Comparison of the clinical outcomes and prognostic factors of dedifferentiated chondrosarcoma and chondroblastic osteosarcoma: a population-based analysis

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Research

Keywords: dedifferentiated chondrosarcoma, chondroblastic osteosarcoma, chemotherapy, outcome, prognostic factors, SEER

Posted Date: April 23rd, 2020

DOI: https://doi.org/10.21203/rs.3.rs-23594/v1

Abstract

Background

Dedifferentiated chondrosarcoma (DDC) and chondroblastic osteosarcoma (COS) have some common morphological characteristics by pathology and involve the same surgical methods and chemotherapy regimen. We explored the prognostic differences and factors of patients with DDC and COS with similar pathological features to analyze the prognostic factors and effect of chemotherapy on the prognosis of each type.

Methods

From the SEER database, we included 228 patients with DDC and 631 patients with COS who underwent surgery from 1975 to 2016. Patient age was stratified with X-tile, and prognosis was analyzed by the Kaplan-Meier method and Cox proportional hazard regression.

Results

The 3- and 5-year overall survival (OS) rates for DDC were 33.3% and 26.5%, respectively, and the 3- and 5-year OS rates for COS were 71.5% and 63.8%, respectively. Compared with COS, DDC had an older onset age, a higher proportion of white patients, an increased likelihood of occurrence in soft tissue, a higher pathological grade, a larger tumor volume, more patients with M1-stage, a higher AJCC stage and a lower chemotherapy utilization rate. Univariate analysis showed that age, M1 stage and high tumor stage were negatively correlated with DDC patient prognosis, with a worse prognosis for patients with lung metastasis. In the multivariate analysis, higher tumor stage was an independent factor for reducing OS in DDC. Univariate analysis showed that COS patients were older and male; had tumors located in the pelvis; had high T-, M-, and AJCC-stage tumors; and had lung metastasis. Moreover, no chemotherapy was negatively correlated with patient prognosis. Furthermore, age, male sex and high tumor stage were independent factors for reducing OS in COS.

Conclusion

The OS of DDC patients is worse than that of COS patients. Chemotherapy cannot benefit patients with DDC. For COS patients, further exploration of the survival benefits of chemotherapy is needed.

Background

Dedifferentiated chondrosarcoma (DDC) and chondroblastic osteosarcoma (COS) are two types of high-grade primary malignant bone tumors, and they account for 1–2%[1,2] and 8–10%[3,4] of primary malignant bone tumors, respectively. These two malignancies have some similarities in terms of pathological

manifestations. Both have some cartilage matrix-like components, and positivity for cartilage-related marker molecules s-100, sma, kp-1, pgm-1 can be observed by immunohistochemistry. The difference between DDC and COS lies in the clear boundary between the cartilage matrix and dedifferentiated components of DCC[5] versus the coexistence and uneven distribution of cartilage components and osteoid-formation area in COS.[6]

DDCs are more malignant than conventional chondrosarcomas.[7–9] The NCCN guidelines recommend that the main treatment for DDC be extensive surgical resection combined with systemic chemotherapy, and the chemotherapy scheme is the same for osteosarcoma chemotherapy (2B). Therefore, DDC and COS have some common characteristics in terms of pathological morphology, and the same surgical methods and systemic chemotherapy regimen are used for both. Large-scale trials show that compared with traditional osteosarcoma, COS has a poor response to chemotherapy, and the prognosis of patients is relatively poor.[10–12] Due to the low incidence and relatively small number of cases, studies on whether DDC and COS respond similarly to chemotherapy are few, and comparisons of the clinical prognoses under the same treatment models and of the related prognostic risk factors of these two high-grade primary malignancies are rare. Using the Surveillance, Epidemiology, and End Results (SEER) Program Database of the National Cancer Institute of the United States, we conducted a population-based analysis of DDC and COS to identify the relevant factors affecting the prognoses of the two diseases and evaluate whether patients can gain survival benefits from chemotherapy.

Patients And Methods

Patient selection

The patient samples used in this study are derived from the SEER database, which was co-established by 18 registries in various states and regions of the United States. It contains data on tumor incidence and outcomes of approximately 28% of the American population, and data include age, sex, race, location, tumor size, order of tumor onset, survival time and cause of death. The SEER database has wide population coverage and high accuracy, so it can provide a large number of samples for the analysis of independent prognostic factors of patients with rare diseases and improve the credibility of the results.

Patients with DDC and COS who were diagnosed between 1975 and 2016 were included in the SEER database. The details were extracted using SEER*Stat version 8.3.6 software (National Cancer Institute, Bethesda, MD, USA). The International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) was used to identify patients with DDC (ICD-O-3 histologic type: 9243/3) and COS (ICD-O-3 histologic type: 9181/3). All the patients received surgical treatment and had a clear pathological diagnosis. From 1975 to 2016, there were 217 DDC patients and 717 COS patients with surgery performed in the database. We excluded 43 patients whose first primary tumors were not DDC and 86 patients whose primary tumors were not COS. Finally, a total of 228 cases of DDC and 631 cases of COS were included in our study (Fig. 1). The data extracted from the SEER database included age, sex, race, tumor site, location, tumor

grade, tumor size, tumor stage including T stage, N stage, M stage, and AJCC stage (American Joint Committee on Cancer, 7th), lung metastasis, surgery type, chemotherapy, survival state, and survival time.

