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Incidence, outcomes and prognostic factors during 25 years of treatment of chondrosarcomas

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ABSTRACT

Background: There are few studies detailing the incidence, patient outcomes and prognostic factors for chondrosarcomas (CS). Those that do exist have small sample sizes and/or use older datasets. The purpose of this study was to determine the incidence, overall survival (OS) and prognostic factors for OS of CS patients, as well as investigate the efficacy of curettage.

Methods: We analyzed data of 2186 patients diagnosed with chondrosarcomas between '89-'13 from the Netherlands Cancer Registry. The effect of risk factors on OS was assessed with a multivariate Cox regression. Median Follow-up was determined with reversed Kaplan-Meier. OS was estimated using Kaplan-Meier method.

Results: The relative incidence of CS was 2.88 per million citizens between '89-'96, 4.15 between '96-'04 and 8.78 between '05-'13. Most of the increase in incidence came from atypical cartilaginous tumours/grade I chondrosarcoma (ACT/CS I). The 3-, 5- and 10-years survival were, respectively, 96%, 93% and 88% for ACT/CS I, 82%, 74% and 62% for grade II CS and 38%, 31% and 26% for grade III CS. Prognostics factors significantly associated with OS were age, histological grade, year of diagnosis, tumour location and size.

Conclusion: The incidence of CS, and especially ACT/CS I, has increased over time, which could be driven by both an ageing population and increased diagnostic imaging. With the increased number of diagnosed ACT/CS I, the number of preventative curettages of this tumour has also increased. Despite the supposed preventative character of this treatment, the incidence of high-grade CS did not decrease.

1. Introduction

Chondrosarcomas (CS) are a heterogeneous group of malignant bone neoplasms with hyaline cartilage differentiation. They are characterized by the production of cartilage matrix. CS central, primary, and secondary are the largest subgroup of cartilage tumours and account for approximately 20% of malignant bone tumours, making CS the second most common bone tumour in adults [1]. Eighty-five percent of the conventional CS arise from the medullar cavity where they are referred to as primary central CS. Secondary CS are malignant transformed enchondromas or osteochondromas [2].

Based upon their histopathology, CS are divided into three grades, where grade I is considered to be low-grade (locally aggressive) and grade II and III high-grade (malignant). The fourth group of CS, which could be seen as grade IV; is called dedifferentiated chondrosarcoma and makes up 10% of all CS [1]. In 2002 low-grade CS were 'downgraded' from malignant to locally aggressive lesions and renamed atypical cartilaginous tumour (ACT) [1]. Two other less common types of CS are mesenchymal and clear cell CS. Both of these have very different characteristics, treatment and prognosis than other CS subtypes. Mesenchymal is a highly malignant tumour with strong tendency towards local recurrence. On the contrary, clear cell is a low-grade variant that can usually be cured with en bloc excision [1,3].

For ACT/CS I, which is locally aggressive, curettage (with either

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cryosurgery or phenolisation) is the standard treatment in the extremities. The effectiveness of curettage in preventing transformation into high-grade CS has, however, not been proven. CS of the axial skeleton and grade II and grade III CS in the extremities are generally resected with free margins (Appendix A). Surgical treatment is considered the only curative treatment modality as CS is less sensitive to both radiotherapy and chemotherapy [4]. Radiotherapy can be of use in two situations: after incomplete resection for local control with curative intent or if resection is not an option. In the latter case the intention is to palliate [5,6].

Consensus exists that age, grade and localization are of prognostic value for survival [7–9]. Additionally, larger tumours and fractures are associated with worse outcome [3,8]. Gender is not associated with survival [8]. Local recurrence and distant metastasis are associated with a worse outcome in univariate analysis [9–11]. Studies investigating prognostic factors often have small sample sizes and use more covariates in their multivariate Cox regression models than is recommended in statistical literature or neglect to include known important prognostic factors (based on clinical experience and literature). Studies that do not suffer from these shortcomings are scarce, and those that exist are several decades old and therefore in need of confirmation in a modern setting.

