Influence of marital status on overall survival in adult chordoma patients: A SEER-based study

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Abstract

Background. As a rare primary bone tumor, no studies have reported the relationship between prognosis and marital status in patients with chordoma.

Methods. We classified chordoma patients identified from the Surveillance, Epidemiology, and End Results (SEER) database from 1975 to 2016 into four groups: married, divorced/separated, widowed and single groups. Kaplan-Meier curves with log-rank test and Cox regression were used to analyse the effect of marital status on overall survival (OS).

Results. A total of 1,080 patients were included in the study, 700 (64.8%) were married, 88 (8.1%) were divorced/separated, 78 (7.2%) were widowed and 214 (19.8%) were single. Among the four groups, the 5-year OS (45.2%), 10-year OS (12.5%) and median OS (56.0 months) were the lowest in the widowed group. After including age, sex, primary site, marital status, disease stage, tumor size, histological type, and treatment pattern, multivariate analysis showed that marital status was still an independent risk factor for chordoma patients, widowed patients have the lowest OS (hazard ratio [HR]: 1.71; 95% confidence interval [CI]: 1.25–2.33, p<0.001) compared with married patients. Similar results were observed after stratifying the primary site and disease stage.

Conclusion. Marital status was an independent prognostic indicator for adult chordoma patients, and marital status was conducive to patient survival. Compared with married patients, widowed patients have a higher risk of death.

Introduction

Chordomas was a rare bone tumor that accounts for approximately 20% of primary spinal tumors and 3% of all bone tumors(1). It was a rare and locally destructive tumor that originates from the residual tissue of the embryonic spinal cord structure and can occur
anywhere along the midline bone, especially the slope of the skull base, the saddle area, and the tail of the spine (2, 3). The survey of European and American population shows that the incidence rate of chordomas was about 0.08/100,000, which was slightly higher in male (4). Although chordomas grow slowly, due to its aggressive and easy metastasis, the chordoma can infiltrate the surrounding bone structure (5). Due to its high recurrence rate, which seriously affects the survival rate and the quality of life of patients, the total 5-year survival rate was only about 67% (6).

There were many factors affect the prognosis of chordoma patients. Previous studies have shown that surgical margin and distant metastasis were independent prognostic factors in patients with chordoma (7, 8). In addition, patient age, histological type and tumor size may also affect the survival of chordoma patients (7, 9, 10).

Marital status has always been closely related to the prognosis of cancer. Many studies have confirmed that marital status may affect the prognosis of various tumors, including osteosarcoma (11), chondrosarcoma (12), penile cancer (13) and breast cancer (14). However, retrospective or prospective studies have not been conducted to report whether marital status affects the survival of adult chordoma patients. Therefore, the purpose of this study was to investigate the effect of marital status on the survival of chordoma patients according to the Surveillance, Epidemiology, and End Results (SEER) database.

Materials & Methods

Patients selection

The patients we studied were selected from the Surveillance Epidemiology and End Results (SEER) database funded by the National Cancer Institute. The SEER database covers approximately 28% of the US population and includes demographic information and cancer characteristics, such as year of diagnosis, age, origin, race, insurance, marital
status, primary tumour location, income status, tumour grade, disease stage, histological type, Tumor-Node-Metastasis (TNM) stage, treatment modality and survival time (15). The National Cancer Institute's SEER*Stat software (version 8.3.6; SEER 18 Regs Custom Data (with additional treatment fields), Nov 2018 Sub (1975–2016 varying) database) was used in this study. We included 1,521 patients diagnosed with chordoma between January 1st, 1975 and December 31st, 2016 based on the International Classification of Diseases for Oncology (9370: chordoma, NOS; 9371: chondroid chordoma; 9372: dedifferentiated chordoma).

The exclusion criteria were as follows: (a) not one primary tumor only (n = 298); (b) primary site code not 41.0, 41.2, 41.4 (n = 9); (c) marital status unknown or domestic partner (n = 61); (d) unknown survival time (n = 2); (e) patients under 18 years of age (n = 71). Finally, based on the above screening criteria, we left 1,080 eligible patients diagnosed with chordoma.

Study Variables

Variable definition information about year of diagnosis, age at diagnosis, sex, primary site, marital status, disease stage, tumor size, histological type, treatment pattern (surgery (16), radiotherapy, chemotherapy) and survival time can be found in the SEER database. The starting point of the follow-up was the date of diagnosis of chordoma. The overall survival (OS) time is the length of time from the date of diagnosis to the end of the patient's follow-up or death.

