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Research Paper

Prognostic factors for patients with chondrosarcoma: A survival analysis based on the Surveillance, Epidemiology, and End Results (SEER) database (1973–2012)

Nie Zhigang[1], Lu Qiang[1], Peng Hao*

Department of Orthopedics, Renmin Hospital of Wuhan University, 99 Zhangzhidong Road, Wuhan 430060, Hubei, China

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ABSTRACT

Current reports on prognostic factors for chondrosarcoma mainly involve patients in treatment centers. Few are based on multicenter or multi-eras. We analyzed existing data from the Surveillance, Epidemiology, and End Results (SEER) database to investigate the risk factors for survival outcomes. All patients with chondrosarcoma from 1973 to 2012 were identified. 3737 patients were eligible and included. In survival analysis, patient had good survival outcome if the patient was female, young, with localized stage, well grade, small tumor size, treated with surgery, while patient was male, old, with distant stage, undifferentiated grade, tumor size < 50 mm, located in vertebral or pelvic bones, underwent radiation had bad survival outcome. Surgery types from having best survival outcomes to worst were local excision, radical excision, amputation, no surgery. 'Well' and 'moderately' grade seems to be suitable for local excision, but 'poorly' and 'undifferentiated' grade suitable for wide local excision. Multivariate COX regression analysis showed year of diagnosis, sex, age of diagnosis, stage, grade, tumor site, surgery, radiation were independent risk factors. Year of diagnosis, sex, age of diagnosis, stage, grade, tumor site, surgery, radiation were independent risk factors. Excision is a better treatment than amputation. Doctors can use wide local excision to treat chondrosarcoma, especially when encountering high grade chondrosarcoma or pelvic chondrosarcoma.

1. Introduction

Chondrosarcoma is the second most common malignancy of skeletal system cancers following osteosarcoma and the treatment of it is challenging for orthopedic oncologists [1]. It is less sensitive to radiation or chemotherapy and the only therapy hitherto proved to be effective is surgical excision [2]. Metastasis has been confirmed to be associated with worse survival outcome of patients with chondrosarcoma [3,4]. However, it is difficult to correlate metastasis potential with histological features under the microscope [1]. Therefore, it is critical to study the risk factors and the effects of different treatments, on the survival outcome of chondrosarcoma.

Prognoses for chondrosarcoma have been studied in single center trials [5], meta-analysis [6] and systematic reviews [1]. Few studies analyse a sample size as large as the Surveillance, Epidemiology, and End Results (SEER) program. SEER covers 17 geographically defined registries and approximately 26% of the U.S. population, which contains a great amount of data for all kinds of tumors from 1973 to now.

In this study, we obtained data from the SEER program, and selected all patients with chondrosarcoma between 1973 and 2012. We investigated the influence of 15 variables on the survival rate of chondrosarcoma using multivariate COX regression analysis. We then performed a pairwise comparison of these factors and analyzed the impact of different therapeutic strategies on the survival rates. We aimed to identify useful factors for the prevention and treatment of chondrosarcoma.

2. Patients and methods

2.1. Data source

All data were obtained from the Surveillance, Epidemiology, and End Results (SEER) program and the SEER*Stat application (version 8.3.4) was used for analysis. We selected patients with chondrosarcoma from 1973 to 2012. Histologic Type ICD-O-3 in the application was input 9220 and Primary Site-Lableled were input C40.0–C41.9 in the

* Corresponding author.
E-mail address: penghaowhu123@163.com (H. Peng).
[1] Both authors contributed equally to this work.

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software to represent chondrosarcoma, NOS. 3737 cases were identified. Survival outcomes were analyzed according to 15 variables.

2.2. Study design

These 15 factors can be split into 3 categories: patient related factors (year of diagnosis, and age of diagnosis, sex, race, CHSDA region, and whether they were from rural or urban areas), tumor related factors (stage, grade, tumor size, laterality, tumor site) and treatment related factors (surgery, surgery type, radiation, treatment).

We divided year of diagnosis into 4 groups: 1973–1982, 1983–1992, 1993–2002, and 2013–2012. Age at diagnosis was also divided into 4 groups: 00–24 years, 25–49 years, 50–69 years, 70 + years. Races determined were White, Black and Other (American Indian/AK Native, Asian/Pacific Islander). CHSDA region was divided as East, Northern Plains, Pacific Coast and Southwest. Rural or urban were defined as urban and rural according to whether the patient was in a metropolitan area. Stages of cancer were either 'localized', 'regional' or 'distant'. In terms of grade patients were either 'well differentiated', 'moderately differentiated', 'poorly differentiated', or 'undifferentiated'. We identified 4 groups regarding tumor size: <50 mm, 50–79 mm, 80–99 mm and ≥ 100 mm. Tumor laterality was categorized as being right or left. In respect of treatment patients either had no surgery, local excision, radical excision or amputation. For tumor site the following were identified: upper limb was the combination of C40.0 and C40.1, lower limb was the combination of C40.2 and C40.3, skull and mandible was the combination of C41.0 and C41.1, chest bones was C41.3, vertebral and pelvic bones were combinations of C41.2 and C41.4.