The main objective of this study was to determine the incidence, overall survival (OS) and prognostic factors associated with OS for CS in the Netherlands over the last 25 years. Secondary objective was to evaluate the effect of curettage of ACT/CS I in preventing transformation into high-grade CS. We hypothesized that the increased number of ACT/CS I treated with preventative curettage has not led to a decrease in the incidence of high-grade CS.

2. Methods

Study design. This is a retrospective observational study. We used data from the Netherlands Cancer Registry (NCR-IKNL), a retrospective national registry that records all cases of cancer in the Netherlands, covering a population of approximately 16.9 million. Patients were seen at a tertiary dedicated bone tumour centre, that has a multidisciplinary team of dedicated bone tumour pathologist(s), radiologists, and orthopaedic surgeons. We evaluated 2186 consecutive patients with a histologically proven chondrosarcoma treated between '80-'13, resulting in 1615 eligible patients after excluding 571 patients for one or more of the following reasons: missing data for relevant covariates, treatment without curative intent, CS subtypes periosteal, dedifferentiated, mesenchymal, clear cell or a multifocal tumour (Fig. 1, flow diagram detailing the inclusion process).

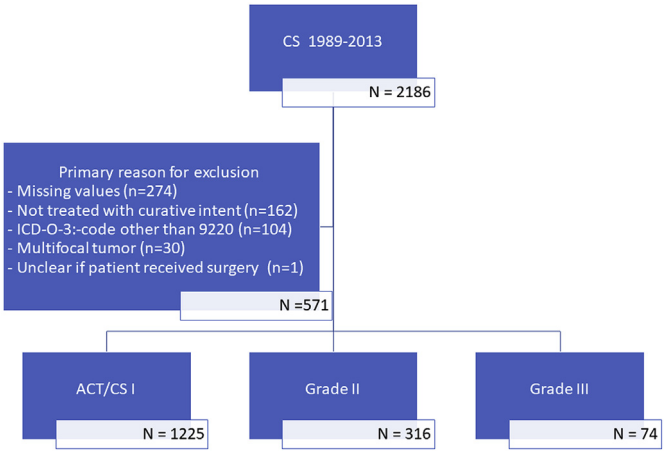

Fig. 1. Flowchart representing the selection process for patients that were incorporated into the analysis.
Abbreviations: N, number of patients; ICD-O-3: International Classification of Diseases for Oncology, 3rd ed. [12]; *ACT/CS I, atypical cartilaginous tumor/chondrosarcoma grade I.*

Variables. Starting point was the date of diagnosis. The radiological diagnosis and -grade was combined with histological tissue diagnosis, according to the WHO classification of bone tumours. Data on diagnosis, grading, treatment and outcome is collected by trained registry personnel of this independent organization through a national pathology database, supplemented by data from medical records. Tumour size was defined as maximum diameter at pathologic analysis. Tumour grade was classified as (ACT/)CS I < grade II < grade III. Tumour location was based on ICD-0-3 codes. Survival data are available through a link with municipal population registries [13]. If patients were lost to follow-up, the last documented endpoint was used.

Participants. Table 1 summarizes characteristics for all patients with a chondrosarcoma. The median follow-up was 7.4 years (range 5 days–26.1 years). Mean age at time of diagnosis was 50.6 ± 16.2 years. Slightly more women (53%) than men (47%) were affected. The majority of CS were conventional (95.2%), for more details on the other subtypes please refer to Appendix B. ACT/CS I was the most common grade with 1437 (65.7%) patients, versus 404 (18.5%) for grade II and 150 (6.9%) for grade III. Tumour size was 8 cm or

Table 1
Demographic and clinical characteristics of the study cohort.

