Original Article

Role of Fine-needle Aspiration and Survival Analysis of Chondrosarcomas

Pravinkumar Vijaykumar Ghongade[1], Bharat Umakant Patil[1], Anupama Gupta[1], Nitin M. Gangane[2]

[1]Department of Pathology, All India Institute of Medical Sciences (AIIMS) Nagpur, Maharashtra, India, [2]Vice-chancellor, KLE Academy of Higher Education and Research (Deemed-to-be-University) JN Medical College, Belagavi, Karnataka, India

Abstract

Background: Chondrosarcomas (CSs) are the second-most common primary malignant tumor of the bone and are a malignant tumor of cartilaginous origin. **Aim:** The aim of the study was to analyze the accuracy of fine-needle aspiration cytology (FNAC) in diagnosing CS and its correlation with histologic diagnosis and evaluate the survival outcome and prognostic factors in CS. **Setting and Design:** Retrospective study conducted from January 2013 to December 2019. **Materials and Methods:** Data regarding clinical findings, FNAC diagnosis, histopathological, radiological findings, and patient status were retrieved. **Statistical Analysis:** Kaplan–Meier curve and Log Rank (Montel Cox) analysis were used for statistical analysis. **Results:** Twenty-six cases of CS were selected. The accuracy of diagnosing CS on FNAC was 61.53%, and the accuracy in interpreting it as a malignant lesion was 92.30. Overall survival outcome in CS patients was 92.23% at 1 year, 73.23% at 3 years, and 61.32% at 5 years. Survival outcomes significantly altered depending on the histological variants, metastases status, and histological grading, which showed Chi-square values of 31.77 ($P \leq 0.001$), 8.43 ($P = 0.011$), and 6.33 ($P = 0.043$), respectively. The median survival time of CS was 2214.98 days, with a standard error of 362.83. Patient age, gender, tumor size, and skeletal versus extraskeletal CS had little impact on CS survival (Chi-square value = 0.464 ($P = 0.496$ NS), 0.570 ($P = 0.450$ NS), 2.83 ($P = 0.242$ NS), 0.125 ($P = 0.724$ NS), respectively. **Conclusion:** FNAC is a beneficial, reliable tool for screening and diagnosing CS. Prognostic factors such as histological variants, histological Grade 1 and 2, and no metastases status are associated with good survival. Patient age, tumor size, and extraskeletal location are not associated with prognosis and survival.

Keywords: Chondrosarcoma, histological variant, metastases, prognostic factors, survival outcomes

Introduction

Chondrosarcomas (CSs) are malignant tumors of cartilaginous origin and the second-most frequent primary malignant tumor of the bone. CS is the most common in those over 40 years, with a peak incidence between 30 and 60. Only 3.8% of cases are reported to arise in a person's first or second decade.[1] Common tumor locations include the lower and upper limbs and the pelvis.[1,2] Prolonged pain over months is a highly diagnostic sign of this malignancy.[3] In addition to CS not-otherwise specified (NOS), juxtacortical, myxoid, and mesenchymal CS (MeCS), clear cell CS, dedifferentiated CS, and periosteal CS, there are seven further histological subtypes of CS. Histological subtypes exhibit distinct variations in biology and clinical behavior. MeCSs account for 30%–50% of all cases outside the skeleton. However, extraskeletal CS account for only 2% of soft-tissue sarcomas.[4] The standard treatment for CS is surgical resection.[5]

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Preoperative diagnosis relies heavily on fine-needle aspiration cytology (FNAC) and imaging studies. Differentiation between benign chondroma and other malignant bone tumors, including chondroblastic osteosarcoma and metastatic malignancies, is essential in diagnosing CS. CS of the bone and soft tissues can be more accurately diagnosed before surgery with the help of FNAC. Except for the thoracic vertebra, lytic bone lesions are ideal candidates for FNAC.[3]

Combined with radiographic investigations, FNAC is a fast and straightforward method for diagnosing CS patients. However,

Address for correspondence: Dr. Bharat Umakant Patil, Department of Pathology, All India Institute of Medical Sciences (AIIMS) Nagpur, Maharashtra, India.
E-mail: bharatpatil@mgims.ac.in

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the CS survival rate varies in each continent. There is not much research on the survival result and accuracy of FNAC in CS in the Indian population, despite extensive literature search. This is the first study in central India to report on CS survival and the accuracy of FNAC. Survival outcomes and prognostic factors in CS were analyzed, and the accuracy of FNAC in diagnosing CS was compared to histopathological diagnosis at tertiary care hospitals in Central India.