Statistical analysis

Chi-square analysis was performed to evaluate clinical characteristics of four marital status in chordoma patients. Kaplan-Meier curve was used to estimate the factors related to the OS, 5-year OS and 10-year OS of chordoma patients, and the log-rank test was used
to analyzed the difference between the curves. Univariate and multivariate Cox regression models were performed to estimate the hazard ratios (HR) and 95% confidence intervals (CI) to analyze independent prognostic factors associated with chordoma patients. All statistical analyses used Statistical Package for the Social Sciences software (version 24.0; SPSS, Chicago, USA) and R version 3.5.3 (R Foundation for Statistical Computing, http://www.r-project.org/). Survminer package including in Kaplan-Meier analysis with log-rank testing was applied to conduct the survival data analysis and visualization (Drawing Survival Curves using 'ggplot2' [R package survminer version 0.2.0]). Univariable Cox proportional hazards regression and Multivariate Cox proportional hazards regression with Wald test was performed to determine risk factors associated with overall mortality and cancer-specific mortality. It was statistically significant when the P value is ≤ 0.05 (both sides).

Results

Demographic and clinicopathologic characteristics of chordoma patients

According to the inclusion and exclusion criteria in Fig. 1, our study included a total of 1,080 eligible chordoma patients from 1975 to 2017. The number of married group, divorced/separated group, widowed group and single group was 700 (64.8%), 88 (8.1%), 78 (7.2%) and 214 (19.8%), respectively. Table 1 shows the clinical characteristics and demographic of all adult chordoma patients. Chi-square test showed that marital status was related to diagnosis year (p = 0.014), age at diagnosis (p < 0.001), sex (p < 0.001), primary site (p = 0.019) and surgery (p < 0.001). With the increase of years, the proportion of chordoma patients also increased. In the whole cohort, the majority of patients were male (59.9%), the primary site was bones of skull and face and associated joints (40.4%), and the localized stage (40.9%). In addition, the proportion of widowed
patients over 60 years old (94.9%), female (73.1%) and surgery not performed (37.2%) was higher than other three groups.

Table 1
Baseline demographic and clinical characteristics of chordoma patients in our study.