Statistical methods

X-tile 3.6.1 software was used to obtain the best truncation value as the classification variable for continuous variables including age. We divided the patients into three age categories (3 ~ 39 years, 40 ~ 70 years, 71 ~ 95 years) according to the X-title software. Tumor size was converted to a categorical variable (≤ 8 cm, or > 8 cm) based on the American Joint Committee on Cancer (AJCC) staging criteria.[13] In this study, overall survival (OS) was the time from the diagnosis of DDC or COS to death of any cause. IBM SPSS version 25.0 was used to describe the clinical data, and the chi-square test was used to identify the difference in the distribution of each factor between the two diseases. Kaplan-Meier analysis was used for univariate analysis, and chemotherapy and other possible related factors ($p < 0.1$) were included in the Cox multivariate analysis to identify the independent risk factors affecting survival. The survival curves of the influencing factors with significant differences were plotted by GraphPad Prism 8 software (the *p* value was the result of the log-rank test). All the hypothetical tests were 2-sided, with $p < 0.05$ indicating a statistically significant difference.

Results

Demographic and clinical characteristics of patients with DDC and COS

Among the 228 patients with DDC, there were 123 males (53.9%) and 105 females (46.1%). The overall median age of the patients was 63 years. In the end, 153 patients (67.1%) with DDC died, the median OS of the patients was 14 ±1.3 months, and the 3- and 5-year OS rates of the patients were 33.3% and 26.5%, respectively. Of the 631 patients with COS, there were 373 males (59.1%) and 258 females (40.9%), with a median age of 18 years. A total of 247 patients (39.1%) with COS died, the median OS of the patients was 233 ±38.1 months, and the 3- and 5-year OS rates of the patients were 71.5% and 63.8%, respectively. The 3- and 5-year OS rates for DDC were significantly lower than those for COS ($p< 0.001$) (Table 1, Figure 2).

Regarding demographic characteristics, most of the patients with DDC were in the age range of 40 to 70 years (64.9%), and most of the patients with COS were in the age range of 39 years (81.0%). The proportions of white and black patients with DDC were 91.7% and 2.6%, respectively, and the percentages of white and black patients with COS were 74.5% and 15.5%, respectively. There were significant differences in age and ethnic distribution between the two diseases ($p< 0.001$, $p< 0.001$), but there was no significant difference in the sex distribution between the two diseases.

In terms of the clinical characteristics of the tumors, the distributions of T stage, N stage and lung metastasis were similar between the two diseases. Most of the two kinds of tumors were located in the bone and joints, and the proportion of tumors originating from soft tissue in DDC was higher than that in COS (6.6% vs 2.5%, $p= 0.019$). Among the two diseases, the specific growth site of the tumors was most

often the lower limbs, followed by the skull and mandibles, pelvic bones, and vertebral or chest bone. The occurrence of DDC in the upper and lower limbs was higher than that of COS (8.8% vs 7.6%, 68.0% vs 60.1%, p=0.019). In the DDC group, a high pathological grade was predominant. In the COS group, the proportion of grade IV cases was significantly higher than that of grade IV cases (51.3% vs 38.4%, p=0.031). The proportion of tumors with diameters ≥ 8 cm in the DDC group was higher than that in the COS group (47.4% vs 29.6%, p= 0.008). More DDCs were diagnosed with distant metastasis (M1), and the difference in M1 staging between the DDC and COS groups was statistically significant (13.6% vs 6.8%, p=0.015); moreover, the corresponding proportion of AJCC IV staged tumors was higher in the DDC group than in the COS group (14.9% vs 7.0%, p= 0.036). The rates of local excision, radical excision, amputation, and partial resection in the COS group were higher than those in the DDC group (p=0.002). The chemotherapy rate in the COS group was significantly higher than that in the DDC group (85.1% vs 39.5%, p< 0.001) (Table 1).

Univariate analysis of OS-related factors in DDC and COS

The univariate analysis of patient survival is shown in Table 2 and Figure 3. In DDC, age was a factor that affected patient survival; the younger the age was, the better the prognosis would be (p< 0.001). The prognosis of patients with DDC was significantly correlated with M stage. The prognosis of patients with stage M1 was worse than that of patients with stage M0 (p< 0.001). The prognosis of patients with stage I or II disease was better than that of patients with stage III or IV disease (p< 0.001). Lung metastasis was also associated with prognosis. Patients with DDC with lung metastasis had a poorer prognosis than those without lung metastasis (p=0.009). Sex, race, tumor location, pathological grade, tumor size, T stage, N stage, mode of operation and chemotherapy had no effect on the prognosis of patients with DDC (Table 2, Figure 3).

Age can affect the prognosis of patients with COS; the younger the age was, the longer the total survival time would be (p< 0.001). Statistical analysis showed that the prognosis of female patients with COS was better than that of male patients (p=0.006). The patients with specific tumor growth sites survived, and the survival time of the patients with tumors located in the skull and lower extremities was significantly better than that of patients with tumors located in the pelvis, spine or sternum (p< 0.001). Regarding AJCC staging, the higher the T stage of COS was, the poorer the prognosis of the patients with M1-stage tumors would be (p< 0.001, p< 0.001, p< 0.001), and the survival rate of patients with lung metastasis would also be shorter (p=0.005). Patients with COS who received chemotherapy during the whole treatment had a longer OS time (p< 0.001). (Table 2, Figure 4)

Multivariate analysis of OS-related factors in DDC and COS

The multivariate analysis of patient survival is shown in Tables 3 and 4. For DDC, tumor stage was an independent factor affecting patient prognosis; the higher the tumor stage was, the worse the prognosis would be. Furthermore, chemotherapy was not an independent factor affecting the patient prognosis. Regarding COS, age, sex, tumor stage and chemotherapy were independent factors affecting patient prognosis. Older age, male sex, high tumor stage and not receiving chemotherapy were negatively correlated with prognosis.