Materials and Methods

The current study is a hospital-based retrospective analysis undertaken from January 2013 to December 2019 in the Department of Pathology of a tertiary care rural hospital in Central India. Year-by-year data on age, sex, sites, radiological findings including tumor size, cytological diagnosis, and final histopathological diagnosis including variants and grading of corresponding CS cases were obtained from the hospital information system (HIS) and patient records from the pathology archives. Smears stained with Papanicolaou and Giemsa were both analyzed. In addition, a histopathological examination of a corresponding biopsy of bone and soft-tissue specimens was performed, and sections were stained with hematoxylin and eosin [Figure 1]. The tumor is classified as Grade I, II, or III on histology. In addition, radiological features such as tumor size, tumor sites, calcifications, extent of surrounding tissue, and metastasis were determined. Only cases with a histologically confirmed diagnosis of CS and follow-up and patient status (living or dead) were included in this study. Furthermore, cases with no data on patient follow-up and just a cytopathological diagnosis of CS were removed from the study.

Histological grading of CS ranged from Grade 1 to 3.[6] A Grade of 1, 2, or 3 is assigned based on the cellularity of the lesion (ranging from hypocellular to hypercellular), changes in the matrix (ranging from abundant and hyaline to sparse and myxoid), the character of the cells (ranging from small and minimally pleomorphic with little nuclear detail to markedly pleomorphic with bizarre forms, giant cells, and hyperchromatic nuclei), and replicative activity (ranging from rare binucleate forms to multiple and bizarre mitotic figures).[2] In addition, information regarding treatment, such as surgery, chemotherapy, radiation therapy, follow-up, and patient status (live or dead) was retrieved from the HIS, a patient file maintained at the Medical Records Department, and a population-based cancer registry located at the department of pathology.

A Kaplan–Meier curve was developed to illustrate the cumulative survival outcome for a single component. It is used in analysis based on a single element. Log Rank (LR) (Montel Cox) was used to calculate it, and different survival curves were compared using this method. Overall survival, sometimes known as OS, was calculated from diagnosis until the patient died. The statistical application SPSS 27 version (IBM Corp. Released 2022) was used throughout the statistical research, and the statistical application SPSS 27 version (IBM Corp. Released 2022) was used. SPSS Statistics for Windows by IBM was created in Armonk, New York, USA.

The institutional ethics committee approved this study (MGIMS/IEC/Path/329/2022 dated August 01, 2022). Patient confidentiality was maintained throughout all research procedures. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards mentioned in these lines in ethics as the Helsinki Declaration.

Results

The male-to-female ratio in CS was 1.88:1. Regarding age distribution, the fifth decade had the most significant number of cases, followed by the sixth decade [Table 1]. Pain and swelling were recorded in 19 cases, with 7 cases reporting merely swelling without pain as complaints. Sinonasal CS showed nasal bleeding symptoms. The lower limb was involved in most CS cases (12), followed by the pelvic and buttocks regions (8 cases), the upper limb (5 cases), and the head and neck (1 case of sinonasal CS). There were also 15 cases of skeletal CS and 11 cases of extraskeletal CS documented. The skeletal-to-extraskeletal CS ratio was 1.5:1 [Table 2]. On histological investigation, 26 cases were identified as CS, although only 22 cases with cytopathology reports were available. Cytology data were missing in HIS in four cases because cytology was performed at a different hospital and then sent to our hospital for further treatment. As a result, the cytohistological correlation was performed in 22 cases [Table 3].

