cardiovascular disease related to lung cancer itself. It is worth noting that the CVD risk in patients with lung cancer is often overlooked and underestimated during survival period (Wang et al., 2020), which means strengthening the prevention and control of CVD may contribute to the survival and prognosis of lung cancer patients (Guan et al., 2020). Previous studies confirmed that anti-cancer treatment (Fillon, 2019), lack of exercise and high blood pressure (Shin et al., 2019) are associated with high CVD risks, and clinic guidelines recommended that more attention should paid to the cardiotoxicity of cancer treatment and the traditional cardiovascular risk factors in order to decrease the CVD risk. However, based on the widely accepted biopsychosocial medical model, the social and psychological factors are also vital link of that cannot be ignored in the prevention and control of CVD in patients with lung cancer.

Marital status (e.g., married, separated, divorced, widowed, etc.), as one of the important social and psychological factors, is independently related to CVD risk that have not been overlooked (Schultz et al., 2017). The possible mechanisms by which marriage might affect CVD risk involved a combination of psychosocial, behavioral, and physiological factors, including increased social support, healthier behaviors, economic stability, better mental health, and shared responsibility for health so on. These factors work together to reduce stress, promote healthy behaviors, and ensure better access to healthcare, all of which contribute to lower CVD risk. Married individuals often benefit from greater social support, which can positively influence health behaviors and reduce stress, thereby lowering the risk of cardiovascular disease. In the general population, married people seem to have lower cardiovascular mortality and CVD incidence (14). The risk of CVD in married men was lower than that of single men (15). In patients with lung cancer, previous studies reported that marital status was a predictive factor and an independent risk factor for the overall survival rate and lung cancer-specific survival rate among (Chen et al., 2020; Ou et al., 2009), but the risk of cancer-related death did not increase in single people (Caleyachetty et al., 2015). The findings suggested that marriage may be an important form of social relations affecting the cancer-related and non-cancer-related mortality in lung cancer patients, especially the lung cancer related cardiovascular death. However, the relationship between marital status and cardiovascular death in lung cancer patients is unclear, and further investigation is needed to determine whether marital status is independently associated with CVD in lung cancer patients.

Marital status may be associated with the risk of cardiovascular death in lung cancer patients, and there are significant differences in cardiovascular death risk among different unmarried subgroups (single, separated, divorced, widowed) of lung cancer patients. Therefore, in this study we utilized Surveillance, Epidemiology, and End Results (SEER) database to assess the impact of marital status on cardiovascular disease risk in lung cancer patients, and further analyzed variations in cardiovascular disease risk across different marital statuses, genders, and age subgroups using propensity scores, so as to provide specific interventions for these patients to improve their prognosis.

2. Method

2.1. Study population

We conducted a retrospective cohort study using data from the SEER database in the United States. The SEER database collects cancer incidence and survival data from population-based cancer registries covering approximately 34.6 % of the United States population. The SEER database primarily comprises register data sourced from cancer registries. These registries collect extensive information on cancer incidence, prevalence, survival, and mortality from diverse sources, including hospitals, pathology laboratories, and vital statistics offices. This study population comprised 130,990 patients diagnosed with lung cancer between 2011 and 2015. Our study utilized register data from patients who met the specified criteria for lung cancer diagnosis and CVD-related mortality. The entry criteria were as follows: (1) lung cancer diagnosis confirmed by pathological evidence; (2) death attributed to CVD; (3) age 25 years or older at the time of diagnosis; (4) known marital status. The unqualified criteria were: (1) absence of clear pathological evidence for lung cancer diagnosis; (2) presence of more than one primary tumor; (3) unknown or homosexual marital status; (4) unknown cause of death; (5) incomplete race information; (6) incomplete staging according to the lung cancer adjusted American Joint Committee on Cancer (AJCC) cancer staging manual 6th edition. As a result, a total of 118,293 eligible patients met the inclusion and exclusion criteria. These patients were categorized into two cohorts based on marital status: married and unmarried. Subsequently, we analyzed the association between marital status and CVD risk in lung cancer patients within these cohorts, and also explored the impact of various marital statuses (married, single, widowed, divorced, or separated) on CVD.