Discussion

In this study, we found that the onset age of COS was lower than that of DDC. This is consistent with the fact that osteosarcoma is predominant among adolescents and that COS predominant in middle-aged adults.[14,15] Among whites, the incidence of DDC is higher than that of COS, while among blacks, the incidence of COS is higher than that of DDC. The incidence rate of COS in the skull and mandibles, vertebral and chest bones, and pelvic bones was higher than that of DDC, while in soft tissue, the incidence rate of DDC was higher than that of COS. DDC has a higher pathological grade, larger tumor volume, more patients with M1 stage at first diagnosis, and higher AJCC stage, which suggests that DDC has a higher degree of malignancy and metastatic potential than COS.

The median survival time of patients with dedifferentiated chondrosarcoma, 14 ± 1.3 months, is similar to that of most studies[7,16–18]. The univariate analysis shows that age is a potential factor affecting the poor prognosis of patients with DDC, but it is not an independent factor in the multivariate analysis. Grimer's research also suggests that the prognosis of older patients is worse.[7] M1 stage, high clinical stage of tumor and the presence of lung metastasis are all indicators of poor prognosis in the univariate analysis. Because the three factors are collinear in the multivariate Cox regression, only the clinical stage of the tumor is included. Cox regression analysis shows that only the clinical stage of the tumor is an independent risk factor affecting the prognosis of patients. The median survival time of COS is 233 ± 38.1 months. Old age and male sex are independent risk factors for prognosis, which has been confirmed in many studies, and it can be related to the poor response of men to treatment[15]. Older patients have poor tolerance to treatment, and the incidence of toxic reactions is higher than that of young people.[19,20] Patients with tumors located in the pelvis, spine and sternum have a poor prognosis, and P. Tsagozis obtained similar results.[21] The reason is that these tumors have an abundant blood supply and are prone to distant metastasis. The volumes of pelvic tumors can become very large, and because of the complex structure of adjacent tissues, it is difficult to remove them; thus, these tumors are not easily resected, so this approach is not widely used. T stage, M stage, tumor stage and lung metastasis are potential factors affecting the prognosis of patients. Because they are collinear in the multivariate Cox regression, only the clinical stage of the tumor is included. High tumor stage is an independent risk factor for poor prognosis. This view is also confirmed by Duchman KR and Iwata S.[15,22]

Whether DDC can benefit from chemotherapy is still controversial. Dhinsa et al.[23] retrospectively investigated 21 patients with DDC between the ages of 35 and 80 from 2000 to 2010. The authors found

that the median survival time of patients who received chemotherapy was 17 months, while the median survival time of the overall cohort was 9.5 months. Patients who received chemotherapy had a longer median time of local recurrence. Based on the multivariate analysis of 34 patients without metastasis, it was found that chemotherapy was an independent factor for improving patient survival. However, the univariate analysis of our study showed that chemotherapy could not improve the survival of patients with DDC, and our multivariate regression analysis showed that chemotherapy was not an independent factor affecting patient prognosis. Staals et al.[8] reviewed the clinical, imaging, histological features and treatment of 123 patients with central DDC and found that there was no significant difference in OS between patients who received surgery alone and those who received surgery combined with chemotherapy (18 months vs 23 months, $p = 0.88$). Grimer et al.[7] collected clinical and demographic data from 337 patients from 9 European centers for analysis to explore the prognostic characteristics of patients. They also did not find that the use of chemotherapy had an impact on patient prognosis.

In the univariate statistical analysis of COS, we found that patients who had received chemotherapy had a longer survival time, but in the multivariate analysis, chemotherapy could not be used as an independent predictor of patient prognosis. This is similar to the conclusion reached by some researchers. P. Tsagozis et al.[21] conducted a retrospective analysis of 256 patients with COS in the extremities and pelvis from 1975 to 2015. It was found that the chemotherapy regimen for conventional osteosarcoma was not as effective in COS, and chemotherapy resistance was more obvious among patients with high cartilage content. Unlike conventional osteosarcoma, the response of COS to chemotherapy is not a prognostic factor in our multiple regression analysis. Bacci et al.[24] believe that the histological subtype of primary central high-grade osteosarcoma of the extremities is closely related to chemotherapeutic response and patient prognosis, and COS has the lowest response to chemotherapy. Hauben et al.[12] analyzed the data of 570 patients with central osteosarcoma of the extremities in the European osteosarcoma group. It was confirmed that the efficacy of chemotherapy was different among different tumor tissue subtypes. Among them, the proportion of patients with COS who had a good response to chemotherapy was the lowest, and it was suggested that patients with COS had a better long-term survival rate. Although the response of patients with COS to chemotherapy is not as good as that of conventional osteosarcoma, chemotherapy for patients with COS may be necessary, based of the obvious survival potential of patients with chemotherapy in the univariate analysis; however, stronger evidence is still needed to support this possibility.

A comprehensive analysis of DDC and COS showed that both had cartilage components. Monderer et al.[25] found that cartilage components may have an inhibitory effect on chemotherapy. They constructed primary central chondrosarcoma cell lines from stage III tumors and DDC cell lines and designed a three-dimensional culture model to maintain their differentiation into chondrocytes. The researchers found that chondrosarcoma cells were significantly resistant to doxorubicin in the presence of cartilage matrix but not to cisplatin. P. Tsagozis believes that the poor response of COS to chemotherapy is related to the presence of a predominantly chondroblastic component (more than 50% of the tumor volume).[21] Therefore, our analysis found that chemotherapy could not improve the prognosis of patients with DDC

and had no absolute clinical benefit for COS, both of which may be attributed to the unique pathological features of the two kinds of tumors, namely, the presence of cartilage components. Staals et al.[8] study found that a high proportion of dedifferentiated components in DDC can also lead to a poor prognosis, which can be a potential reason for the pathological similarity between DDC and COS, though the difference in total survival time is large. Therefore, it is necessary to further explore the effects of various components and their proportions in tumor tissue on patient prognosis, as this can enable patients to obtain a more reasonable and accurate individualized treatment plan and optimize the cost-effectiveness of treatment. At the same time, this study also suggests that the simple application of chemotherapy for osteosarcoma may not necessarily benefit patients with DDC and COS. We can look for chemotherapeutic drugs that can break through the cartilage barrier or change the molecular configuration of chemotherapeutic drugs to make this kind of tumor containing cartilage more sensitive to chemotherapy.