Table 1: Age and gender distribution of patients of chondrosarcoma

Age group	Male	Female	Number of cases
21–30	2	0	2
31–40	3	1	4
41–50	2	2	4
51–60	5	2	7
61–70	3	2	5
71–80	2	2	4
Total	17	9	26

Table 2: Site of involvement of chondrosarcoma

Sites	Skeletal CS	Extra skeletal CS	Number of cases
Head and neck	0	1	1
Lower limb	8	4	12
Pelvis	3	5	8
Upper limb	4	1	5
Total cases	15	11	26

CS: Chondrosarcoma

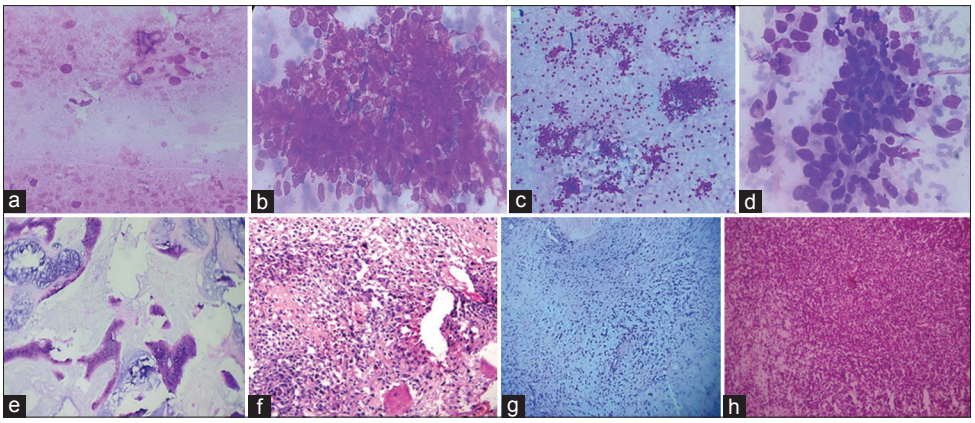

Figure 1: Chondrosarcoma (CS) cytology microphotograph on a-d, (a) Conventional CS at ×100 (Giemsa staining) – (b) Mesenchymal CS ×400 (Giemsa stained) (c) Myxoid CS ×40 Giemsa-stained (d) Poorly differentiated CS ×400 (Giemsa stained). CS histology microphotograph on hematoxylin staining E to H, (e) Well-differentiated CS at ×40 (f) Mesenchymal CS at ×100 (g) Myxoid CS ×40 (h) Dedifferentiated CS ×100

Table 3: Correlation of cytopathological and corresponding histopathological diagnoses in chondrosarcoma cases

Histopathology	Total cases whose both reports available	Correlation with cytological diagnosis				Utility of cytology in CS (%)	
		Accurately categorized	Diagnosed as malignant but not accurately categorized	Suspicious CS	Inadequate smear	Accuracy of diagnosing CS on cytology	Overall accuracy in diagnosing CS as malignant lesion on cytology
CS	22	12	7	2	1	54	95.45

CS: Chondrosarcoma

On cytology, 12 of the 22 patients were correctly identified as CS. Seven cases were diagnosed as malignant but not as CS, whereas two cases were suspected of being CS. In one case, inadequate smear was recorded due to smear bleeding, and the patient was unwilling to repeat the procedure. On cytology, the accuracy of diagnosing CS was 61.53%. On cytopathology, however, the total accuracy in interpreting it as a malignant lesion was 92.30% [Table 3]. There were 26 cases documented on histology, including biopsy and specimen. On histology, six CS variations were found in our cases. Classical/NOS CS supplied 42.30% of the CS variation, whereas myxoid CS (MyCS) contributed 15.38%. Other variations were also responsible for well-differentiated CS (15.38%) and MeCS (7.7%). Dedifferentiated CS (7.69%), clear cell CS (3.84%), and high-grade CS (19.23%) were all found [Figure 1]. Histopathology grading revealed that seven cases were Grade I, nine were Grade II, and ten were Grade III [Table 4].