2.2. Participant variables and outcomes

The demographic and clinical variables include marital status (married, unmarried), age at diagnosis (25–60 years, >60 years), sex (male, female), race (white, non-white), year of diagnosis (2011, 2012, 2013, 2014, 2015), laterality (left, right, one side, paired site), AJCC state (I, II, III, IV), chemotherapy (yes, no evidence), radiotherapy (yes, no evidence). Further, marital status was listed into five categories: (1) married; (2) single (never married); (3) divorced; (4) widowed; (5) separated. CVD was defined as any death with a certifiable cardiovascular cause or any death that is not distinctly ascribed to a non-CV cause, which was considered as the primary endpoint of this analysis. The CVD includes heart disease (I00-I09, I11, I13, I20-I51), hypertension without heart disease (I10, I12), cerebrovascular disease (I60-I69), atherosclerosis (I70), aortic aneurysm and dissection (I71) and other diseases of arteries, arterioles and capillaries (I72-I78), according to the International Classification of Disease-10 (ICD-10) codes (Fung et al., 2015). Then lung cancer patients who were alive at the time of last follow-up or who had died from non-CVD were viewed as censored observations.

2.3. Propensity-score matching

In this study, we assumed that marriage was not a prognostic factor in cardiovascular death in lung cancer patients since the cause of cancer was biological instead of sociological factor. Marital status was separated into married (married cohabitation, unmarried cohabitation) and unmarried (singe, divorced, widowed, separated). In order to confirm the vital function of marital status on CVD risk in lung cancer patients, propensity-score matching (PSM) was applied. Propensity score was used to match each patient in the married group to a comparable patient in the unmarried group in a ratio of 1:1, and the caliper width was 0.01. Logistic regression was applied to impute propensity scores. The acceptable standard means that P value of the above covariates was larger than 0.05.

2.4. Statistical analysis

Categorical variables in baseline characteristics of the patients, including sex, race, marital status, the cause of death, were assessed by using chi-squared test. The Kaplan-Meier method was applied to access cancer-specific survival between different marital statuses, and the Log-rank test was used to estimate the distinction. To accurately assess the association of marital status in prognosis of lung cancer patients, a Fine-Gray competing risk regression model was employed (Wolbers et al., 2014). To assess whether the effect of marital status on prognosis varied by sex (Lindstrom et al., 2024), we conducted stratified subgroup analyses to explore potential sex-specific effects on outcomes. Statistical significance was deemed as p value less than 0.05. SPSS version 25.0 (SPSS, Chicago, IL), GraphPad Prism version 7.0 (GraphPad Software, San Diego, California, USA) and X-tile program (Yale University, New

Haven, USA) were utilized to statistical analysis.

3. Results

3.1. Baseline characteristics

The baseline characteristics before and after PSM are shown in Table 1. A total of 118,293 patients with lung cancer were finally included in our study, of whom 62,812 (53.1 %) were married and 55,481 (46.9 %) were unmarried. Before PSM, the baseline features (age at diagnosis, sex, race, year of diagnosis, laterality, AJCC stage, radiotherapy and chemotherapy) were all imbalanced (all $P<0.05$). A 1:1 PSM was used to compensate the inherent of baseline characteristics in 92,292 lung cancer patients. After PSM, all baseline characteristics were well matched (all $P>0.05$).

3.2. The independent relationship of marital status on CVD of lung cancer patients

At univariate analysis, marital status, age at diagnosis, sex, year of diagnosis, AJCC stage, radiotherapy and chemotherapy were all correlated with CVD in lung cancer patients before and after PSM (Table 2) (all $P<0.05$). Unmarried lung cancer patients were at higher CVD risk compared to their married counterparts [before PSM, unadjusted hazard ratio (HR) = 1.355, 95 % confidence interval (CI): 1.246–1.473, $P<0.001$; after PSM, unadjusted HR = 1.398, 95 %CI: 1.268–1.542, $P<0.001$). These results remained consistent after multivariable adjustment (Table 3). Marital status was considered as an independent predicted factor of CVD. CVD risk of unmarried patients was higher than that of married patients (after PSM, adjusted HR = 1.407, 95 %CI: 1.276–1.551, $P<0.001$) (model 1: adjusted for age at diagnosis, sex, year of diagnosis, AJCC stage, radiotherapy and chemotherapy) (Table 3 and Table S1). Additionally, similar to the result in Model 1, the regression coefficient of marital status was robust (after PSM, adjusted HR = 1.407, 95 %CI: 1.276–1.551; $P<0.001$) (Model 2: the same as Model 1, and also adjusted for race and laterality) (Table 3 and Table S2).

