Original Article
Analysis of the influence of marital status on prognosis of prostate cancer patients based on big data

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Abstract: Objective: To study the effect of different marital status on the prognosis of patients with prostate cancer. Methods: The general data of 169,533 patients with prostate cancer confirmed by biopsy or surgery in SEER database were retrospectively analyzed. The COX univariate analysis was performed first, and the meaningful variables of the univariate analysis were incorporated into the Cox proportional hazards model for multivariate analysis, and the independent factors affecting the prognosis of patients with prostate cancer were obtained. Results: The collected patients accounted for 59% of married patients and 22% of unmarried patients. COX multivariate analysis, the results showed: age (HR: 1.063; P<0.001), tumor differentiation grade (HR: 1.367; P<0.001), marital status: married (HR: 0.648; P<0.001), unmarried (HR: 0.602; P<0.001), bone metastasis (HR: 6.077; P<0.001), brain metastasis (HR: 2.296; P<0.001), liver metastasis (HR: 2.582; P<0.001), lung metastasis (HR: 1.256; P<0.001), distant lymph node metastasis (HR: 1.698; P<0.001), T stage (HR: 1.047; P>0.005), N stage (HR: 0.970; P>0.005), M stage (HR: 0.880; P>0.005) were all factors affecting the prognosis of patients with prostate cancer. The average survival time of married patients was 16.05±10.32 months, and the average survival time of unmarried patients was 15.46±10.37 months. The average survival time of married patients was longer than that of unmarried patients (X^2=1173.133; P<0.001), and the difference was statistically significant. Conclusion: Based on big data analysis, marital status has a great influence on postoperative prostate cancer patients, and the survival time of married prostate cancer patients is longer than that of unmarried patients.

Keywords: Prostate cancer, marital status, SEER database, survival analysis

Introduction

Globally, prostate cancer is the second most common malignant tumor in men. According to the data of the Global Cancer Research Organization, in 2018, there were more than 1.276 million new cases of prostate cancer in the world, and more than 359,000 patients died of prostate cancer. The world population-standardized incidence rate and world population-standardized mortality rate were 29.3/100,000 and 7.6/100,000 [1]. Despite extensive research on prostate cancer, only a few risk factors for prostate cancer have been identified, including age, Gleason score, PSA level, tumor differentiation, family history, ethnicity, and certain genetic polymorphisms. The lack of modifiable risk factors limits the etiological prevention, early detection, early diagnosis, and early treatment of prostate cancer

[2, 3]. Although foreign research results have shown that there is a close relationship between the incidence of prostate cancer and changes in sexual behavior and marital status, the relevant research conclusions are not unified, or conflict with each other. Studies have shown that marital status does not affect the clinical and pathological characteristics of radical prostatectomy patients treated in high-volume centers. In addition, marital status did not affect biochemical recurrence-free and metastasis-free survival after radical prostatectomy [4, 5]. Therefore, it is necessary to clarify the effect of different marital status on cancer patients after surgery, especially the mechanism of the effect on prostate cancer. Due to cultural differences, the records on marital status of prostate cancer patients in my country lack credibility. Therefore, this study conducted a statistical analysis by collecting the prognosis

of prostate cancer patients with different marital status in the National Cancer Institute Surveillance, Epidemiology and Outcomes Database (SEER database), so as to clarify the relationship between marital status and prostate cancer impact on patient outcomes.

Materials and methods

Source

Pathologically diagnosed patients with prostate cancer from 2013 to 2018 in the National Cancer Institute Surveillance, Epidemiology, and Outcomes Database (SEER database) were collected by SEERSTAT software. Inclusion criteria: 1. The year of diagnosis was from 2013 to 2018; 2. The tumor site was prostate cancer; 3. The patient underwent radical prostatectomy (including open resection and laparoscopic resection). Exclusion criteria: 1. Concomitant with other types of cancer (excluding secondary cancers); 2. Incomplete follow-up information of the patient, including the type of the patient's tumor, the degree of tumor differentiation, and the clinical stage of the patient's cancer; 3. Short-term Cases who died within (one month). A total of 169,533 prostate cancer patients who met the above inclusion and exclusion criteria were collected, and the patients were staged by the seventh edition of the UICC/AJCCTNM staging system.