There is a lack of data for all 3737 patients with respect to laterality, surgery type and tumor size. Information on laterality was available for 2670 patients. Information on surgery type was only available for 2319 patients and all available records were dated from 1998. For tumor size records began from 2004 with only 1215 cases. Therefore, in the survival curve, the x-axis for surgery type and tumor size did not correspond to 40 years.

2.3. Statistical analysis

SEER*Stat application (version 8.3.4) was used and we collected data for each patient from case listing sessions. These data were then analyzed using SPSS version 17.0 (SPSS, Chicago, IL, USA). Analysis was done on five-year survival rate, log-rank testing, pairwise comparison, univariate analysis and multivariate COX regression. 15 factors were considered. Laterality, tumor size and surgery type had incomplete data. In addition, surgery type and treatment overlapped with other factors. As such these 4 factors were excluded. Only 11 factors were included and analyzed by multivariate COX regression. Model 1 includes all 11 factors whereas Model 2 only includes 8 factors as 3 factors were excluded on the basis that they had no significant difference in univariate analysis. We also compared outcomes between surgery types wholly and at the same stage and grade. Number of cases at each situation, the order from best survival outcomes to worst, and pairwise comparisons were analyzed, respectively. Relationships between surgery, radiation and metastasis were subsequently analyzed to figure out the influence of treatment type on survival.

3. Results

3.1. The five-year survival rate, univariate analysis and pairwise comparisons

Table 1 conducted five-year survival rates and univariate analyses for 15 factors. Fig. 1 consists of drawn survival curves and presented results of pairwise comparisons on pictures. From the table and the figure, we can see prognosis of chondrosarcoma getting better when comparing outcomes by decade. 1973–1982 had the worst five-year survival rate (64.4%), whereas 2003–2012 had the best five-year survival rate (77.6%). Female patients had better survival outcome than male ($P < 0.001$). Survival of chondrosarcoma got worse as age increased, and each group (00–24 years, 25–49 years, 50–69 years, 70+ years) had significant difference ($P < 0.05$ for all). No significant differences were found between different races ($P > 0.05$) and different CHSDA regions ($P > 0.05$). There was no significant difference in survival rates for patients from rural and urban areas ($P > 0.05$). There were, however, significant differences for stage in pairwise comparisons and whole comparison ($P < 0.001$ for all). 'Localized' was best, followed by 'regional', and 'distant' being the worst. A similar result was shown for grade of chondrosarcoma. Patients with 'well' grade had better outcomes than those with 'undifferentiated' grade. The differences was more obvious ($P < 0.001$ for all). The most prominent thing shown in the 9th picture of the survival curve was that tumor size ≥ 100 mm had the lowest survival rate ($P < 0.05$). As tumor size increases prognosis becomes poorer. Whether the tumor was located on the left or right side had no effect on survival rates ($P > 0.05$). Tumors located in vertebral and pelvic bones had worst prognosis ($P < 0.001$). Those located in other sites had no differences between each other. Patients who underwent surgery had better survival rates than who not ($P < 0.001$). When compared with each other, the surgery type groups from having best survival outcomes to worst were local excision, radical excision, amputation, no surgery. Every pairwise comparison between surgery types shows a significant difference ($P < 0.05$ for all). Patient who underwent radiation had worse prognosis than those who did not ($P < 0.001$). When looking at every pairwise comparison, it is clear that treatment methods from having the best survival outcomes to worst were as follows: surgery, surgery + radiation, none, radiation ($P < 0.001$ for all). From the results of the five-year survival rate statistics it is interesting to see that 'distant' stage, 'undifferentiated' grade had a five-year survival rate lower than 30%. Moreover, more situations had five-year survival rates higher than 80%. In addition, the five-year survival rate of patients who underwent radiation but did not underwent surgery was 17.3%, which was in shark contrast to 'radiation' (49.9%) and 'no surgery' (43.0%).

3.2. Association between surgery type and survival outcome

The relationship between surgery type and survival outcomes was further analyzed as stage and grade to avoid confusion. Results are shown in Table 2. From the table, we can see more patients at the 'localized' stage underwent excision and less patients underwent amputation. Patients at a 'distant' stage tended to not be surgically treated. Fewer patients with 'well' grade underwent amputation. From looking at the effect of surgery type on survival we can see the consistency of the order from best to worst (excision, amputation, and no surgery) except that we cannot determine the order of local excision and radical excision. We found that radical resection has a better outcome for higher grade chondrosarcoma ('poorly' and 'undifferentiated'). But local resection appears to be better for lower grade chondrosarcoma ('well' and 'moderately').

3.3. Association between treatment type and survival outcome

We identified patients with 'distant' stage in the SEER database as metastatic patients. Analysis of the relationship between treatment types and metastasis in Table 3 shows that patients who underwent single radiation had the highest metastasis rate (at 41.4% shown in the table). Patients who underwent single surgery had lowest rate of metastasis at 4.4%. Only 6.5% of all patients who did not undergo radiation were metastatic patients. 22% of all patients who did undergo radiation were metastatic patients.