In this study, there are some limitations in using the SEER database to predict the prognostic variables of diseases. There is a lack of information on chemotherapy regimens and doses, and surgical information, such as the extent of resection and the status of the cutting edge, is lacking for many patients, which limits the analysis of these important treatment variables. Additionally, a large number of patients do not have access to comprehensive staging and metastasis-related analyses. Furthermore, OS is merely used as a surrogate for local control, as the SEER database does not directly provide information regarding local control outcomes for different treatment modalities.

Conclusion

In conclusion, we compared the clinical prognostic factors of patients with DDC and COS. Chemotherapy showed no superiority in prolonging the OS of DDC patients. More evidence is needed to support the survival benefits of patients with COS from chemotherapy.

Abbreviations

DDC
Dedifferentiated chondrosarcoma
COS
Chondroblastic osteosarcoma
OS
Overall survival
SEER
Surveillance, Epidemiology, and End Results
NCCN
National Comprehensive Cancer Network
AJCC
American Joint Committee on Cancer

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Declarations

Acknowledgments

The authors acknowledge the efforts of the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in providing high-quality open resources for researchers.

Funding

This work was supported by the National Natural Science Foundation of China [81772861 to Jingnan Shen; 81202118, 81572638 and 81772864 to Xianbiao Xie]

Availability of data and materials

The datasets generated and analyzed during this study are available from Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence—SEER 18 Regs Custom Data (with additional treatment fields), Nov 2018 Sub (1975-2016 varying), National Cancer Institute, DCCPS, Surveillance Research Program, released August 2019, based on the November 2018 submission.

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Contributions

Yiying Bian, Ziliang Zeng, Jingnan Shen, and Xianbiao Xie designed the study and performed interpretation of the data; Hao Yao, Yutong Zou, Jian Tu, Bo Wang, Qinglin Jin, and Dongming Lv performed the acquisition and analysis of the data; Yiying Bian drafted the manuscript; and Jingnan Shen and Xianbiao Xie revised the manuscript. The authors read and approved the final manuscript.

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Ethics declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Tables

Table 1. Demographic and clinical characteristics of dedifferentiated chondrosarcoma patients (n=228) and chondroblastic osteosarcoma patients (n=631)

Variable	Dedifferentiated chondrosarcoma	Chondroblastic osteosarcoma	*p* value
Age			<0.001
3~39 years	8 (3.5%)	511 (81.0%)	
40~70 years	148 (64.9%)	103 (16.3%)	
71~95 years	72 (31.6%)	17 (2.7%)	
Sex			0.176
Male	123 (53.9%)	373 (59.1%)	
Female	105 (46.1%)	258 (40.9%)	
Race			<0.001
White	209 (91.7%)	470 (74.5%)	
Black	6 (2.6%)	98 (15.5%)	
Other	11 (4.8%)	61 (9.7%)	
Unknown	2 (0.9%)	2 (0.3%)	
Tumor site			0.019
Bones and joints	210 (92.1%)	607 (96.2%)	
Soft tissue	15 (6.6%)	16 (2.5%)	
Other	3 (1.3%)	8 (1.3%)	
Location			0.019
Upper limb	20 (8.8%)	48 (7.6%)	
Lower limb	155 (68.0%)	379 (60.1%)	
Skull and mandibles	19 (8.3%)	102 (16.2%)	
Vertebral and chest bones	6 (2.6%)	21 (3.3%)	
Pelvic bones	12 (5.3%)	56 (8.9%)	
Others	16 (7.0%)	25 (4.0%)	
Grade			0.031
I	10 (4.4%)	9 (1.4%)	
II	13 (5.7%)	31 (4.9%)	
III	65 (28.5%)	195 (30.9%)	
IV	117 (51.3%)	242 (38.4%)	
Unknown	23 (10.1%)	154 (24.4%)	
Tumor size			0.008
<8 cm	43 (18.9%)	131 (20.8%)	
≥8 cm	108 (47.4%)	87 (29.6%)	
Unknown	77 (33.8%)	313 (49.6%)	
T stage			0.624
T1	46 (20.2%)	110 (17.4%)	
T2	101 (44.3%)	199 (31.5%)	
T3	3 (1.3%)	8 (1.3%)	
Unknown	78 (34.2%)	314 (49.8%)	
N stage			0.198
N0	157 (68.9%)	330 (52.3%)	
N1	2 (0.9%)	11 (1.7%)	
Unknown	69 (30.3%)	290 (46.0%)	
M stage			0.015
M0	135 (59.2%)	306 (48.5%)	
M1	31 (13.6%)	43 (6.8%)	

Unknown	62 (27.2%)	282 (44.7%)	
Tumor stage			0.036
I	13 (5.7%)	47 (7.4%)	
II	86 (37.7%)	206 (32.6%)	
III	6 (2.6%)	13 (2.1%)	
IV	34 (14.9%)	44 (7.0%)	
Unknown	89 (39.0%)	321 (50.9%)	
Lung metastasis			0.917
Yes	19 (8.3%)	30 (4.8%)	
No	106 (46.5%)	173 (27.4%)	
Unknown	103 (45.2%)	428 (67.8%)	
Surgery type			0.002
Local excision	11 (4.8%)	41 (6.5%)	
Radical excision	90 (39.5%)	271 (42.9%)	
Amputation	28 (12.3%)	142 (22.5%)	
Partial resection	8 (3.5%)	43 (6.8%)	
Other	12 (5.3%)	12 (1.9%)	
Unknown	79 (34.6%)	122 (19.3)	
Chemotherapy			<0.001
Yes	90 (39.5%)	537 (85.1%)	
No	138 (60.5%)	94 (14.9%)	
3-year OS rate	33.3%	71.5%	
5-year OS rate	26.5%	63.8%	