| Characteristic                                      | Total No. (%) | Married No. (%) | Divorced/Separated No. (%) | Widowed No. (%) | Single No. (%) | P value |
|-----------------------------------------------------|---------------|-----------------|----------------------------|-----------------|----------------|---------|
| Year of diagnosis                                   |               |                 |                            |                 |                |         |
| 1975–1988                                           | 98 (9.1)      | 70 (10.0)       | 4 (4.5)                    | 12 (15.4)       | 12 (5.6)       | 0.014   |
| 1988–2002                                           | 262 (24.3)    | 181 (25.9)      | 19 (21.6)                  | 20 (25.6)       | 42 (19.6)      |
| 2003–2016                                           | 720 (66.7)    | 449 (64.1)      | 65 (73.9)                  | 46 (59.0)       | 160 (74.8)     |
| Age at diagnosis                                    |               |                 |                            |                 |                | < 0.001 |
| < 40                                                | 242 (22.4)    | 131 (18.7)      | 18 (20.5)                  | 0 (0.0)         | 93 (43.5)      |
| 40–60                                               | 412 (38.1)    | 294 (42.0)      | 35 (39.8)                  | 4 (5.1)         | 79 (36.9)      |
| > 60                                                | 426 (39.4)    | 275 (39.3)      | 35 (39.8)                  | 74 (94.9)       | 42 (19.6)      |
| Sex                                                 |               |                 |                            |                 |                | < 0.001 |
| Male                                                | 647 (59.9)    | 441 (63.4)      | 46 (52.3)                  | 21 (26.9)       | 136 (63.6)     |
| Female                                              | 433 (40.1)    | 256 (36.6)      | 42 (47.7)                  | 57 (73.1)       | 78 (36.4)      |
| Primary site                                        |               |                 |                            |                 |                | 0.019   |
| Bones of skull and face and associated joints       | 436 (40.4)    | 285 (40.7)      | 34 (38.6)                  | 17 (21.8)       | 100 (46.7)     |
| Vertebral column                                    | 279 (25.8)    | 179 (25.6)      | 25 (28.4)                  | 27 (34.6)       | 48 (22.4)      |
| Pelvic bone, sacrum, coccyx and associated joints   | 365 (33.8)    | 236 (33.7)      | 29 (33.0)                  | 34 (43.6)       | 66 (30.8)      |
| Disease stage                                       |               |                 |                            |                 |                | 0.587   |
| Localized                                           | 442 (40.9)    | 288 (41.1)      | 38 (43.2)                  | 30 (38.5)       | 86 (40.2)      |
| Regional                                            | 454 (42.0)    | 290 (41.4)      | 41 (46.6)                  | 32 (41.0)       | 91 (42.5)      |
| Distant                                             | 90 (8.3)      | 55 (7.9)        | 5 (5.7)                    | 7 (9.0)         | 23 (10.7)      |
| Unstaged                                            | 94 (8.7)      | 67 (9.6)        | 4 (4.5)                    | 9 (11.5)        | 14 (6.5)       |
| Tumor size                                          |               |                 |                            |                 |                | 0.084   |
| < 5 cm                                              | 357 (33.1)    | 229 (32.7)      | 32 (36.4)                  | 18 (23.1)       | 78 (36.4)      |
| 5-10 cm                                             | 256 (23.7)    | 155 (22.1)      | 21 (23.9)                  | 21 (26.9)       | 59 (27.6)      |
| > 10 cm                                             | 101 (9.4)     | 64 (9.1)        | 10 (11.4)                  | 5 (6.4)         | 22 (10.3)      |
| Unknown                                             | 366 (33.9)    | 252 (36.0)      | 25 (28.4)                  | 34 (43.6)       | 55 (25.7)      |
| Histologic al type                                   |               |                 |                            |                 |                | 0.953   |
| Conventional                                        | 1019 (94.4)   | 659 (94.1)      | 83 (94.3)                  | 75 (96.2)       | 202 (94.4)     |
| Chondroid chordoma | 54 (5.0) | 37 (5.3) | 4 (4.5) | 3 (3.8) | 10 (4.7) |
|---------------------|----------|----------|---------|---------|---------|
| Dedifferentiated chordoma | 7 (0.6) | 4 (0.6) | 1 (1.1) | 0 (0.0) | 2 (0.9) |
| Surgery | | | | | < 0.001 |
| Surgery not performed | 177 (16.4) | 99 (14.1) | 20 (22.7) | 29 (37.2) | 29 (13.6) |
| STR | 452 (41.9) | 295 (42.1) | 38 (43.2) | 23 (29.5) | 96 (44.9) |
| GTR | 301 (27.9) | 199 (28.4) | 23 (26.1) | 12 (15.4) | 67 (31.3) |
| Unknown extent of resection | 150 (13.9) | 107 (15.3) | 7 (8.0) | 14 (17.9) | 22 (10.3) |
| Radiotherapy | | | | | 0.734 |
| Yes | 544 (50.4) | 354 (50.6) | 48 (54.5) | 40 (51.3) | 101 (47.7) |
| No | 536 (49.6) | 346 (49.4) | 40 (45.5) | 38 (48.7) | 112 (52.3) |
| Chemothery | | | | | 0.639 |
| Yes | 40 (3.7) | 24 (3.4) | 3 (3.4) | 2 (2.6) | 11 (5.1) |
| No | 1040 (96.3) | 676 (96.6) | 85 (96.6) | 76 (97.4) | 203 (94.9) |

Note: P-value < 0.05 are shown in bold.
Abbreviations: STR, subtotal resection; GTR, gross total/radical resection.
Percentages may not total 100 because of rounding.

### Survival Of Patients With Chordoma

By analyzing the Kaplan-Meier curve with a log-rank test, we found that age at diagnosis (p < 0.001), marital status (p < 0.001), primary site (p < 0.001), disease stage (p < 0.001), tumor size (p < 0.001), histological type (p = 0.002), surgery (p < 0.001) and chemotherapy (p = 0.001) were associated with OS (Table 2). The 5-year OS and 10-year OS of married, divorced/separated, widowed and single patients were 73.7% and 51.5%, 69.5% and 42.8%, 45.2% and 12.5%, 75.6% and 57.0%, respectively, and the median survival time of married, divorced/separated, widowed and single patients was 125.0 months, 103.0 months, 56.0 months and 157.0 months, respectively (Fig. 2). Widowed patients had the lowest 5-year OS, 10-year OS and median overall survival time, while single patients had the highest 5-year OS, 10-year OS and median overall survival time.