Patients were followed for a median of 62 months. Only 26 cases of CS were included in the survival analysis; the overall cumulative probability of survival in CS patients was 92.23% at 1 year, 73.2% at 3 years, and 61.3% at 5 years [Table 5 and Figure 2a]. Similarly, the cumulative likelihood of death in CS patients at 3 and 5 years was 26.8% and 38.7%, respectively. The most CS cases (16 cases) were seen in people over 50. Only ten of the CS patients were under the age of 50 years. On radiography, six instances were <5 cm in size, 11 cases were 5–10 cm in size, and 9 cases were more significant than 10 cm in size [Table 6]. Calcification was found in 9 of the instances. CS metastasis was detected in seven patients (26.91%), whereas 19 (73.13%) cases had no metastases from CS. Two CS cases developed metastases in histological Grade II tumors [Table 6]. A decreased survival rate was related to positive metastatic status (P = 0.011, S) and high-grade histology of CS (P = 0.043, S) [Table 7 and Figure 3].

Table 4: Histological variant of chondrosarcoma

Histopathological diagnosis	Number of cases (%)
Classical/NOS CS	11 (42.3)
Clear cell CS	1 (3.84)
Dedifferentiated CS	2 (7.69)
Mesenchymal CS	2 (11.51)
Myxoid CS	4 (15.44)
High-grade CS	5 (19.23)
Total cases	26 (100)

CS: Chondrosarcoma, NOS: not otherwise specified

Table 5: Cumulative probability of survival of chondrosarcoma cases

Time (years)	Overall cumulative probability of survival of CS (%)	Overall chances of death in CS cases (%)
1	92.23	7.77
3	69.7	30.3
5	52.3	47.7

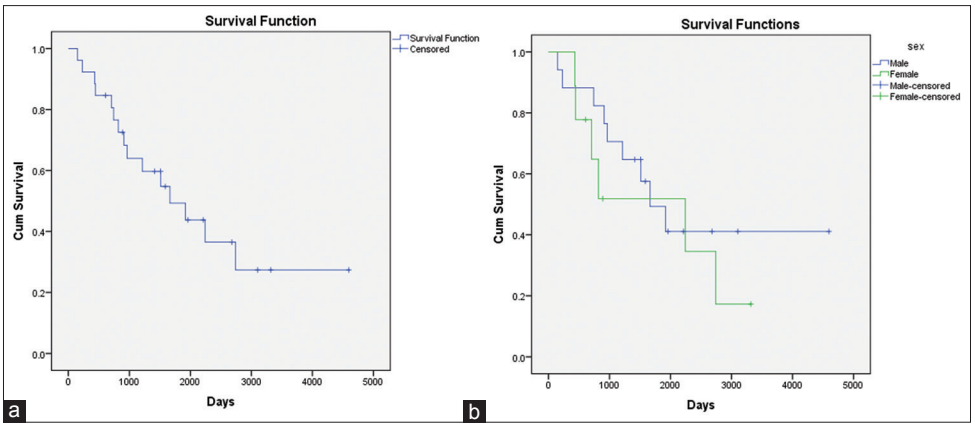

Figure 2: (a) Kaplan–Meier (KM) survival curve showing overall survival outcome in chondrosarcoma (CS) cases. (b) KM survival curve showing overall survival outcome depending on gender in CS cases