Table 2. Median survival data (months) for dedifferentiated chondrosarcoma patients and chondroblastic osteosarcoma patients

Variable	Dedifferentiated chondrosarcoma			Chondroblastic osteosarcoma		
	OS (estimate±SE)	95% CI	*p* value	OS (estimate±SE)	95% CI	*p* value
Age	14±1.340	11.374-16.626	0.001	233±38.081	158.361-307.639	<0.001
3~39 years	57±27.000	4.080-109.920		428±127.033	179.016-676.984	
40~70 years	16±1.887	12.301-19.699		88±31.392	26.471-149.529	
71~95 years	9±1.287	6.478-11.522		20±3.929	12.299-27.701	
Sex	14±1.340	11.374-16.626	0.516	233±38.081	158.361-307.639	0.006
Male	14±2.106	9.872-18.128		167±36.171	96.104-237.896	
Female	14±1.656	10.754-17.246		301±65.340	172.934-429.066	
Race	14±1.385	11.285-16.715	0.139	233±38.138	158.249-307.751	0.896
White	14±1.217	11.614-16.386		233±43.385	147.965-318.035	
Black	8±28.000	0.000-62.80		204±45.741	114.347-293.653	
Other	162±115.030	0.000-387.459		-	-	
Tumor site	14±1.340	11.374-16.626	0.598	233±38.081	158.361-307.639	0.235
Bones and joints	14±1.152	11.742-16.258		300±44.752	212.286-387.714	
Soft tissue	24±8.854	6.645-41.355		52±35.038	0.000-120.675	
Others	17±4.899	7.398-26.602		19±93.944	0.000-203.131	
Location	14±1.340	11.374-16.626	0.630	233±38.081	158.361-307.639	<0.001
Upper limb	16±21.522	0.000-58.183		140±54.069	34.025-245.975	
Lower limb	13±0.706	11.616-14.384		378±112.928	156.662-599.338	
Skull and mandibles	16±21.360	0.000-57.865		-	-	
Vertebral and chest bones	25±18.616	0.000-61.488		44±6.746	30.778-57.222	
Pelvic bones	18±3.416	11.305-24.695		28±4.391	19.393-36.607	
Other	24±11.279	1.894-46.106		88±56.178	0.000-198.109	
Grade	14±1.440	11.178-16.822	0.930	213±31.914	150.448-275.552	0.064
I	14±5.534	3.153-24.847		-	-	
II	13±2.193	8.702-17.298		-	-	

III	16±3.204	9.720-22.280		181±38.712	105.124-256.876	
IV	13±2.287	8.518-17.482		203±23.164	157.598-248.402	
Tumor size	14±1.606	10.853-17.147	0.883	154±-	-	0.126
<8 cm	17±3.925	9.307-24.693		-	-	
≥8 cm	13±1.585	9.893-16.107		154±48.695	58.557-249.443	
T stage	14±1.689	10.690-17.310	0.826	-	-	<0.001
T1	17±3.876	9.404-24.596		-	-	
T2	13±1.532	9.997-16.003		134±-	-	
T3	2±-	-		21±2.828	15.456-26.544	
N stage	-	-	0.117	-	-	0.134
N0	-	-		-	-	
N1	-	-		-	-	
M stage	14±1.346	11.362-16.638	<0.001	-	-	<0.001
M0	19±3.021	13.079-24.921		-	-	
M1	6±1.458	3.143-8.857		37±3.24	11.049-62.951	
Tumor stage	14±1.829	10.416-17.584	<0.001	-	-	<0.001
I	20±8.538	3.266-36.734		-	-	
II	19±3.523	12.095-25.905		-	-	
III	24±-	-		24±3.032	18.056-29.944	
IV	6±1.458	3.143-8.857		44±13.982	16.595-71.405	
Lung metastasis	13±0.952	11.133-14.867	0.009	-	-	0.005
Yes	8±4.342	0.000-16.510		32±-	-	
No	14±2.405	9.286-18.714		-	-	
Surgery type	14±2.416	9.265-18.735	0.820	196±-	-	0.118
Local excision	18±11.276	0.000-40.101		148±	-	
Radical excision	13±2.534	8.034-18.966		-	-	
Amputation	13±5.541	2.140-23.860		196±87.080	25.324-366.676	
Partial resection	48±45.180	0.000-136.552		-	-	
Other	50±45.314	0.000-138.815		171±133.698	0.000-433.048	

Chemotherapy	14±1.340	11.4-16.626	0.473	233±38.081	158.361-307.639	<0.001
Yes	14±1.176	11.7-16.304		378±114.832	152.929-603.071	
No	14±2.904	8.3-19.691		48±52.859	0.000-151.604	

Table 3. Multivariate analyses for OS for dedifferentiated chondrosarcoma patients

Variable	Hazard Ratio (95% CI)	*p* value
Age		0.104
3-39 years	1	
40-70 years	0.267 (0.035-2.013)	
71-95 years	0.668 (0.425-1.049)	
Tumor stage		0.001
I	1	
II	0.363 (0.164-0.803)	
III	0.424 (0.269-0.668)	
IV	0.254 (0.077-0.840)	
Chemotherapy		0.828
Yes	1.053 (0.662-1.675)	
No	1	