After stratifying the primary site and disease stage, we still observed similar results (Table 3 and Fig. 3).
Table 2

Kaplan-Meier analysis overall survival for chordoma patients.

| Characteristic                                      | 5-year Overall Survival, % | 10-year Overall Survival, % | Median Overall Survival (months) | Kaplan-Meier Log Rank χ² test | P value |
|----------------------------------------------------|----------------------------|------------------------------|---------------------------------|-------------------------------|---------|
| Age at diagnosis                                   |                            |                              |                                 |                               |         |
| < 40                                                | 83.8                       | 74.4                         | -                               | 164.433                       | < 0.001 |
| 40–60                                              | 82.8                       | 58.7                         | 138.0                           |                               |         |
| > 60                                                | 54.3                       | 25.2                         | 68.0                            |                               |         |
| Sex                                                |                            |                              |                                 |                               |         |
| Male                                               | 70.5                       | 45.9                         | 105.0                           |                               |         |
| Female                                             | 72.9                       | 52.0                         | 132.0                           |                               |         |
| Marital status                                     |                            |                              |                                 |                               |         |
| Married                                            | 73.7                       | 51.5                         | 125.0                           |                               |         |
| Divorced/Separated                                 | 69.5                       | 42.8                         | 103.0                           |                               |         |
| Widowed                                            | 45.2                       | 12.5                         | 56.0                            |                               |         |
| Single                                             | 75.6                       | 57.0                         | 157.0                           |                               |         |
| Primary site                                       |                            |                              |                                 |                               |         |
| Bones of skull and face and associated joints      | 79.2                       | 65.1                         | 253.0                           |                               |         |
| Vertebral column                                   | 66.7                       | 37.9                         | 90.0                            |                               |         |
| Pelvic bone, sacrum, coccyx and associated joints  | 66.4                       | 40.1                         | 91.0                            |                               |         |
| Disease stage                                      |                            |                              |                                 |                               |         |
| Localized                                          | 77.6                       | 55.3                         | 147.0                           |                               |         |
| Regional                                           | 71.6                       | 48.2                         | 105.0                           |                               |         |
| Distant                                            | 49.7                       | 32.7                         | 53.0                            |                               |         |
| Unstaged                                           | 65.2                       | 39.0                         | 89.0                            |                               |         |
| Tumor size                                         |                            |                              |                                 |                               |         |
| < 5 cm                                              | 82.3                       | 70.9                         | 243.0                           |                               |         |
| 5-10 cm                                            | 70.5                       | 45.9                         | 106.0                           |                               |         |
| > 10 cm                                            | 55.9                       | 32.1                         | 70.0                            |                               |         |
| Unknown                                            | 67.0                       | 41.0                         | 94.0                            |                               |         |
| Histological type                                  |                            |                              |                                 |                               |         |
| Conventional chordoma                              | 71.5                       | 47.6                         | 110.0                           |                               |         |
| Chondroid chordoma                                 | 76.6                       | 72.8                         | -                               |                               |         |
| Dedifferentiated chordoma                          | 28.6                       | 28.6                         | 14.0                            |                               |         |
| Surgery                                            |                            |                              |                                 | 97.790                        | < 0.001 |
| Surgery not performed                              | 48.3                       | 26.0                         | 56.0                            |                               |         |
| STR                                                | 78.1                       | 58.5                         | 154.0                           |                               |         |
| GTR                                                | 82.9                       | 59.3                         | 178.0                           |                               |         |
| Unknown extent of resection                        | 59.1                       | 31.9                         | 80.0                            |                               |         |
| Radiotherapy                                        |                            |                              |                                 | 0.140                         | 0.708   |
| Yes                                                | 72.7                       | 47.1                         | 106.0                           |                               |         |
| No                                                 | 70.0                       | 49.7                         | 120.0                           |                               |         |
| Chemotherapy                                       |                            |                              |                                 | 11.445                        | 0.001   |
| Yes                                                | 47.9                       | 28.1                         | 51.0                            |                               |         |
| No                                                 | 72.4                       | 49.4                         | 119.0                           |                               |         |

Note: P-value < 0.05 are shown in bold.