3.3. Association of different marital status with CVD in lung cancer patients

We observed the association of different marital statuses on CVD in

Table 1
Baseline characteristics in patients with lung cancer based on SEER from 2011 to 2015 before and after propensity score matching.

Variable	Before PSM (N/%)			After PSM (N/%)		
	Married	Unmarried	*P* Value[b]	Married	Unmarried	*P* Value[b]
N	62,812	55,481	–	46,146	46,146	–
Age at diagnosis			<0.001			0.619
25–60 years	15,386 (24.5)	14,624 (26.4)		13,017 (28.2)	12,949 (28.1)	
> 60 years	47,426 (75.5)	40,857 (73.6)		33,129 (71.8)	33,197 (71.9)	
Sex			<0.001			1.000
Male	38,240 (60.9)	23,649 (42.6)		22,680 (49.1)	22,680 (49.1)	
Female	24,572 (39.1)	31,832 (57.4)		23,466 (50.9)	23,466 (50.9)	
Race			<0.001			0.572
White	52,121 (83.0)	43,354 (78.1)		37,161 (80.5)	37,093 (80.4)	
Non-white[a]	10,691 (17.0)	12,127 (21.9)		8,985 (19.5)	9,053 (19.6)	
Year of diagnosis			0.037			0.103
2011	12,194 (19.4)	10,415 (18.8)		8,942 (19.4)	8,688 (18.8)	
2012	12,376 (19.7)	10,938 (19.7)		9,110 (19.7)	9,061 (19.6)	
2013	12,517 (19.9)	11,075 (20.0)		9,213 (20.0)	9,196 (19.9)	
2014	12,788 (20.4)	11,339 (20.4)		9,381 (20.3)	9,432 (20.4)	
2015	12,937 (20.6)	11,714 (21.1)		9,500 (20.6)	9,769 (21.2)	
Laterality			<0.001			0.309
Left	24,903 (39.6)	21,791 (39.3)		18,276 (39.6)	18,101 (39.2)	
Right	35,336 (56.3)	31,127 (56.1)		25,919 (56.2)	25,997 (56.3)	
One side	169 (0.3)	157 (0.3)		130 (0.3)	128 (0.3)	
Paired site	2,404 (3.8)	2,406 (4.3)		1,821 (3.9)	1,920 (4.2)	
AJCC stage			<0.001			0.336
I	12,850 (20.5)	10,711 (19.3)		9,285 (20.1)	9,166 (19.9)	
II	5,349 (8.5)	4,607 (8.3)		3,770 (8.2)	3,821 (8.3)	
III	12,436 (19.8)	11,122 (20.0)		8,900 (19.3)	9,080 (19.7)	
IV	32,177 (51.2)	29,041 (52.3)		24,191 (52.4)	24,079 (52.2)	
Chemotherapy			<0.001			0.654
Yes	30,017 (47.8)	31,266 (56.4)		23,822 (51.6)	23,754 (51.5)	
No evidence	32,795 (52.2)	24,215 (43.6)		22,324 (48.4)	22,392 (48.5)	
Radiotherapy			<0.001			0.204
Yes	36,488 (58.1)	33,041 (59.6)		27,263 (59.1)	27,073 (58.7)	
No evidence	26,324 (41.9)	22,440 (40.4)		18,883 (40.9)	19,073 (41.3)	

[a] Non-white includes Black or African American, American Indian or Alaska Native, and Asian or Pacific Islander.
[b] *P*-values were derived from Chi-square tests.

Table 2
Univariate competing-risks regression analysis of cardiovascular death in patients with lung cancer based on SEER from 2011 to 2015.