Table 4. Multivariate analyses for OS for chondroblastic osteosarcoma patients

Variable	Hazard Ratio (95% CI)	*p* value
Age		<0.001
3-39 years	1	
40-70 years	0.123 (0.038-0.394)	
71-95 years	0.309 (0.100-0.960)	
Gender		0.030
Male	1	
Female	1.583 (1.045-2.399)	
Location		0.164
Upper limb	1	
Lower limb	2.494 (0.575-10.819)	
Skull and mandibles	2.734 (0.722-10.358)	
Vertebral and chest bones	1.164 (0.324-4.183)	
Pelvic bones	1.567 (0.270-9.094)	
Others	3.873 (0.956-15.689)	
Tumor stage		<0.001
I	1	
II	0.219 (0.091-0.532)	
III	0.398 (0.244-0.647)	
IV	0.908 (0.350-2.355)	
Chemotherapy		0.279
No	1	
Yes	1.510 (0.716-3.184)	

Figures

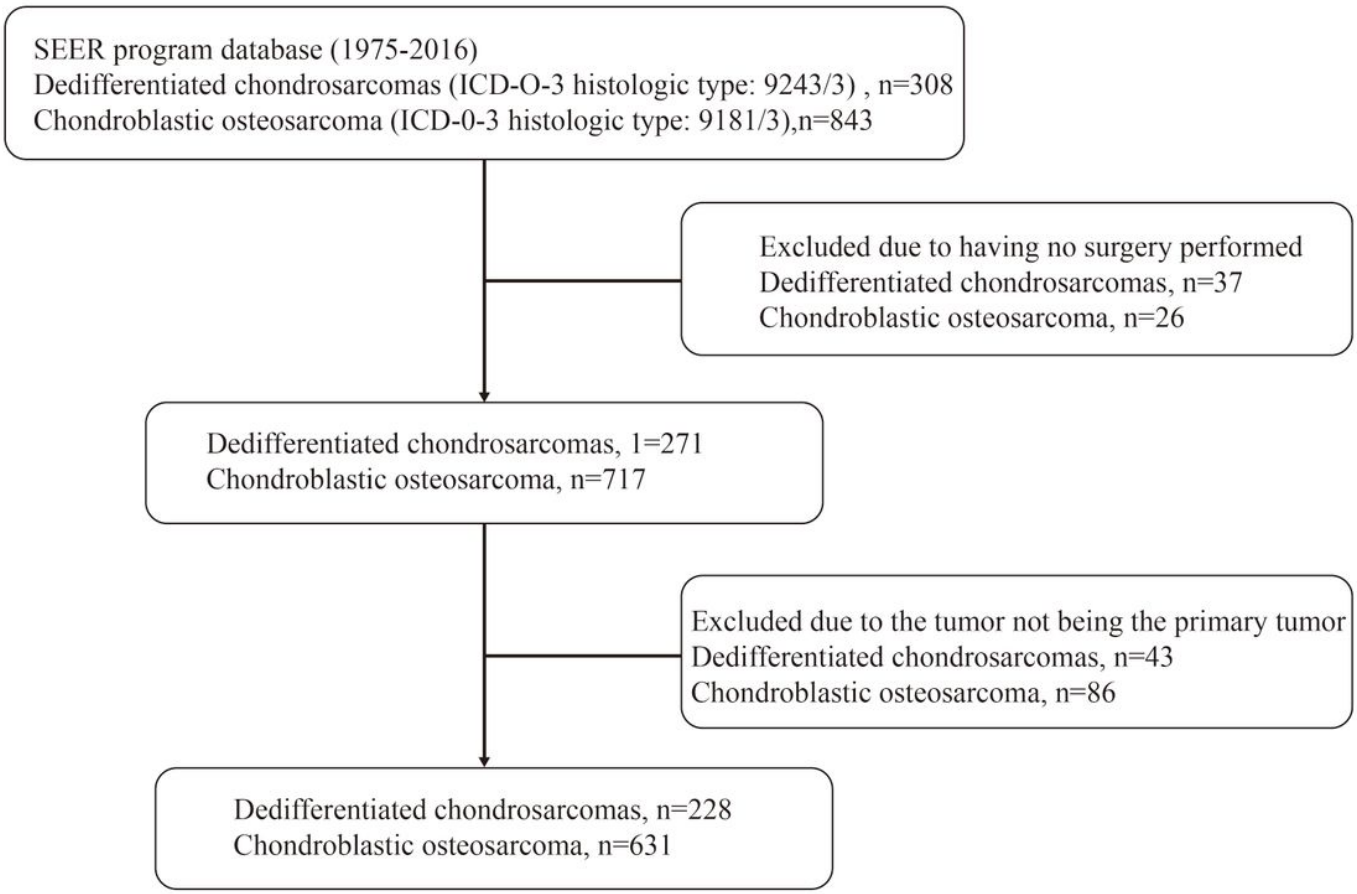

Figure 1

Flow chart for the selection of the study population. (Abbreviations: SEER, Surveillance, Epidemiology, and End Results; ICD-O-3, International Classification of Diseases for Oncology, 3rd edition.).