Abbreviations: STR, subtotal resection; GTR, gross total/radical resection.
### Table 3
Kaplan-Meier analysis overall survival for chordoma patients based on primary site and disease stage.

| Characteristic                      | 5-year Overall Survival, % | 10-year Overall Survival, % | Median Overall Survival (months) | Kaplan-Meier Log Rank $\chi^2$ test | P value |
|-------------------------------------|----------------------------|------------------------------|----------------------------------|-------------------------------------|---------|
| **Primary site**                    |                            |                              |                                  |                                     |         |
| Bones of skull and face and associated joints |                            |                              |                                  |                                     |         |
| Married                             | 81.0                       | 68.3                         | 253.0                            | 35.462                              | < 0.001 |
| Divorced/Separated                 | 65.8                       | 44.9                         | 106.0                            |                                     |         |
| Widowed                             | 45.3                       | 18.1                         | 42.0                             | 38.754                              | < 0.001 |
| Single                              | 85.0                       | 71.8                         | -                                | 7.278                               | 0.064   |
| Vertebral column                   |                            |                              |                                  |                                     |         |
| Married                             | 68.2                       | 38.9                         | 97.0                             | 33.341                              | < 0.001 |
| Divorced/Separated                 | 82.8                       | 40.9                         | 102.0                            |                                     |         |
| Widowed                             | 32.5                       | 0.0                          | 33.0                             |                                     |         |
| Single                              | 74.1                       | 58.3                         | 141.0                            |                                     |         |
| Pelvic bone, sacrum, coccyx and associated joints |                            |                              |                                  |                                     |         |
| Married                             | 69.6                       | 44.9                         | 106.0                            |                                     |         |
| Divorced/Separated                 | 62.6                       | 45.0                         | 81.0                             |                                     |         |
| Widowed                             | 54.7                       | 19.6                         | 63.0                             |                                     |         |
| Single                              | 63.1                       | 32.4                         | 80.0                             |                                     |         |
| Disease stage                       |                            |                              |                                  |                                     |         |
| Localized                           |                            |                              |                                  |                                     |         |
| Married                             | 78.1                       | 57.8                         | 166.0                            | 33.341                              | < 0.001 |
| Divorced/Separated                 | 78.5                       | 58.5                         | 146.0                            |                                     |         |
| Widowed                             | 47.0                       | 10.4                         | 59.0                             |                                     |         |
| Single                              | 87.2                       | 65.8                         | 178.0                            |                                     |         |
| Regional                            |                            |                              |                                  |                                     |         |
| Married                             | 74.4                       | 50.3                         | 121.0                            | 31.648                              | < 0.001 |
| Divorced/Separated                 | 68.4                       | 40.7                         | 87.0                             |                                     |         |
| Widowed                             | 40.0                       | 13.3                         | 46.0                             |                                     |         |
| Single                              | 76.5                       | 59.7                         | -                                |                                     |         |
| Distant                             |                            |                              |                                  |                                     |         |
| Married                             | 59.4                       | 39.9                         | 80.0                             | 17.771                              | < 0.001 |
| Divorced/Separated                 | 0.0                        | 0.0                          | 12.0                             |                                     |         |
| Widowed                             | 28.6                       | 0.0                          | 16.0                             |                                     |         |
| Single                              | 42.3                       | 30.2                         | 32.0                             |                                     |         |

Note: P-value < 0.05 are shown in bold.

### Identification Of Prognostic Factors Of Chordoma Patients OS

Univariate and multivariate Cox regression were used to analyze the prognostic factors associated with OS of chordoma patients (Table 4). Univariate Cox regression analysis showed that age at diagnosis, marital status, primary site, disease stage, tumor size, histological type, surgery and chemotherapy were related factors (all $p < 0.05$) of OS in
chordoma patients (Fig. 4). Moreover, after the all factors were included in multivariate analysis, primary site, histological type, radiotherapy and chemotherapy were not independent risk factors for patients with chordoma (Fig. 5). In addition, multivariate analysis showed that widowed patients had the worst OS (HR: 1.71; 95% CI: 1.25–2.33, p < 0.001) compared with married patients.
Table 4
Univariate and multivariate analysis of overall survival rates.