Characteristic[a]	Total, n = 2186
Period of diagnosis, *n (%)*	
'89-'96	351 (16.1)
'97-'04	530 (24.2)
'05-'13	1305 (59.7)
Age: Mean ± SD, y	50.6 ± 16.2
'89-'96	51.3 ± 19.0
'97-'04	50.7 ± 17.4
'05-'13	50.3 ± 14.9
Gender, *n (%)*	
Male	1033 (47.3)
Female	1153 (52.7)
Histological, *n (%)*	
Conventional	2082 (95.2)
Periosteal	36 (1.6)
Mesenchymal	11 (0.5)
Clear cell	13 (0.6)
Dedifferentiated	44 (2.0)
Grade, *n (%)*	
ACT/CS I	1437 (65.7)
II	404 (18.5)
III	150 (6.9)
Unknown	195 (8.9)
Size in cm, *n (%)*	
≤8 cm	1488 (68.6)
>8 cm	445 (20.5)
Multifocal	30 (1.4)
Unknown	205 (9.3)
Site, *n (%)*	
Extremities	1592 (72.8)
- Upper (excl. hand and wrist)	412 (18.8)
- Hand/Wrist	149 (6.8)
- Lower (excl. knee/ankle/foot)	987 (45.2)
- Knee/Ankle/Foot	44 (2.0)
Axial skeleton	387 (17.7)
- Rib/Sternum/Clavicle	242 (11.1)
- Skull (excl. mandible)	93 (4.3)
- Mandible	5 (0.2)
- Spine	47 (2.2)
Pelvic bones/sarcum/coccyx	207 (9.5)

[a] Full cohort. Abbreviations: N, number of patients; SD, standard deviation; ACT/CS I, atypical cartilaginous tumor/chondrosarcoma grade I.

smaller in 68.6% of the cases. Tumour locations were in descending order: lower extremity (45.2%), upper extremity (18.8%), rib, sternum or clavicle (11.1%), pelvis, sacrum or coccyx (9.5%) hand or wrist (6.8%), skull (4.3%), spine (2.2%), knee, ankle or foot (2.0%), mandible (0.2%).

Statistical analysis. OS was estimated using Kaplan-Meier. The effect of possible prognostic factors on OS were estimated with a multivariate Cox regression model. We stratified for histological grade in this model, as grade violated the proportional-hazards-assumption. To determine if the increase in incidence might be attributed to an ageing population, incidences were calculated per number of citizens in all age groups per time period. For this, data from the governmental institution 'Statistics Netherlands' was used [14]. Median follow-up time was estimated with reversed Kaplan-Meier method.

3. Results

Incidence. When adjusting the absolute number of CS per year for number of citizens per year, the incidence of chondrosarcoma was 2.88 per million citizens between '89-'96, 4.15 between '96-'04 and 8.78 between '05-'13. Most of the increase in incidence came from ACT/CS I, with incidence increasing from 1.20 per million in '89-'96 to 6.63 in '05-'13. Average incidence for high-grade (grade II