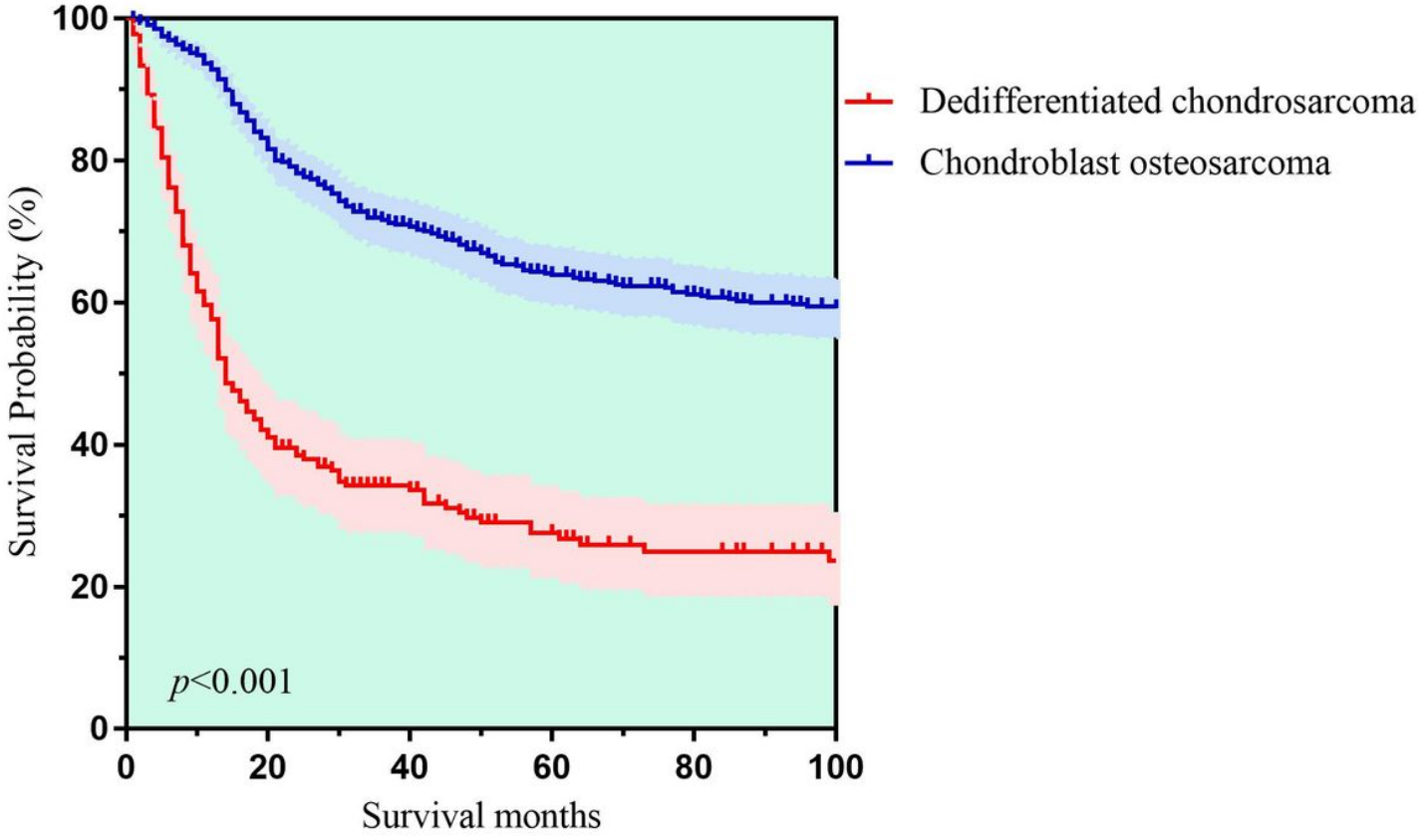

Figure 2

Overall survival of patients with dedifferentiated chondrosarcoma (n=228) and dedifferentiated chondrosarcoma (n=631). Individuals with dedifferentiated chondrosarcoma have a worse median survival rate than those with chondroblastic osteosarcoma (p<0.001).