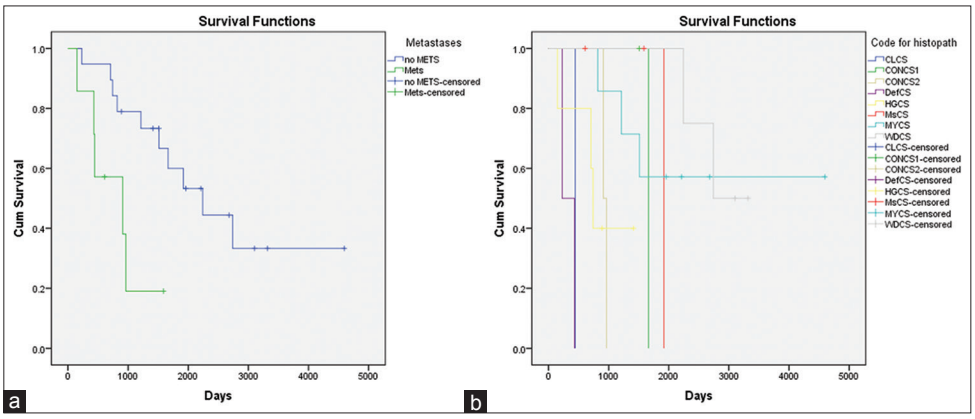

Figure 3: (a) Kaplan–Meier (KM) survival curve showing cumulative survival outcome depending on the status of metastases in chondrosarcoma (CS) cases (b) KM survival curve showing cumulative survival outcome depending on the histological variant of CSchondrosarcoma. CLCS: Clear cell chondrosarcoma, CONSC1: Conventional chondrosarcoma grade 1,2, CONCS: Conventional chondrosarcoma grade 3, DefCS- Dedifferentiated chondrosarcoma, HGCS: High grade chondrosarcoma, MsCS: Myxoid chondrosarcoma, MYCS: Mysenchymal chondrosarcoma, WDCS: Well differentiated chondrosarcoma

Table 6: Median survival time in chondrosarcoma according to a different variable

Variable	Number of cases	Median survival time (days)	SE (days)	95% CI (days)	
				Lower bound	Upper bound
Overall survival	27	2214.986	362.833	1503.833	2926.139
Male	17	2539.312	459.977	1637.758	3440.866
Female	9	1729.623	400.514	944.616	2514.631
Age <50 years	10	2686.822	592.560	1525.404	3848.239
Age >50 years	16	1714.803	306.550	1113.964	2315.641
Grade 1 CS	7	2383.114	352.190	1692.822	3073.407
Grade 2 CS	9	2645.556	585.146	1498.670	3792.441
Grade 3 CS	10	1130.200	272.841	595.431	1664.969
Extraskeletal CS	11	2138.044	502.006	1154.112	3121.976
Skeletal CS	15	1955.250	347.408	1274.330	2636.170
Tumor <5 cm	6	3387.111	684.459	2045.571	4728.652
Tumor 5–10 cm	11	1670.843	266.071	1149.344	2192.342
Tumor >10 cm	9	1341.778	340.068	675.244	2008.311
No metastases	19	2574.900	406.722	1777.724	3372.076
Metastases present	7	805.381	185.619	441.567	1169.195

CS: Chondrosarcoma, CI: Confidence interval, SE: Standard error

Table 7: Log rank (Montel-Cox) analysis for survival outcome of chondrosarcoma cases

LR (Mantel-Cox)	χ^2	Df	*P*
Survival outcome depending on the age	0.464	1	0.496, NS
Survival outcome depending on the sex	0.570	1	0.450, NS
Survival outcome depending on the histological variant of CS	31.771	7	0.0001, S
Survival outcome depending on metastases status	8.439	1	0.011, S
Survival outcome depending on the size of the tumor	2.834	2	0.242, NS
Survival outcome depending on extra skeletal CS versus skeletal CS	0.125	1	0.724, NS
Survival outcome depending on histological grading of CS	6.338	2	0.043, S

CS: Chondrosarcoma, NS: Nonsignificant, DF: Degree of freedom, S: Significant, LR: Log rank