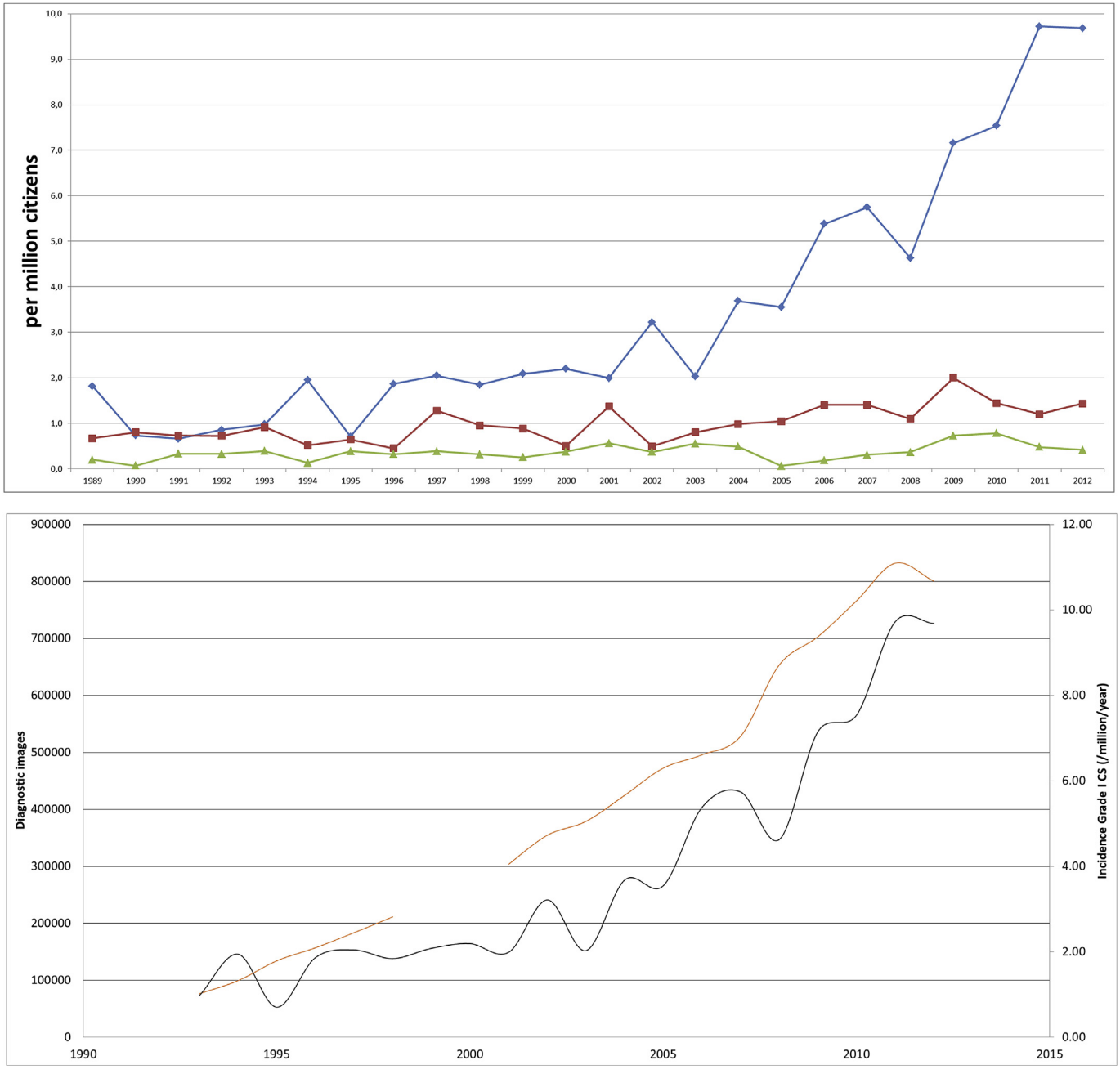

Fig. 2. Incidence of CS between 1989 and 2013 by grade.
Blue, grade I; **red**, grade II and **green**, grade III.
b) Incidence of low-grade chondrosarcoma in comparison with number of MRI examinations over time.
Black, incidence of CS grade I and **red**, number diagnostic images per year [15]. The amount of diagnostic images in 1999 and 2000 are unknown. The data collection started in 1993.

Table 2
Incidence rates per time period.

Period of diagnosis	Grade	N	Incidence (/million/year)
89-'96	ACT/CS I	146	1.20
	II	83	0.68
	III	33	0.27
	Unknown	89	0.73
	Total	**351**	**2.88**
	High-grade (II&III)	*116*	0.95
97-'04	ACT/CS I	306	2.40
	II	116	0.91
	III	53	0.41
	Unknown	55	0.43
	Total	**530**	**4.15**
	High-grade (II&III)	*169*	*1.32*
05-'13	ACT/CS I	985	6.63
	II	205	1.38
	III	64	0.43
	Unknown	51	0.34
	Total	**1305**	**8.78**
	High-grade (II&III)	*269*	*1.81*

Incidence per million citizens.
AbbreviationsN, number of patients; ACT/CS I, atypical cartilaginous tumor/chondrosarcoma grade I.

Table 3
Cox multivariate analysis of the effect of patient- and tumor characteristics on overall survival stratified for tumor grade (n = 1615).