Variable	Before PSM		After PSM	
	HR (95 % CI)	*P* Value[b]	HR (95 % CI)	*P* Value[b]
Marital status				
Married	Reference		Reference	
Unmarried	1.355 (1.246–1.473)	< 0.001	1.398 (1.268–1.542)	< 0.001
Age at diagnosis				
25–60 years	Reference		Reference	
> 60 years	2.203 (1.952–2.485)	< 0.001	2.256 (1.975–2.577)	< 0.001
Sex				
Male	Reference		Reference	
Female	0.765 (0.703–0.833)	< 0.001	0.689 (0.625–0.759)	< 0.001
Race				
White	Reference		Reference	
Non-white[a]	1.091 (0.984–1.210)	0.098	1.040 (0.923–1.173)	0.516
Year of diagnosis		< 0.001		< 0.001
2011	Reference		Reference	
2012	0.976 (0.871–1.094)	0.677	0.951 (0.834–1.085)	0.458
2013	0.900 (0.801–1.012)	0.078	0.904 (0.790–1.033)	0.139
2014	0.673 (0.590–0.767)	< 0.001	0.674 (0.580–0.783)	< 0.001
2015	0.624 (0.530–0.736)	< 0.001	0.612 (0.506–0.741)	< 0.001
Laterality		0.086		0.067
Left	Reference		Reference	
Right	0.919 (0.843–1.001)	0.053	0.897 (0.812–0.990)	0.030
One side	0.515 (0.166–1.603)	0.252	0.425 (0.106–1.706)	0.228
Paired site	0.809 (0.631–1.038)	0.095	0.804 (0.605–1.069)	0.134
AJCC stage		< 0.001		< 0.001
I	Reference		Reference	
II	0.859 (0.742–0.994)	0.041	0.817 (0.688–0.970)	0.021
III	0.694 (0.616–0.782)	< 0.001	0.701 (0.612–0.804)	< 0.001
IV	0.536 (0.484–0.594)	< 0.001	0.519 (0.462–0.584)	< 0.001
Chemotherapy				
Yes	0.514 (0.471–0.560)	< 0.001	0.515 (0.466–0.569)	< 0.001
No evidence	Reference		Reference	
Radiotherapy				
Yes	0.887 (0.815–0.966)	0.006	0.871 (0.790–0.961)	0.006
No evidence	Reference		Reference	

[a] Non-white includes Black or African American, American Indian or Alaska Native, and Asian or Pacific Islander.
[b] *P*-values were derived from univariate competing-risks regression analysis.

lung cancer patients. In univariate analysis, single patients ($P = 0.003$), divorced patients ($P = 0.004$) and widowed patients ($P<0.001$) were all at higher CVD risk compared with married lung cancer patient (Table 4 and Table S3). The differences between separated patients and married patients did not reach statistical significance ($P = 0.093$).

Upon adjusting for potential confounding biases in multivariable analysis, the differences between separated patients and married patients became statistically significant (adjusted HR = 1.630, 95 % CI: 1.153–2.305, $P = 0.006$). Compared with married lung cancer patients, CVD risk was 1.561 time higher in widowed patients (adjusted HR = 1.561, 95 % CI: 1.393–1.749, $P<0.001$), 1.397 time higher in single patients (adjusted HR = 1.397, 95 % CI: 1.236–1.580, $P<0.001$) and 1.318 time higher in divorced patients (adjusted HR = 1.318, 95 % CI: 1.158–1.500, $P<0.001$).

Further subgroup analysis by sex revealed that compared to male lung cancer patients with married, CVD risk was significant increased in their counterparts with widowed (adjusted HR = 1.509, 95 % CI: 1.291–1.764, $P<0.001$), single (adjusted HR = 1.361, 95 % CI: 1.168–1.585, $P<0.001$) and divorced (adjusted HR = 1.353, 95 % CI: 1.177–1.555, $P<0.001$) rather than those with separated. However, similar phenomena was only observed in female lung cancer patients with widowed (adjusted HR = 1.414, 95 % CI: 1.220–1.640, $P<0.001$) and single (adjusted HR = 1.438, 95 % CI: 1.195–1.730, $P<0.001$).