| Characteristic                        | Univariate analysis | Multivariate analysis |
|---------------------------------------|---------------------|-----------------------|
|                                       | Hazard Ratio (95% CI) | P value | Hazard Ratio (95% CI) | P value |
| Age at diagnosis                      | < 0.001             |          | < 0.001             |          |
| <40                                   | Reference           |          | Reference           |          |
| 40–60                                 | 1.92 (1.40–2.64)    | < 0.001 | 1.97 (1.42–2.73)    | < 0.001 |
| >60                                   | 4.83 (3.57–6.53)    | < 0.001 | 4.28 (3.08–5.96)    | < 0.001 |
| Sex                                   |                      |          |                      |          |
| Male                                  | Reference            |          | Reference            |          |
| Female                                | 0.86 (0.71–1.04)    | 0.109   | 0.82 (0.67–1.00)    | 0.048   |
| Marital status                        | < 0.001             |          | < 0.001             |          |
| Married                               | Reference            |          | Reference            |          |
| Divorced/Separated                    | 1.29 (0.92–1.80)    | 0.136   | 1.42 (1.01–1.99)    | 0.046   |
| Widowed                               | 2.82 (2.13–3.73)    | < 0.001 | 1.71 (1.25–2.33)    | < 0.001 |
| Single                                | 0.83 (0.64–1.09)    | 0.175   | 1.16 (0.88–1.53)    | 0.303   |
| Primary site                          | < 0.001             |          | < 0.001             |          |
| Bones of skull and face and associated joints | Reference          |          | Reference            |          |
| Vertebral column                      | 1.93 (1.52–2.44)    | < 0.001 | 1.19 (0.92–1.54)    | 0.196   |
| Pelvic bone, sacrum, coccyx and associated joints | 1.94 (1.54–2.44)    | < 0.001 | 0.97 (0.73–1.28)    | 0.809   |
| Disease stage                         | < 0.001             |          | < 0.001             |          |
| Localized                             | Reference            |          | Reference            |          |
| Regional                              | 1.41 (1.13–1.75)    | 0.002   | 1.43 (1.15–1.79)    | 0.002   |
| Distant                               | 2.22 (1.62–3.05)    | < 0.001 | 2.31 (1.66–3.20)    | < 0.001 |
| Unstaged                              | 1.68 (1.24–2.29)    | 0.001   | 1.17 (0.85–1.62)    | 0.327   |
| Tumor size                            | < 0.001             |          | < 0.001             |          |
| <5 cm                                 | Reference            |          | Reference            |          |
| 5-10 cm                               | 1.96 (1.47–2.61)    | < 0.001 | 1.25 (0.91–1.71)    | 0.173   |
| >10 cm                                | 2.98 (2.08–4.27)    | < 0.001 | 1.85 (1.22–2.80)    | 0.004   |
| Unknown                               | 2.04 (1.57–2.65)    | < 0.001 | 1.50 (1.13–1.98)    | 0.005   |
| Histological type                     | 0.004               |          | 0.124               |          |
| Conventional chordoma                 | Reference            |          | Reference            |          |
| Chondroid chordoma                    | 0.52 (0.29–0.92)    | 0.025   | 0.78 (0.43–1.42)    | 0.419   |
| Dedifferentiated chordoma             | 3.03 (1.25–7.32)    | 0.014   | 2.11 (0.83–5.35)    | 0.115   |
| Surgery                               | < 0.001             |          | < 0.001             |          |
| Surgery not performed                 | Reference            |          | Reference            |          |
| STR                                   | 0.39 (0.30–0.52)    | < 0.001 | 0.58 (0.44–0.76)    | < 0.001 |
| GTR                                   | 0.35 (0.26–0.46)    | < 0.001 | 0.41 (0.30–0.55)    | < 0.001 |
| Unknown extent of resection           | 0.82 (0.63–1.07)    | 0.144   | 0.95 (0.71–1.26)    | 0.723   |
| Radiotherapy                          |                      |          |                      |          |
| Yes                                   | Reference            |          | Reference            |          |
| No                                    | 0.97 (0.80–1.16)    | 0.709   | 1.07 (0.89–1.30)    | 0.466   |
| Chemotherapy                          |                      |          |                      |          |
| Yes                                   | Reference            |          | Reference            |          |
| No                                    | 0.51 (0.34–0.76)    | 0.001   | 0.71 (0.47–1.09)    | 0.120   |

Abbreviations: STR, subtotal resection; GTR, gross total/radical resection.

In the stratification of primary site and disease stages (Table 5), univariate analysis showed that marital status was a risk factor for OS in the primary site of “Bones of skull and face and associated joints”, “Vertebral column”, and “Localized”, “Regional”, and “Distant” disease stages. In addition, multivariate analysis showed that marital status was
an independent risk factor for the primary site of “Bones of skull and face and associated joints” and “Vertebral column”. Moreover, although marital status was not an independent risk factor for the prognosis of chordoma patients at the disease stages of “Localized”, “Regional”, and “Distant”, widowed patients were at higher risk of survival compared with married, divorced/separated or single patients.