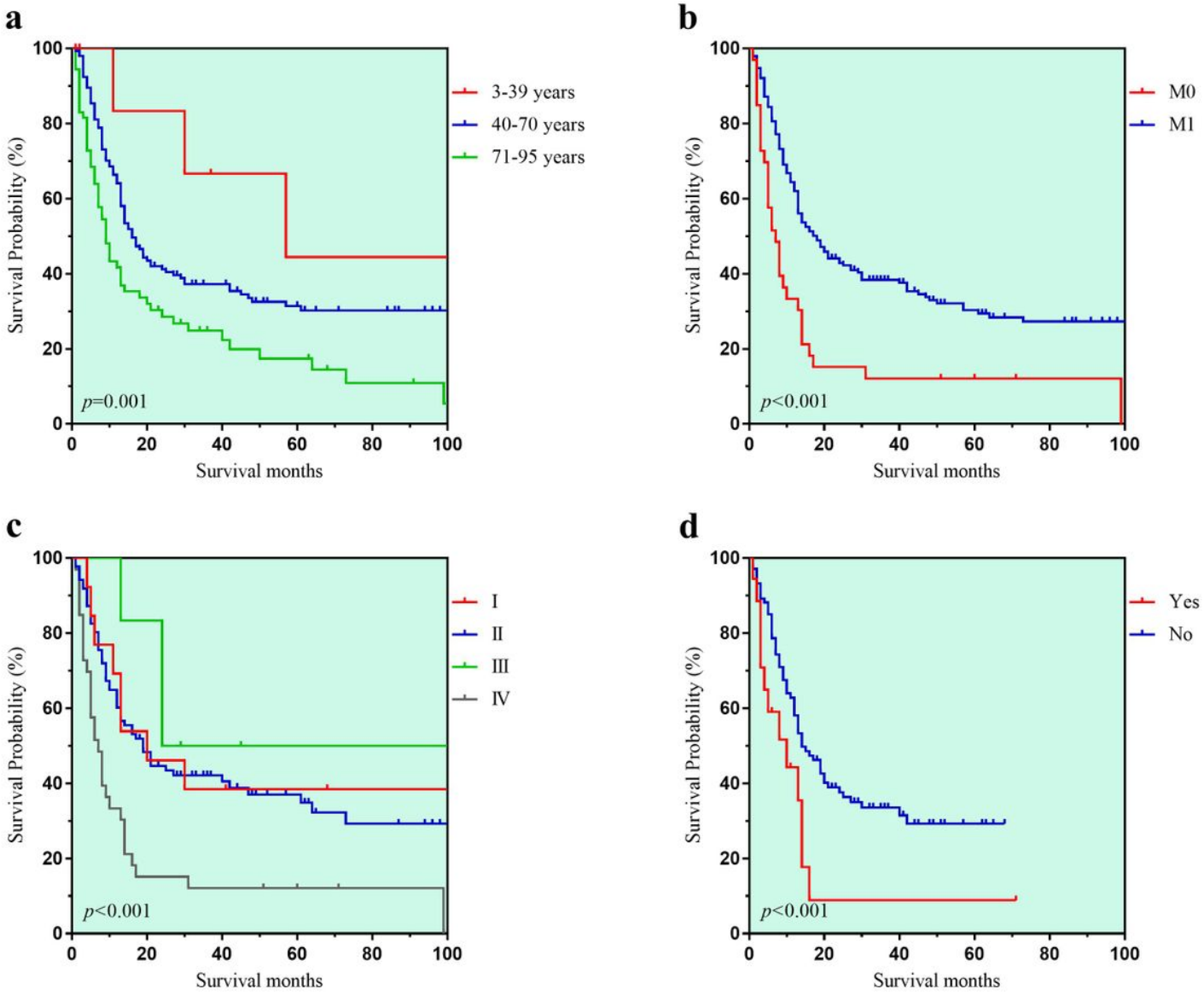

Figure 3

Kaplan-Meier method-estimated OS in dedifferentiated chondrosarcoma patients with surgery performed. OS stratified by a. age b. M stage, c. tumor stage, and d. lung metastasis.

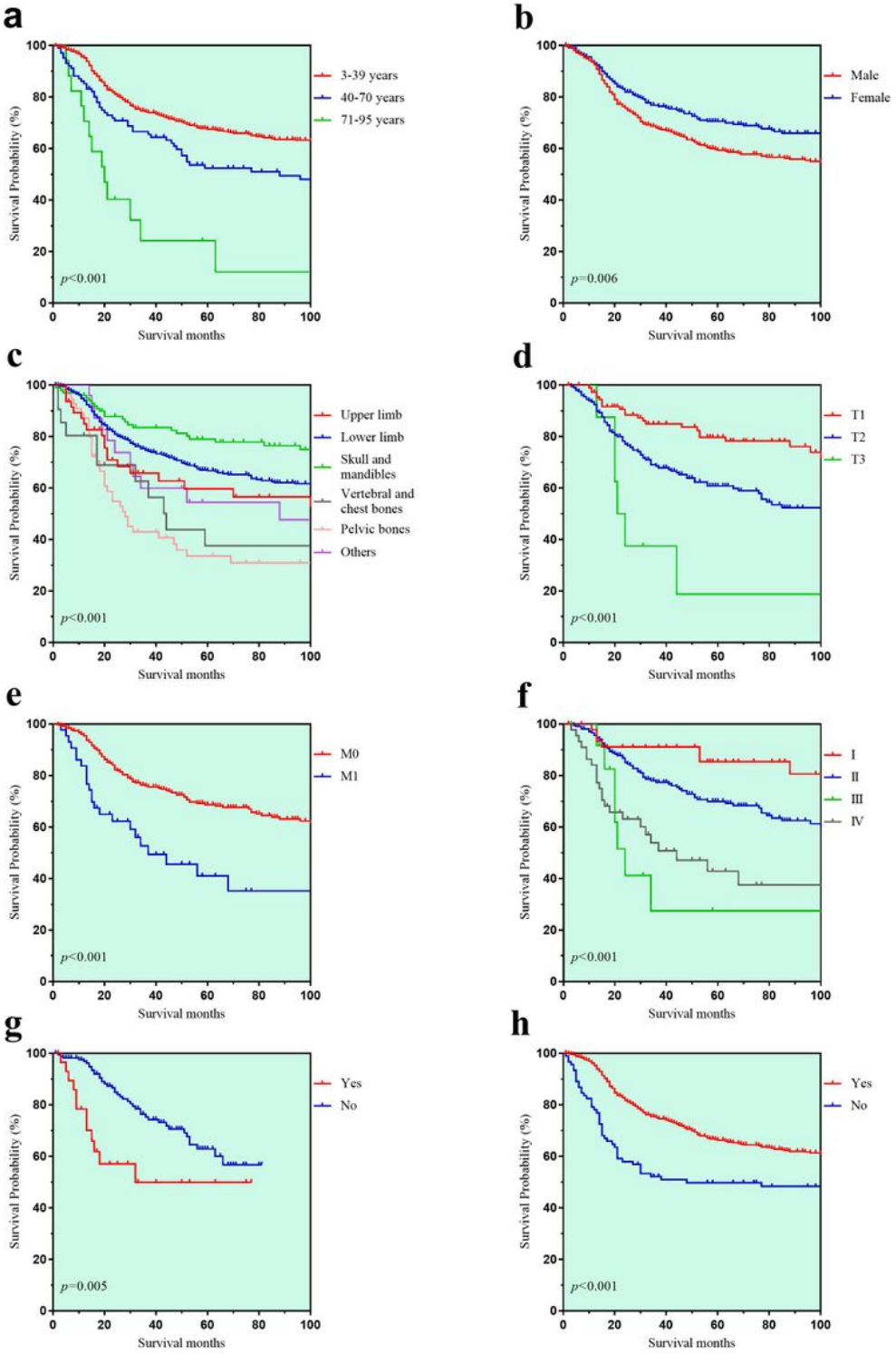

Figure 4

Kaplan-Meier method estimated OS of dedifferentiated chondrosarcoma patients with surgery performed. OS stratified by a. age, b. sex, c. location, d. T stage, e. M stage, f. tumor stage, g. lung metastasis, and h. chemotherapy.