4. Discussion

Lung cancer is still a disease with the highest mortality rate among cancers. In lung cancer patients, cardiovascular disease accounts for about half of their non-cancer deaths. The association of marital status on cardiovascular disease in patients with lung cancer is unclear. We are the first to explore the relationship between the marital status of lung cancer patients and cardiovascular disease. Our results show that marital status is an independent predictor of cardiovascular disease in lung cancer survivors. After using PSM to reduce the bias between groups and using a multivariable competitive risk model to analyze and adjust for potential confounding factors, the CVD risk of unmarried lung cancer survivors was still higher than that of married survivors by 40 %. Our results were consistent with other similar researches (Lai et al.,

Table 3
Multivariable competing-risks regression analysis of cardiovascular death in patients with lung cancer based on SEER from 2011 to 2015.

Variable	Before PSM		After PSM	
	HR (95 % CI)	*P* Value	HR (95 % CI)	*P* Value
Unadjusted HR				
Married	Reference		Reference	
Unmarried	1.355 (1.246–1.473)	< 0.001	1.398 (1.268–1.542)	< 0.001
Model 1[a]				
Married	Reference		Reference	
Unmarried	1.439 (1.320–1.569)	< 0.001	1.407 (1.276–1.551)	< 0.001
Model 2[b]				
Married	Reference		Reference	
Unmarried	1.430 (1.312–1.559)	< 0.001	1.407 (1.276–1.551)	< 0.001

[a] Model 1: Hazard ratios (HRs) were adjusted for statistically significant factors according to univariate analysis (age at diagnosis, sex, year of diagnosis, AJCC stage, radiotherapy and chemotherapy).
[b] Model 2: It is the same as Model 1, and also includes race and laterality.

1999; Manzoli et al., 2007; Tannenbaum et al., 2013; Wong et al., 2018). Among late-stage cancer patients in SEER database (N = 261,070), Lai et al. found that the survival prognosis in cancer patients under the single, separated, divorced, or widowed status was much worse than that of married cancer patients (Lai et al., 1999). Based on the Florida Cancer Data System data (1996–2007), Agency for Health Care Administration data and U.S. Census data (N = 161,228), Tannenbaum et al. then reported that the death risk of never married lung cancer patients increased approximately by 43 % compared to that their married counterparts (Tannenbaum et al., 2013). Two *meta*-analyses on the relationship of marital status with mortality confirmed that unmarried individuals was not only associated with increased mortality risk (about by 6.4 %) in the elderly (Manzoli et al., 2007) but also with atherosclerotic cardiovascular disease related mortality risk, such as coronary heart disease (by 43 %) and stoke (by 55 %) (Wong et al., 2018). Maselko et al. also found that never married individuals had a 40 % increased risk for stroke than married among American adults aged 50 and older (Maselko et al., 2009). Similar phenomenon was observed in Northern China based on a cross-sectional study (N = 56,716), and unmarried subjects had higher 10-year CVD risk (30.4 %) compared to their married counterparts (23.6 %) (Zhu et al., 2020). Indeed, a recent retrospective case-control study (N = 5,707) by Celeng et al. observed that unmarried status was correlated to increased CVD-related death risk (by 75 %) in lung cancer screening population after adjusting for traditional cardiovascular risk factors (Celeng et al., 2020). These findings obviously indicated that marital status is related to CVD risk in patients with lung cancer, at least partially.

Further analysis showed that various categories of unmarried were related to increased risk of CVD compared to married individuals, such as single (by 39.7 %), divorced (by 31.8 %), widowed (by 56.1 %), and separated (by 63.0 %). Our result was consistent with other studies. Leon's survey revealed that the mortality of coronary heart disease in single/widowed was higher than that of married in middle-aged men (Mendes de Leon et al., 1992). A prospective study of 13,889 Scottish showed that single men and separated/divorced women had the highest risk of CVD (Molloy et al., 2009). Recent studies further showed that divorced people had a higher risk of myocardial infarction and cardiovascular disease compared with married people (Dupre et al., 2015; Kaiser et al., 2010). In this study, we also found that the CVD risk for single female lung cancer patients was 6.3 % higher than that of male patients. Conversely, the CVD risk for widowed male lung cancer patients was 6.7 % higher than that of female patients. The CVD risk for divorced male lung cancer patients increased by 36.1 %, while the risk increase for female patients was not significant. This indicated that the relationship between marital status and CVD was more pronounced in widowed and divorced male lung cancer patients compared to their female counterparts, which is consistent with recent studies by Lindström et al. who reported that the associations between marital status and mortality are stronger among men than women (Lindstrom et al., 2024). These findings suggested that more attention should be

Table 4
Univariate and multivariable competing-risks regression analysis base on different marital statuses and sex of 118,293 patients with lung cancer based on SEER from 2011 to 2015.