Information collection

The patient's age, cancer classification, marital status, bone metastasis, brain metastasis, liver metastasis, lung metastasis, lymph node metastasis, TNM staging of cancer, patient survival time, and the patient's living conditions at the end of observation, etc.

Statistical methods

SPSS 16.0 was used for statistical analysis, and the COX proportional hazards model was used as the research model. Firstly, we put the collected factors that may affect the prognosis of prostate cancer patients into the COX model for univariate analysis, and then use the COX model to conduct multivariate analysis to obtain independent factors that affect the prognosis of prostate cancer patients. We use the mean ± standard deviation for the measurement data that meet the conditions of normal distribution, and the comparison between the two groups passes the t test; the data that does not meet the conditions of normal distribution is expressed as the median, and the comparison between the two groups The Wilcoxon rank sum test was used; the comparison between rates was statistically significant using the χ^2 test $P<0.05$.

Result

General situation

The general condition of the patients was (66.45±8.01) years old in the married group and (65.63±8.90) years old in the single group. The number of people with lymphatic metastasis, bone metastasis, brain metastasis, liver metastasis and lung metastasis in the married group (respectively: 1.7%, 6.6%, 0.1%, 0.3%, 0.7%) were all higher than those in the single group. Brain metastases, liver metastases, and lung metastases were small (3.2%, 12%, 0.2%, 0.7%, and 1.2%, respectively). The age, tumor grade, lymphatic metastasis, bone metastasis, brain metastasis, liver metastasis, and lung metastasis of the married group and the single group were all $P<0.001$, and these factors were all related to prostate cancer (**Table 1**). The average postoperative survival of the married prostate cancer patients was 16.05±10.32 months, and the average postoperative survival of the unmarried prostate cancer patients was 15.46±10.37 months. The average survival time of married prostate cancer patients was longer than that of unmarried prostate cancer patients (χ^2=1173.133; $P<0.001$), so the difference was statistically significant.

Univariate analysis

The collected factors that may affect the prognosis of patients with prostate cancer were included in the COX risk proportional model for univariate analysis. The results obtained after the univariate analysis were: age (χ^2=4618.474; $P<0.001$), pathological grade (χ^2=3468.554; $P<0.001$), marital status (χ^2=1173.133; $P<0.001$), bone metastasis (χ^2=22469.056; $P<0.001$), brain metastasis (χ^2=1131.953; $P<0.001$), liver metastasis (χ^2=5225.860; $P<0.001$), lung metastasis (χ^2=3749.134; $P<0.001$), distant lymph node metastasis (χ^2=5255.897; $P<0.001$), T stage

Table 1. General information of patients with prostate cancer

variable		Total (169533)	marital status		P
			married	unmarried	
Age			66.45±8.01	65.63±8.90	P<0.001
BIOGrade	Grade I		16975 (17%)	5739 (15.3%)	P<0.001
	Grade II		28791 (28.9%)	9793 (26.1%)	
	Grade III		15980 (16%)	6420 (17.1%)	
	Grade IV		31 (0%)	16 (0%)	
Distant lymph node metastases			1717 (1.7%)	1213 (3.2%)	P<0.001
Done metastasis			6539 (6.6%)	4483 (12%)	P<0.001
Brain metastasis			74 (0.1%)	70 (0.2%)	P<0.001
Liver metastasis			325 (0.3%)	266 (0.7%)	P<0.001
Lung metastasis			691 (0.7%)	450 (1.2%)	P<0.001

(χ^2=0.289; P>0.05), N stage (χ^2=1.235; P>0.05), M stage (χ^2=0.613; P>0.05). Although the univariate analysis of TNM stage P>0.05, the difference was not statistically significant, but combined with clinical experience and related literature reports, it is related to the prognosis of prostate cancer.

Multi-factor analysis

The results of the above univariate analysis were analyzed by COX proportional hazards model, and the factors affecting the prognosis of patients with prostate cancer (**Table 2**) were: age, tumor differentiation grade, marital status, bone metastasis, brain metastasis, and liver metastasis, lung metastasis, distant lymph node metastasis, T stage, N stage, and M stage are all factors that affect the prognosis of patients with prostate cancer, and the survival curve is drawn (**Figure 1**).