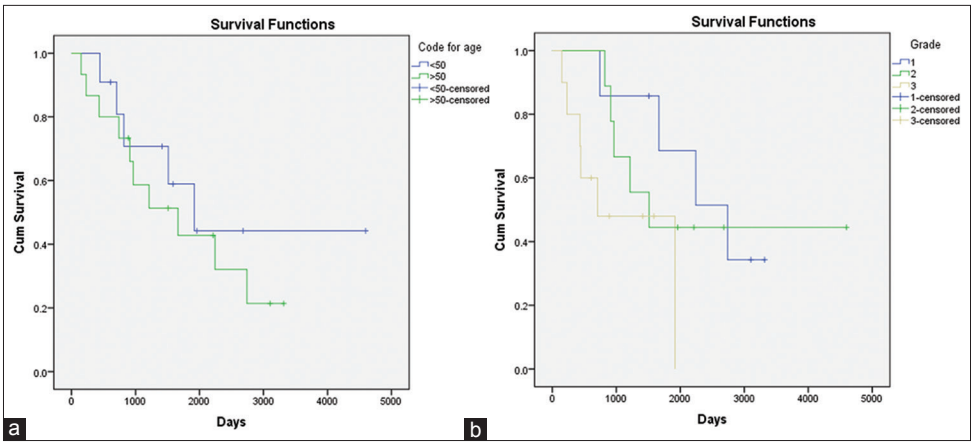

Figure 4: (a) Kaplan–Meier (KM) survival curve showing overall survival outcome depending on the age of patients (<50 and >50) in chondrosarcoma (CS) cases (b) KM survival curve showing overall survival outcome depending on histological grading (Grade 1, 2, and 3) in CS cases

The LR (Mantel-Cox) test was used to assess survival outcomes in CS cases; cumulative survival outcome was significantly different depending on histological variants, metastasis status, and histological grading, with Chi-square values of 31.77 (*P* = 0.000 S), 8.43 (*P* = 0.011), and 6.33 (*P* = 0.043), respectively [Table 7 and Figures 3 and 4]. Similarly, the LR test revealed that patient age, gender, tumor size, and skeletal versus extraskeletal CS had little impact on CS survival (Chi-square value = 0.464 (*P* = 0.496 NS), 0.570 (*P* = 0.450 NS), 2.83 (*P* = 0.242 NS), and 0.125 (*P* = 0.724 NS), respectively [Table 7 and Figures 2a, 2b and 3a, 3b and 4a, 4b].

Discussion

In the present study, the mean of the CS patients was 55.3 years. Studies commonly affect males [Table 1] consistent with another author.[7] The persistent discomfort over several months is a key clinical sign in distinguishing between malignant and benign cartilage lesions. Nineteen CS cases reported pain, whereas seven (26.07%) had no classic symptoms.[3]

However, the current study found that cytology was only 61.53% effective at detecting CS. However, cytopathology had a 92.30% overall accuracy rate in classifying it as a malignant tumor. Cytology positively identified CS in 12 instances, ruled out malignancy in 7 cases, and raised suspicions in 2 cases [Table 3]. Three patients were diagnosed with high-grade sarcoma, including metastases of poorly differentiated carcinoma/sarcoma, a likely round cell tumor, an intermediate-grade sarcoma, and a liposarcoma. CSs of Grade 3 were found in ten people [Table 6]. In the absence of cartilaginous particles, cases of Grade 3 CS may be difficult to distinguish from metastatic, poorly differentiated epithelial malignancies.[7] This is probably why cytology could not label these lesions as CS, and FNAC reported them as malignant. Due to their rarity, reports of FNAC diagnosis for other types of CSs, such as mesenchymal, clear cell, and dedifferentiated, are scarce.[3]

MyCS demonstrates a strong tendency for local recurrence (37%–48%) and metastatic disease (50%), usually pulmonary.[8] The large amounts of mucoid material and focal areas of myxoid degeneration posed a diagnostic dilemma. Areas of dedifferentiation with MyCS are scarce, reported before in few cases, and associated with poor survival rates.[4] Other myxoid tumors of soft tissue that should be considered in the differential diagnoses on cytology include myxoid liposarcoma, soft-tissue chondroma, a myxoid variant of malignant fibrous histiocytoma, myxoma, and CS. Thus, FNAC has proved to be a valuable tool in diagnosing adult myxoid sarcomas.[9]