	HR	0.95% CI	*P-value*
Sex			
Male	Ref	–	–
Female	0.94	0.73–1.23	.671
Age, *y**			
50	Ref	–	–
	1.78	1.63–1.95	<.001
Period of diagnosis			
'05-'13	Ref	–	–
'97-'04	1.68	1.20–2.35	.003
'89-'96	2.23	1.57–3.15	<.001
Location			
Extremities	Ref	–	–
Spine	1.23	0.91–1.67	.173
Pelvis/sacrum/coccyx	1.76	1.24–2.50	.002
Tumor size			
≤8 cm.	Ref	–	–
>8 cm.	1.48	1.11–1.97	.007

All patients have received surgical treatment for their chondrosarcoma. A p-value of <.05 is considered statistically significant.*Age is in steps of 10 years with a reference of 50 years.Abbreviations: CI, confidence interval; HR, hazard ratio; Ref, reference category.

and grade III) tumours was 0.95 per million in '89-'96 and 1.81 in '05-'13 (Fig. 2a). The number of diagnostic images in the Netherlands also increased over time (Table 2). The relation between incidence rates of ACT/CS and the number of diagnostic images in the Netherlands are presented in Fig. 2b. For a more detailed overview of incidence rates per grade per year, we refer to appendix C.

Survival and prognostic factors. The 3-, 5- and 10-years overall survival for ACT/CS I were, respectively, 96% (95%CI: 94–98%), 93% (95%CI: 91–95%) and 88% (95%CI: 86–90%). For grade II CS this was 82% (95%CI: 78–86%), 74% (95%CI: 70–78%) and 62% (95%CI: 56–68%), respectively. Lastly for grade III CS this was 38% (95%CI: 30–46%), 31% (95%CI: 23–39%) and 26% (95%CI: 18–34%) (Fig. 3).

A multivariate Cox regression model, based on clinically relevant variables, was used to assess the effect of prognostic factors on OS. Only a small number of patients received (neo)adjuvant radiotherapy and/or chemotherapy. Therefore (neo)adjuvant therapies were not included in the analysis. At the end of follow-up, a total of 252 patients had died. Variables are categorical, except for age which is linear. The hazard ratio is per 10 years with a reference of 50 years (mean age at diagnosis). This means that the HR of age of 1.78 represents the increase in risk of a 60-years-old compared to a 50-years-old. Prognostic factors that had a significant negative association with OS were increasing age (HR = 1.78; 95%CI:1.63–1.95; p < .001) earlier period of diagnosis (for '97-'04: HR = 1.68; 95% CI:1.20–2.35; p = .003; for '89-'96: HR = 2.23; 95%CI:1.57–3.15; p < .001) and tumour size >8 cm (HR = 1.48; 95%CI:1.1.-1.97; p = .007). Location in the pelvis, sacrum or coccyx (HR = 1.76; 95% CI:1.24–2.50; p = .002) and spine (HR = 1.23; 95%CI:0.91 = 1.67; p = .173) had a worse outcome than location in the extremities (Table 3).

Patients diagnosed with extremely rare chondrosarcoma subtypes (periosteal (juxta-cortical), mesenchymal, clear cell and dedifferentiated) are described in Appendix B.

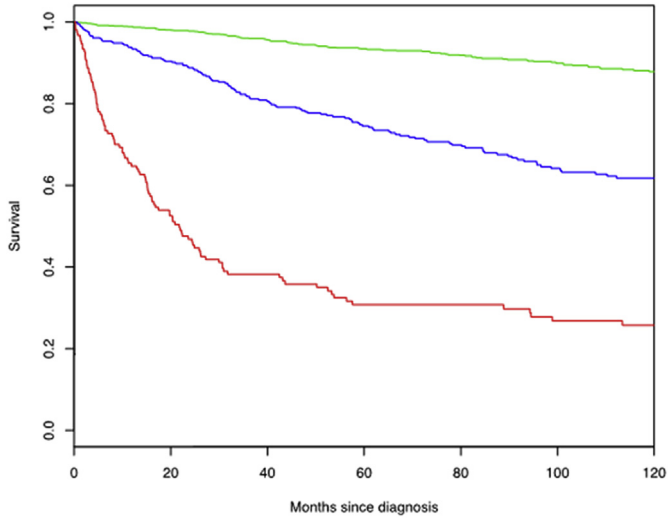

Fig. 3. Overall survival for chondrosarcoma.
Green, atypical cartilaginous tumors/grade I chondrosarcoma; **blue**, grade II; **red**, grade III. Log-rank test of the association of grade and overall survival (p < .001).