Discussion

The incidence and progression of prostate cancer are inextricably linked with sex hormones. In 1941, Professors Huggind and Hodges discovered that androgens are an essential substance for the growth and development of prostate cancer cells. A series of studies on hormone therapy for prostate cancer have thus started [6]. In a study by Holmbo et al., after long-term follow-up of 1113 men, they found that testosterone levels in different marital status were lower in married than unmarried. The German scholar Exton et al. have also obtained similar results. In their study, they found that after 3 weeks of abstinence from men, the tes-

tosterone levels of these men were significantly increased, and then the subjects were allowed to ejaculate through masturbation. After ejaculation, they found that the subjects' testosterone levels had Therefore, the study concluded that testosterone levels in patients with different marital status are different, and testosterone is also released in large quantities during sexual intercourse [7, 8], and married men are usually more regular than unmarried men. Therefore, married men have better prostate cancer outcomes than unmarried men.

At the same time, during sexual intercourse, men release a series of signals that affect male social behavior and hormone balance, including prolactin, oxytocin, testosterone, vasopressin, and dopamine [9]. At the physiological level, some studies have shown that marital status may have a certain influence on the improvement of patients' cardiovascular, endocrine and immune function, and the quality of marriage may play a decisive role in the existence and magnitude of this influence [10, 11]. In other cancer patients, there is sufficient evidence to prove that after receiving sufficient social support, the patient's blood cortisol level has a significant decrease, and this change in cortisol level is related to natural killer cells and survival rate of cancer patients related. After the cortisol level decreased, the natural killer cell count of cancer patients also decreased significantly [12, 13], thus the survival rate of patients was significantly improved, indicating that cancer patients have a good marital status and better prognosis. There is a very important connection. And a recent study showed that individuals with prostate cancer who were sep-

Table 2. Multivariate analysis table of prostate cancer patients with different marital status

| variable	B	SE	Wald	df	P	HR
Age	0.061	0.002	799.119	1.000	0.000	1.063
BIOGrade	0.312	0.026	142.147	1.000	0.000	1.367
Marital status	-	-	200.922	2.000	0.000	-
Married	-0.433	0.057	57.191	1.000	0.000	0.648
Unmarried	-0.508	0.036	196.507	1.000	0.000	0.602
Bone metastasis	1.805	0.044	1652.462	1.000	0.000	6.077
Brain metastasis	0.831	0.267	9.692	1.000	0.002	2.296
Liver metastasis	1.048	0.114	84.108	1.000	0.000	2.852
Lung metastasis	0.228	0.105	4.726	1.000	0.030	1.256
Distant lymph node metastases	0.529	0.068	60.550	1.000	0.000	1.698
T stage	0.046	0.058	0.636	1.000	0.425	1.047
N stage	-0.030	0.063	0.231	1.000	0.631	0.970
M stage	-0.128	0.120	1.136	1.000	0.286	0.880
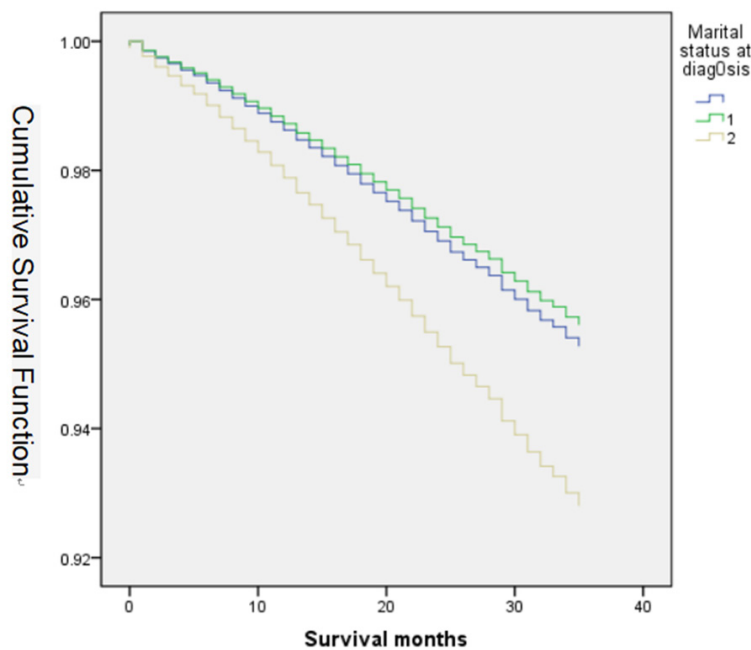
Figure 1. Survival curves of prostate cancer patients in two marital statuses. Note: 1 is married, 2 is unmarried (no domestic partner), separated, divorced, single, widowed. Blue represents a group representing unknown marital status.