Subjects	Marital status	Univariate analysis HR (95 % CI)	*P* value	Multivariable analysis HR (95 % CI)[a]	*P* value
Total	Married	Reference		Reference	
	Single	1.206 (1.067–1.363)	0.003	1.397 (1.236–1.580)	< 0.001
	Separated	1.345 (0.951–1.902)	0.093	1.630 (1.153–2.305)	0.006
	Divorced	1.209 (1.064–1.374)	0.004	1.318 (1.158–1.500)	< 0.001
	Widowed	1.615 (1.451–1.798)	< 0.001	1.561 (1.393–1.749)	< 0.001
Female	Married	Reference		Reference	
	Single	1.351 (1.123–1.626)	0.002	1.438 (1.195–1.730)	< 0.001
	Separated	1.421 (0.848–2.382)	0.180	1.606 (0.957–2.695)	0.073
	Divorced	1.143 (0.943–1.385)	0.170	1.107 (0.913–1.342)	0.300
	Widowed	1.763 (1.527–2.037)	< 0.001	1.414 (1.220–1.640)	< 0.001
Male	Married	Reference		Reference	
	Single	1.192 (1.039–1.368)	0.012	1.353 (1.177–1.555)	< 0.001
	Separated	1.203 (0.789–1.835)	0.390	1.395 (0.915–2.127)	0. 120
	Divorced	1.288 (1.106–1.500)	0.001	1.361 (1.168–1.585)	< 0.001
	Widowed	1.742 (1.492–2.033)	< 0.001	1.509 (1.291–1.764)	< 0.001

[a] Hazard ratio (HR) was adjusted for statistically significant factors according to univariate analysis (age at diagnosis, sex, year of diagnosis, AJCC stage, chemotherapy and radiotherapy).

paid to CVD risk of unmarried patient (e.g., single, separated, or widowed) with lung cancer in future clinical practice, especially those male lung cancer patients with widowed or divorced as well as female lung cancer patients with single.

The relationship between the marital status of lung cancer patients and CVD can be explained from the following two aspects: physical support for improved medical outcome and mental support from families. The effects of physical support include prevention (Son et al., 2017), diagnosis (Aizer et al., 2013; Atzema et al., 2011; Chen et al., 2021), treatment (Aizer et al., 2013), follow-up visit (Sesti et al., 2020), compliance (Chen et al., 2021) and recovery. Unmarried patients receive less physical support from families than married patients, so the former have a higher risk of CVD (Wong et al., 2018). Firstly, lifestyle plays a vital role in the occurrence of CVD. Unmarried people intend to have unhealthy lifestyles (Krieger, 1992; Magrin et al., 2015), like smoking habits and lack of exercise (Chida et al., 2008) which may lead to a higher risk of lung cancer or CVD and it is not good for to the primary prevention of the disease. Secondly, the spouse can also contribute a lot to secondary prevention. When a person has developed symptoms (like chest pain, palpitations and chest tightness, etc), he/she will be encouraged by their spouse to seek medical treatment. That would be beneficial to early diagnosis and treatment, and therefore medical treatment rate would be increased (Chen et al., 2021). Thirdly, the spouse plays an important role in supervising their partner to actively follow treatment protocol, including taking medications on time and following doctor's advice (Wong et al., 2018), which then increased the treatment rate and patient compliance. Prognosis was worse in unmarried patients compared with married patients with heart failure since unmarried patients may had a higher risk for non-adherence (Wu et al., 2012). Surgery remains the main and most effective treatment for lung cancer. Greenberg *et al.* found that married patients with lung cancer are more likely to undergo surgery. In contrast, Goodwin et al. proved that unmarried lung cancer patients are less likely to receive specific treatments (Aizer et al., 2013). Sesti et al. (Sesti et al., 2020) found that the follow-up rate of married patients with lung cancer was higher. These physical supports may be associated with a lower risk of cardiovascular death.