Table 5

Univariate and multivariate analysis of overall survival rates based on primary site and disease stage.

| Characteristic                        | Univariate analysis | Multivariate analysis |
|---------------------------------------|---------------------|-----------------------|
|                                       | Hazard Ratio (95% CI) | P value  | Hazard Ratio (95% CI) | P value |
| Primary site                          |                     |                      |                       |         |
| Bones of skull and face and associated joints | < 0.001            |          | 0.017                |         |
| Married                               | Reference           |                      | Reference             |         |
| Divorced/Separated                    | 2.01 (1.14-3.56)    | 0.016               | 2.31 (1.26-4.22)      | 0.007   |
| Widowed                               | 4.33 (2.35-8.00)    | < 0.001             | 2.34 (1.18-4.65)      | 0.015   |
| Single                                | 0.74 (0.45-1.21)    | 0.233               | 1.15 (0.67-1.95)      | 0.618   |
| Vertebral column                      | < 0.001             |          |                      |         |
| Married                               | Reference           |                      | Reference             |         |
| Divorced/Separated                    | 0.81 (0.44-1.51)    | 0.514               | 0.94 (0.48-1.86)      | 0.863   |
| Widowed                               | 3.33 (2.11-5.26)    | < 0.001             | 2.43 (1.44-4.12)      | 0.001   |
| Single                                | 0.66 (0.39-1.10)    | 0.111               | 0.82 (0.48-1.43)      | 0.488   |
| Pelvic bone, sacrum, coccyx and associated joints | 0.064              |          | 0.277                |         |
| Married                               | Reference           |                      | Reference             |         |
| Divorced/Separated                    | 1.26 (0.72-2.19)    | 0.423               | 1.24 (0.69-2.25)      | 0.477   |
| Widowed                               | 1.74 (1.12-2.71)    | 0.014               | 0.96 (0.57-1.60)      | 0.867   |
| Single                                | 1.36 (0.90-2.05)    | 0.140               | 1.54 (0.99-2.38)      | 0.056   |
| Disease stage                         |                     |                      |                       |         |
| Localized                             | < 0.001             |          | 0.483                |         |
| Married                               | Reference           |                      | Reference             |         |
| Divorced/Separated                    | 1.15 (0.62-2.17)    | 0.655               | 1.17 (0.60-2.29)      | 0.650   |
| Widowed                               | 3.54 (2.16-5.80)    | < 0.001             | 1.54 (0.89-2.67)      | 0.126   |
| Single                                | 0.79 (0.48-1.29)    | 0.340               | 1.20 (0.70-2.06)      | 0.519   |
| Regional                              | < 0.001             |          | 0.055                |         |
| Married                               | Reference           |                      | Reference             |         |
| Divorced/Separated                    | 1.22 (0.77-1.93)    | 0.401               | 1.31 (0.81-2.11)      | 0.266   |
| Widowed                               | 2.80 (1.82-4.32)    | < 0.001             | 1.95 (1.23-3.10)      | 0.005   |
| Single                                | 0.69 (0.45-1.04)    | 0.073               | 1.09 (0.71-1.67)      | 0.702   |
| Distant                               | < 0.001             |          | 0.159                |         |
| Married                               | Reference           |                      | Reference             |         |
| Divorced/Separated                    | 6.83 (2.25-20.73)   | 0.001               | 4.43 (1.19-16.53)     | 0.027   |
| Widowed                               | 2.78 (1.14-6.80)    | 0.025               | 3.14 (0.71-13.99)     | 0.133   |
| Single                                | 1.31 (0.69-2.48)    | 0.405               | 1.33 (0.58-3.04)      | 0.497   |

Discussion

In this 42-year retrospective study, we conducted univariate and multivariate Cox regression analysis of a large number of adult chordoma patients through the SEER database. We found that marital status was an independent risk factor for OS in patients
with adult chordoma, and marital status had a protective effect on the survival outcome of adult chordoma patients.