Family relationships, as a form of social support, play a very important role in the individual's health and pursuit of health. Among the factors influencing the prognosis of prostate cancer patients, family relationships, especially marital status, may run through the whole process of the occurrence, development, diagnosis and treatment of prostate cancer patients. First, married and unmarried individuals differ greatly in their lifestyle choices after a diagnosis of prostate cancer. Married men lead healthier lifestyles after diagnosis compared to unmarried men. Smoking and alcohol use were more common among single, divorced, and widowed identities, while physical inactivity was more common among men with inadequate social support. Second, studies have shown that women often monitor the health behavior of their family members and ensure that family members play an important role in seeking medical care [16, 17]. Evidence suggests that men seldom actively seek prostate cancer screening in the absence of clinical symptoms of prostate cancer, and their wives prefer screening for their husbands [18, 19]. Therefore, at the diagnosis stage of prostate

arated from their spouses at diagnosis had significantly lower individual survival rates [14]. This finding shares the same path as some previous studies, which have previously reported support that patient declines in health are associated with a patient's transition from married to divorced, rather than from married to widowed, or from single or divorced to married [15].

cancer patients, marital status may affect the timing of diagnosis, as spouses may encourage patients to actively seek medical help because of urinary symptoms in patients with prostate cancer.

After being diagnosed with prostate cancer, in addition to surgery, chemotherapy and biological targeted therapy, they also face practical, emotional and psychological needs that are very important, but in fact these needs are often undetected and Satisfy [20]. Notably, for unmarried men, distress peaked when prostate cancer was first diagnosed, and peaked again when the cancer recurred. For married men, the peak of this distress appears to be delayed [21]. In other groups of cancer survivors, up to 66% of cancer patients experience long-term psychological distress and up to 30% experience significant anxiety problems, ranging from 20% to 35% of these patients Depression [22]. An Australian survey found that unfortunately only 25% of cancer patients with depression had ever received counselling [23]. A recent European study showed that patients diagnosed with advanced disease or with distant metastases had twice the risk of suicide compared with their peers, demonstrating the importance of early identification of symptoms of depression in patients with prostate cancer and optimal treatment [24]. Married men who are diagnosed with prostate cancer receive care from their spouses, and love, hope and faith are considered important motivators in the lives of prostate cancer patients and their wives. With the support of the spouse and the responsibility of the family, prostate cancer patients can regain their hope of life, and with the encouragement of their spouses, they can take active coping measures and listen to the advice of specialists for active treatment. Second, the spouse of a patient with prostate cancer may influence the patient's appointment and transport to a urologist for follow-up observation, as well as adjuvant chemotherapy, adjuvant radiotherapy, or targeted therapy. The patient's spouse can greatly influence the patient's compliance. There is an important and substantial link between social support and adherence, which also suggests that adherence is also an important mediating mechanism between social support and health outcomes [25, 26]. The author believes that after the diagnosis of prostate cancer patients with

partners, out of family responsibility and the care and help from their partners, compared with patients without partners, they will have a better prognosis. In addition, prostate cancer patients with partners were also more compliant with postoperative adjuvant therapy than those without partners. Therefore, the results of this study are in line with the actual clinical situation.

Although this study collected a large number of samples from SEER data to conduct a comprehensive and detailed analysis of the influence of marital status on prostate cancer patients after surgery, it clarified the role of marital status in the whole process of screening, diagnosis and treatment of prostate cancer patients. However, this study still has various limitations. First, the SEER database lacks records of postoperative chemotherapy and other treatments for prostate cancer patients. Secondly, the SEER database does not include details other than the marital status of each person, including the length of the patient's marriage at the time of diagnosis, the strength of the patient's happiness in this marriage, and previous marriage history, etc. In addition, some people may live with their partners at the time of diagnosis, but they are still classified as "never married". Finally, since most of the cases included in the SEER database are whites and blacks in the United States, and yellows in my country, due to different races, the applicability of the results of this study to Chinese patients with prostate cancer requires more follow-up studies. It also provides directions for future research in this area.

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Disclosure of conflict of interest

None.

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