4. Discussion

To our knowledge, this is the only recent study that incorporated both the effect modifiers age and grade in their analysis with (overall) survival as an endpoint. Only one study used a statistic model to determine prognostic factors for different locations [11]. In that study, 194 patients were included in a multivariate Cox analysis, with 94 deaths and 11 covariates. This should be regarded as a relatively marginal sample size, justifiable by the rareness of the disease. Inclusion ended after '93, while in our study the 89% of the patients were included later that '93, meaning that the majority of our patients were treated according to more recent guidelines. Others that used statistical models unfortunately did not perform multivariate analysis [8]. Additionally, other important papers on the topic need confirmation in a modern setting, as patients in one study were included between '11-'90 and in another study between '48-'74 [3,10].

Incidence. We observed a marked increase in overall incidence over time during the period covered. This finding is in line with data from the UK [16]. The observed increase could be due to an increase in the true incidence, as the Netherlands is an ageing society and development of CS is age dependent [1,17]. Furthermore, it could reflect an increase in incidental findings due to an increase

in diagnostic imaging [18]. For example, the number of MRI scans increased tenfold between '99-'14 in the Netherlands (Fig. 2b). Previous studies how shown that the majority of ACT/CS I were incidental findings [19,20]. On the contrary, incidental findings are uncommon for high-grade CS, because they destruct the cortex and have faster infiltrative growth patterns with corresponding symptoms [21–24].

The share of CS consisting of ACT/CS I increased from 42% '89-'96 to 75% '05-'13. Although it has been reported in literature that low-grade CS can transform into higher grades, true observational studies reporting the risk of progression are lacking. Increased diagnostic imaging could therefore have the effect of showing a one-off increase in ACT/CS I′ share of the total, given some grade II and III tumours would be detected in their earlier stage, before possible transformation.

The use of curettage to treat ACT/CS I has increased over time as detection rates have gone up. If the treatment is effective in preventing transformation into high-grade CS, we would expect to see a decreased incidence of grade II and III over time. In fact, incidence of grade II and III has increased from 0.95 (89-96) to 1.81 (05-13) per million. Part of this can be explained by the ageing of society; applying 89-96 incidence per age group to 05-13 demographics would see incidence rise to 1.1. Therefore, ageing population is not the only cause for the incidence rise to 1.81. The remainder of the increase could be explained by increased diagnostic imaging.

Our incidence numbers exceed the few that are available in existing literature. A study using national cancer registration data in the UK between '79-'03 found an incidence of 1.56 per million between '79-'03, while a study on the population of East Denmark found an incidence of 1.46 between '83-'96 [17,25]. We believe that divergent outcomes may be explained by the historical data used by previously mentioned studies, and by progressive difference in grading approaches, including grading of borderline lesions as malignant grade I CS, which account for the majority of CS.

Survival and prognostic factors. The 5-years overall survival in our study was 93% (95%CI: 91–95%) for ACT/CS I, 74% (95%CI: 70–78%) for grade II and 31% (95%CI: 23–39%) for grade III. These survival percentages at 5 years after diagnosis are broadly in line with existing literature, which shows for grade I 89%, 90% and 96%, for grade II 62%, 63%, 81% and for grade III of 39%, 43% and 53% (Appendix D) [3,8,10,11]. When interpreting results on survival, one must take into account that of the patients with ACT/CS I, more received surgical treatment recently in comparison to grade II and III. Therefore, a time-effect might overestimate the better survival results for ACT/CS I in comparison to grade II and III.

Also in line with literature, age, tumour grade, -size and -localization are prognostic factors for OS [3,7–9,26]. Additionally, being diagnosed '05-'13 rather than in earlier periods, '89-'96 and '97-'04, was associated with better OS (Table 3). This could be due to better treatment; however, it could also reflect lead time bias, due to increased diagnostic imaging, and/or changes in CS grading.