Marital status was widely considered to be an independent prognostic factor for many malignancies (17–20). However, the effect of marital status on adult chordoma patients has not been fully investigated. In this study, we first explored the effect of marital status on the OS of adult chordoma patients, and we found that married patients had better OS than divorced/separated and widowed patients. In multivariate analysis, after adjusting for diagnosis age, sex, marital status, primary site, disease stage, histological type, tumor size, surgery, radiotherapy and chemotherapy, marital status was still a risk factor for chordoma patients. The widowed group patients have the highest risk ratio (HR: 1.71; 95% CI: 1.25–2.33, p < 0.001), and the benefits of married patients remain. Compared with married, divorced/separated or single groups, widowed patients had the worst 5-year OS (45.2%), 10-year OS (12.5%) and median survival time (56.0 months). Similar results were observed in the subgroup analysis of primary site and disease stages.

The effect of marital status on the survival of chordoma patients has been studied before. Pan et al (8) analyzed 808 patients with primary spinal chordoma from 1973 to 2014 and found that marital status was not main factor affecting OS. Huang et al (16) also showed that marital status was not a prognostic factor for patients with primary spinal chordoma.

In our study, we included chordoma in the skull base, excluded all patients younger than 18 years old, and divided patients into four groups (married group, divorce/separation group, widowed group and single group). It was found that marital status was an independent prognostic factor for adult chordoma patients, which reduced the bias in case selection.

We speculate that the reasons for the worst survival of widowed patients may be as follows: first, the widowed group patient's proportion over 60 years old was 94.9%, while
the proportion of the elderly was significantly higher than other groups. Elderly patients are more likely to die due to their poor physical quality and more complications(21). Second, the proportion of women (73.1%) in widowed patients was highest, and women tend to suffer higher psychological troubles(22). In addition, the proportion of surgery not performed (37.2%) was highest in the widowed group, and inadequate treatment may also lead to deterioration of the prognosis of the widowed group(23). Moreover, widowed patients may have more complex psychological and mental stress due to the lack of a partner(24). On the contrary, married patients have better family conditions and can get more social support from their spouses and families(25).

There are limitations to be recognized in this study. First, this study was a retrospective study with obvious limitations. Second, marital status was recorded at the time of diagnosis, and this information may change during follow-up, which may affect the patient's OS. In addition, the specific contents of radiotherapy and chemotherapy were not included, which may also be a prognostic factor for chordoma patients.

Conclusions

Our study found that marital status was an independent prognostic indicator for adult chordoma patients and marital status was conducive to patient survival. Widowed patients had worst OS than other group patients, and similar results were observed in the subgroup analysis.

Abbreviations

SEER, Surveillance, Epidemiology and End Results; OS, overall survival; CT, Chemotherapy; RT, radiotherapy; HR, hazard ratios; CI, confidence interval; TNM, Tumor-Node-Metastasis.

Declarations
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Authors’ contributions CT, XN and HZ studied the concept and design. CT, RW and QL collected the data. CT, SW, GJ and PC analyzed and interpreted the data. CT, and RW drafted the manuscript. XN and HZ critically revised the manuscript for important intellectual content. CT and RW performed the statistical analysis.

Conflicts of interest We declare that there are no conflicts of interest between authors.

Consent for publication Not applicable.

Ethics approval and consent to participate This article does not contain any studies with human participants or animals performed by any of the authors.

Data Availability Statement The datasets generated for this study are available on request to the corresponding author.

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Figures
Chordoma, NOS; chondroid chordoma; dedifferentiated chordoma patients diagnosed between 1975-2016
n = 1,521

- Not on primary tumor only
  n = 298

- Primary site code not 41.0, 41.2, 41.4
  n = 9

- Marital status unknown or domestic partner
  n = 61

- Unknown survival time
  n = 2

- Patients under 18 years of age
  n = 71

1,080 patients cases included in analytic cohort

Figure 1

Schematic flow diagram of inclusion and exclusion criteria for our study cohort.
Figure 2

Kaplan-Meier survival curves according to marital status in chordoma patients.
Figure 3

Overall survival curves of chordoma patients according to marital status in different primary site and disease stage. A, Bones of skull and face and associated joints; B, Vertebral column; C, Pelvic bone, sacrum, coccyx and associated joints; D, Localized stage; E, Regional stage; F, Distant stage.
Figure 4

Forest plot of univariate Cox analyses of overall survival. The black squares on the transverse lines represent the hazard ratio (HR), and the transverse lines represent 95% CI.
**Figure 5**

Forest plot of multivariable Cox analyses of overall survival. The black squares on the transverse lines represent the hazard ratio (HR), and the transverse lines represent 95% CI.