Poorly differentiated monomorphic, small, spindle-shaped, or polygonal cells with a high nuclear-cytoplasmic ratio are embedded in a dense metachromatic matrix, and malignant

chondroid component (atypical cartilage) is the defining cellular features of MeCS on FNA smears. MeCS is a fast-progressing, highly malignant tumor frequently spreading through the blood and lymphatic system. The metastatic disease most frequently manifests in the lung.[4,8,10]

Based on FNA findings, MeCS's differential diagnoses might include rhabdomyosarcoma, Ewing's sarcoma, hemangiopericytoma, synovial sarcoma, and other CS variations that also exhibit small round blue cells.[11] The diagnosis of MeCS by FNA is challenging due to the difficulty in sampling both phases of the tumor, the lack of distinctive clinical and radiographic features, and the tumor's rarity.[4] When a FNA bone or soft-tissue mass specimen has tiny, spherical, blue cells in a basophilic background matrix, MeCS should be considered in the differential diagnosis.[11] Among tumor histologies, mesenchymal and dedifferentiated CS predicted a bad prognosis. FNAC effectively identifies bone and soft-tissue cancers with meticulous radiologic and clinical examination.[7,11]

The present study showed a 92.23% chance of survival at 1 year, 73.23% at 3 years, and 61.32% at 5 years [Table 5 and Figures 2-4]. However, other studies reported survival rates ranging from 72.00% to 95.00% at 5 years and 53.00%–69.00% at 10 years.[12-14] Few studies showed that the 5-year overall survival of unresectable CS was 53.00%.[15,16]

In the current study, age ($P = 0.496$) and gender ($P = 0.450$) had no significant impact on survival [Table 7], consistent with another study.[12] Grade 3 CS cases showed a substantially poor median survival of 1130.20 days, with a standard error of 272.84 days than Grade 1 and 2 CS cases. A high tumor grade was found to have a statistically significant negative impact on overall survival ($P = 0.043$) [Table 7 and Figure 4b]. This could be because only 10%–15% of Grade 1 and 2 CS metastasized, but Grade 3 CS has a higher risk of metastasis.[6] Metastatic disease was seen in 26.92%. These results are congruent with those described by other authors.[12,16] Patients with metastases had a median survival time of 805.38 days, with a standard error of 185.61 days, which was considerably ($P = 0.011$, S) shorter than patients without metastases (2574.93 days with a standard error of 406.72 days) [Tables 6 and 7]. At the time of follow-up, seven patients (26.92%) developed metastatic disease: five in the lung, one in the thigh, and one in the spine. Regardless of tumor grade or localization, the development of local recurrence and distant metastases significantly decreased overall survival.[12] Even in the current investigation, metastatic CS was documented, with significantly high mortality rates. The occurrence of metastasis in these patients indicates a highly aggressive disease profile.[12]

In the present study, the pelvic location of CS has a worse prognosis. Our five survival rates in those patients are 56.23%, respectively. Study results are consistent with Fromm *et al*.[13] In central CS, published 10-year survival rates vary between 54.00% and 88.00%.[13,17] The pelvis's CS exhibits more aggressive behavior and should not be cured even in low-grade tumors. Local recurrence might lead to dedifferentiation and metastatic disease.[13] The 5-year survival rate for CS is 61.32%, much higher than that of osteosarcoma and Ewing sarcoma.[14] The present study showed that tumor grade, histological variant, pelvic location, and metastasis status are all associated with the prognosis of CS.

The study's strength is that it helps determine the incidence and survival rate of CS in the rural populations of central India. Second, this information will help develop CS cancer diagnosis, clinical intervention, and palliative care methods for these individuals.

Conclusion

FNAC is a beneficial, reliable, time-consuming tool for screening and diagnosing CS. Overall survival outcome in CS patients was 92.23% at 1 year, 73.23% at 3 years, and 61.32% at 5 years. Prognostic factors such as histological variants, histological Grade 1 and 2, and no metastases status are associated with good survival. The patient age, tumor size, and extraskeletal location are not associated with prognosis and survival.

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Conflicts of interest

There are no conflicts of interest.

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