In this study we did not evaluate the association between radio- and chemotherapy and OS for primary resectable CS. However, findings of a small study in patients with unresectable CS and a study in rats suggest chemotherapy might be beneficial [5,27]. No randomized controlled trials have been undertaken to support this. Furthermore, some studies suggest that OS improves when applying adjuvant radiotherapy to patients with high-risk CS with non-wide surgical margins [6].

The true incidence of enchondromas might be close to 2.8%–2.9% according to two studies reviewing routine knee MR images for enchondromas [19,20], and the incidence of high-grade CS at that same time period in our results is 0.0001%. Thus, if this actually happens, it is expected that the amount of malignant transformation is small. Therefore, even if preventative curettage does have some effect on preventing malignant transformation, we are confident that this percentage is presumably small. As we are not able to explicitly split the potential effect of lower transformation rates from the counter effect of increased diagnostic imaging, we cannot draw any definitive conclusions on the efficacy of curettage. However, we do not find any proof that it achieved its desired outcome in our study.

5. Conclusions

The 3-, 5- and 10-years survival were respectively, 96%, 93% and 88% for ACT/CS I, 82%, 74% and 62% for grade II CS and 38%, 31% and 26% for grade III. Prognostic factors for survival were in line with existing literature. The incidence of CS, and especially ACT/CS I, has increased over time. This could be driven by an ageing population and/or the increased amount of diagnostic imaging. The question whether the negative side-effects of treating the rapidly growing group of diagnosed ACT/CS I with curettage outweigh the potential benefits, is therefore an important one, and requires more research.

Level of significance

Level II: retrospective study, with consecutive patients, well designed cohort from nmore than one center, determining of prognostic factors.

Conflicts of interest

None declared.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.suronc.2018.05.009.

Appendix A

A simplified overview of conventional treatments for different histological grades of CS.

Grade	
Benign lesions	Watchful waiting
ACT/CS I	Watchful waiting/Curettage [28–30] Resection in axial skeleton
Grade II*	Resection [6]
Grade III*	Resection [6]

*Possible adjuvant radiotherapy in intralesional resections [6].
Abbreviation: ACT/CS I, atypical cartilaginous tumor/chondrosarcoma grade I.

Appendix B

In total 36 (1,7%) patients were diagnosed with **periosteal** chondrosarcoma (CS), of which all received surgery for their CS without adjuvant therapy. After an average follow-up (FU) duration of 11.5 years, 4 (11%) had died. **Mesenchymal** CS was the most rare type with only 11 patients diagnosed over 25 years (0,5% of the whole population diagnosed with CS). Ten patients had received surgical treatment, of which 3 with adjuvant radiotherapy (RT) and 2 with both RT and chemotherapy (CT). After an average FU of 7.9 years, 8 (73%) had died. In the group with **clear cell** CS only 3 patients (23%) that had died at time of FU, 5.2 years. Only one patient did not receive any treatment, the other 12 received solely surgical treatment. The second largest subtype consisted of patients diagnosed with **dedifferentiated** CS, with a total of 44 patients (2.0%). Probably imputable to the infaust prognosis only 27 (61%) received surgery for their CS. After an average follow-up (FU) duration of 1.8 years, 38 (86%) of the patients with dedifferentiated CS had died. The six surviving were all surgically treated, two with adjuvant RT.

Chondrosarcomas (n)	N (%)	Age at diagnosis (average)	Surgical treatment					No surgical treatment				
			No RT		RT		Total	No RT		RT		Total
			No CT	CT	No CT	CT		No CT	CT	No CT	CT	
9220 NNO	2082 (95,2%)	50 years	1842	8	61	2	1913	127	7	31	3	168
9221 Periosteal	36 (1,7%)	38 years	36	0	0	0	36	0	0	0	0	0
9240 Mesenchymal	11 (0,5%)	38 years	3	2	3	2	10	0	1	0	0	1
9242 Clear cell	13 (0,6%)	43 years	12	0	0	0	12	1	0	0	0	1
9243 Dedifferentiated	44 (2,0%)	61 years	19	2	6	0	27	13	1	2	1	17
Grand Total	**1982 (100%)**	**50 years**	**1912**	**12**	**70**	**4**	**1861**	**141**	**9**	**33**	**4**	**187**

Appendix C

Incidence of chondrosarcomas for both histological grade and population size.