The influence of mental factors on cardiovascular disease cannot be ignored. Married people acquired more positive emotional support from their partners and so had a certain preventive effect on CVD (Wong et al., 2018). On the one hand, adverse mental factors promoted the occurrence and development of cardiovascular diseases in patients. After the diagnosis of cancer, patients bears a larger psychological shock (Kaiser et al., 2010), which may eventually deteriorate CVD events risk elements such as hypertension, hyperlipemia, atherosclerosis and diabetes (Arestedt et al., 2013). On the other hand, unmarried patients had a higher risk of major depression, and to some extent, it is possible to be a mediator of the association between marital status and adherence to medical recommendations (DiMatteo et al., 2000), affecting the progress of CVD events. On the contrary, the married patients benefit from the spiritual support of their partners, which effectively slows down the development of CVD. Partner can often be known to play a vital role in sharing the emotional burden (Goldzweig et al., 2010; Luszczynska et al., 2013), which help to relieve psychological pressure and negative emotion of patients, so the married patients are at lower risk of presentation with cardiovascular disease, especially in the patients with heart failure (Arestedt et al., 2013).

Inflammatory mediators, endocrine dysfunction and changes in gene expression cause direct and serious damage to blood vessels physiologically. The ending of a marriage or the death of a spouse may cause high stress (Wong et al., 2018). That was likely result to immune dysfunction and inflammatory processes, and increase the susceptibility to cardiovascular disease (Segerstrom and Miller, 2004). Chin et al. showed that the saliva cortisol level of married people was lower (Chin et al., 2017). Another possible factor is that single people have shorter telomeres and are at higher risk of cardiovascular disease compared with other married or cohabiting people (Chen et al., 2021). Research had confirmed that acute psychological stress caused by cancer diagnosis may lead to vulnerable plaque rupture, thrombosis, or fatal arrhythmia (e.g., increased sympathetic tone, increased blood pressure, endothelial dysfunction; and hypercoagulable state) and emotional pain-related health damage behaviors, which will eventually be related to cardiovascular events (Harashima et al., 2019).

5. Limitations

There are some limitations in our research. Firstly, retrospective research has its own limitations. Due to the retrospective study design, our data cannot be randomly assigned to more accurately report the survival characteristics of lung cancer patients (Elbardissi et al., 2008; Oliveira et al., 2015). Secondly, the SEER database does not contain variables such as pre-diagnosis comorbidities, which may affect the final result (Martinez et al., 2017). Thirdly, although it can be considered that the assessment of marital status at the time of diagnosis is appropriate, we cannot assess the changes of their marital status after lung cancer is diagnosed (Aizer et al., 2013; Liu et al., 2019). Fourthly, our research data cannot describe in detail the physical and mental support of patients. Finally, SEER's database does not provide accurate marriage details, such as the duration and quality of marriage, which can affect the outcome of survival rates (Trivedi et al., 2008). Despite these limitations, our study is the first to explore the relationship between marital status and cardiovascular events in patients with lung cancer. In addition, our results are reliable as this study includes a very large sample size.

6. Conclusion

Marital status was an independent predictor, and had different associations on the risk of lung cancer patients suffering from cardiovascular disease. These findings indicate that we should pay attention to the impact of social factors on the prognosis and provide patients with more psychological support in clinical practice, not limiting to curing of disease. Therefore, patients can be supported to benefit from the medical model of "biological-psychological-social", which can significantly improve the cardiovascular survival rate of patients. Further investigation is needed to determine the clinical treatment and the sociodemographic characteristics of caring for lung cancer survivors.

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Availability of data and materia

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval

The SEER database is a publicly available resource with anonymized data, and specific ethical approval is not required for studies utilizing this data. 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.

Patient and public involvement

Neither the patients nor the public were involved in the design, conduct, reporting or dissemination plans of our research.

CRediT authorship contribution statement

Yanxian Lai: Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization. **Tianwang Guan:** Writing – original draft, Validation, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation. **Haifeng Zhang:** Writing – review & editing, Supervision, Conceptualization. **Yingyuan Zhang:** Validation, Methodology, Data curation. **Shenghui Zhang:** Validation, Methodology, Formal analysis. **Zhengxia Yang:** Validation, Methodology, Data curation. **Cheng Liu:** Writing – review & editing, Validation, Methodology, Investigation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pmedr.2024.102846.

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