Year	Population size	Overall		ACT/CS I		Grade II		Grade III		Unknown	
		Incidence	N	Incidence	N	Incidence	N	Incidence	N	Incidence	N
1989	14849000	3.7	55	1.8	27	0.7	10	0.2	3	1.0	15
1990	14951000	2.3	35	0.7	11	0.8	12	0.1	1	0.7	11
1991	15070000	2.5	37	0.7	10	0.7	11	0.3	5	0.7	11
1992	15184000	2.5	38	0.9	13	0.7	11	0.3	5	0.6	9
1993	15290000	2.8	43	1.0	15	0.9	14	0.4	6	0.5	8
1994	15383000	3.4	53	2.0	30	0.5	8	0.1	2	0.8	13
1995	15459000	2.5	39	0.7	11	0.6	10	0.4	6	0.8	12
1996	15528000	3.3	51	1.9	29	0.5	7	0.3	5	0.6	10
1997	15611000	4.4	69	2.0	32	1.3	20	0.4	6	0.7	11
1998	15706000	3.4	54	1.8	29	1.0	15	0.3	5	0.3	5
1999	15812000	3.7	58	2.1	33	0.9	14	0.3	4	0.4	7
2000	15924000	3.5	56	2.2	35	0.5	8	0.4	6	0.4	7
2001	16044000	4.4	70	2.0	32	1.4	22	0.6	9	0.4	7
2002	16149000	4.5	73	3.2	52	0.5	8	0.4	6	0.4	7
2003	16225000	3.8	61	2.0	33	0.8	13	0.6	9	0.4	6
2004	16282000	5.5	89	3.7	60	1.0	16	0.5	8	0.3	5
2005	16320000	4.9	80	3.6	58	1.0	17	0.1	1	0.2	4
2006	16346000	7.4	121	5.4	88	1.4	23	0.2	3	0.4	7
2007	16358000	7.8	127	5.7	94	1.4	23	0.3	5	0.3	5
2008	16405000	6.3	103	4.6	76	1.1	18	0.4	6	0.2	3
2009	16485000	10.3	170	7.2	118	2.0	33	0.7	12	0.4	7
2010	16575000	10.1	168	7.5	125	1.4	24	0.8	13	0.4	6
2011	16656000	11.6	193	9.7	162	1.2	20	0.5	8	0.2	3
2012	16730000	11.8	197	9.7	162	1.4	24	0.4	7	0.2	4
2013	16780000	8.7	146	6.1	102	1.4	23	0.5	9	0.7	12
Average		**5.4**		**3.5**		**1.0**		**0.4**		**0.5**	
Total			**2186**		**1437**		**404**		**150**		195

Incidence per million citizens.

Appendix D

Overall survival reported in literature

Study	Number of patients*	Grade	Overall survival (%)	
			5-years	10-years
Andreou et al., 2011 [8]	N = 115	I	89	89
	(68 extremities, 47 axial/pelvis)	II	63	58
		III	39	33
		Dedifferentiated	-	-
		All	*72*	*69*
Björnsson et al., 1998 [10]	N = 344	I	89	–
	(208 long bones,	II & III	57	–
	109 pelvis,	Dedifferentiated	–	–
	27 scapula)	All	77	–
Evans et al.	N = 81	I	90	83
1977 [3]	*(20 axial,*	II	81	64
	20 long bones,	III	43	29
	23 pelvis, 5 scapula)	Dedifferentiated	–	–
		All	–	–
Fiorenza et al., 2002 [11]	N = 153	I	96	89
	(101 long bones	II	62	53
	52 pelvis)	III	53	38
		Dedifferentiated	–	–
		All	*78*	*70*

*All patients were diagnosed with both primary chondrosarcomas and treated at tertiary centers.

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