Correlation between survival and tumour characteristics in patients with chondrosarcoma

Achmad Fauzi Kamal, Kurniadi Husodo, Yogi Prabowo, Errol Untung Hutagalung
Department of Orthopaedic and Traumatology, Ciptomangunkusumo National Central Hospital / Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia

ABSTRACT

**Purpose.** To evaluate the correlation between survival and tumour characteristics in 23 patients with chondrosarcoma.

**Methods.** Records of 15 men and 8 women aged 14 to 66 (mean, 37) years who were diagnosed with primary (n=19) or secondary (n=4) chondrosarcoma of the axial skeleton (n=8), proximal extremity (n=9), or distal extremity (n=6) were reviewed. The tumour diameter was <10 cm in 4 patients, 10–19 cm in 12, and 20–30 cm in 7. The tumour involved the intramedullary in 17 and the periosteum in 6 patients; tumour extension was intracompartamental in 5 and extracompartamental in 18 patients. The Evans histological grade for the tumours was grade 1 in 6 patients, grade 2 in 10, and grade 3 in 7. The mean tumour size was 12.3 cm for grade 1 tumours, 18.2 cm for grade 2 tumours, and 18.3 cm for grade 3 tumours. 13 patients had no metastasis and 3 of 10 patients with grade 2 tumours and all 7 patients with grade 3 tumours had metastasis at the lung at presentation. 17 patients underwent surgery, one underwent adjuvant treatment only, and 5 declined treatment.

**Results.** The mean follow-up period for the 23 patients was 3.1 years (range, 3 weeks to 9 years). The 5-year survival rate was 43% overall, 83.3% for grade 1 tumours, 50% for grade 2 tumours, and 0% for grade 3 tumours. The median survival duration was 20 (95% confidence interval, 11–29) months. Two patients had local recurrence and 16 did not, and the 5 patients who declined treatment died. Survival correlated with Evans histological grading (p=0.004), the presence of metastasis at presentation (p=0.026) and local recurrence (p=0.004).

**Conclusion.** The survival rate was lower in patients with higher Evan grading, metastasis, or local recurrence.

**Key words:** chondrosarcoma; survival analysis

INTRODUCTION

Chondrosarcoma is a malignant tumour consisting
of cartilaginous tissue without osteoid matrix.\textsuperscript{1,2} It accounts for 10 to 20\% of all bone malignancies, with an annual incidence of 1.7 per million people in the UK.\textsuperscript{3} It typically occurs in adults aged 30 to 60 years.\textsuperscript{4} Primary chondrosarcoma usually occurs within bone or cartilage and accounts for 86\% of chondrosarcoma.\textsuperscript{5} Secondary chondrosarcoma usually arises from benign tumours such as osteochondroma, enchondroma, and fibrous dysplasia.\textsuperscript{6}

Chondrosarcoma can be classified based on its histologic grade for cellularity, atypia, and pleomorphism.\textsuperscript{3,7} Grade 1 lesions have slow growth and metastasise infrequently, whereas grades 2 and 3 have a higher metastatic rate and lower survival rate.\textsuperscript{8} Dedifferentiated chondrosarcoma is an aggressive subtype and is associated with poorer prognosis, with a 5-year survival rate of 20 to 30\%.\textsuperscript{9} Borderline or grade ½ chondrosarcoma typically has a more benign course and is difficult to be differentiated from enchondroma.\textsuperscript{10}

Wide surgical resection is the primary treatment for chondrosarcoma;\textsuperscript{11} radiation therapy is reserved for non-resectable lesions or when wide margin resection is not feasible.\textsuperscript{12} Chemotherapy has a minimal role in treatment, although it is suggested for use in young, healthy patients with dedifferentiated chondrosarcoma and extraskeletal myxoid chondrosarcoma.\textsuperscript{3,13}

This study evaluated the correlation between survival and tumour characteristics in 23 patients with chondrosarcoma.

**MATERIALS AND METHODS**

Records of 15 men and 8 women aged 14 to 66 (mean, 37) years who were diagnosed with primary (n=19) or secondary (n=4) chondrosarcoma of the axial skeleton (n=8), proximal extremity (n=9), or distal extremity (n=6) in our hospital from 1995 to 2013 were reviewed (Table). 20 patients presented with a mass and 3 with pain. The tumour diameter was <10 cm in 4 patients, 10–19 cm in 12, and 20–30 cm in 7. The tumour involved the intramedullary in 17 and the periosteum in 6 patients; tumour extension was intracompartamental in 5 and extracompartamental in 18 patients. The Evans histological grade for the tumours was grade 1 in 6 patients, grade 2 in 10, and grade 3 in 7. The mean tumour size was 12.3 cm for grade 1 tumours, 18.2 cm for grade 2 tumours, and 18.3 cm for grade 3 tumours. Three of 10 patients with grade 2 tumours and all 7 patients with grade 3 tumours had metastasis to the lung at presentation. 17 patients underwent surgery, one underwent adjuvant treatment only, and 5 declined treatment.

Complications associated with the tumour included pleural effusion secondary to pulmonary metastasis, a pathologic fracture, bowel obstruction secondary to a pelvic lesion, haematuria secondary to a lower rib lesion, and neurological deficit secondary to a vertebral lesion.

The Kaplan-Meier survival rate was evaluated. The correlation of survival with tumour characteristics, treatment methods, presence of metastasis at presentation, and local recurrence were analysed using the log rank test. A p value of <0.05 was considered statistically significant.

**RESULTS**

The mean follow-up period for the 23 patients was 3.1 years (range, 3 weeks to 9 years). The 5-year survival rate was 43\% overall, 83.3\% for grade 1 tumours, 50\% for grade 2 tumours, and 0\% for grade 3 tumours (Fig.). The median survival duration was 20 (95\% confidence interval, 11–29) months. Two patients had local recurrence, 16 did not, and 5 who declined treatment died.

Survival correlated with Evans histological grading (p=0.004), the presence of metastasis at presentation (p=0.026) and local recurrence (p=0.004) [Fig.].

**DISCUSSION**

For patients with chondrosarcoma, only 51 of 358 patients at the Mayo Clinic\textsuperscript{14} and only 21 of 45 patients in another study\textsuperscript{15} completed full follow-up. Chondrosarcoma has a male predominance,\textsuperscript{4,14} and usually occurs as primary chondrosarcoma\textsuperscript{15} of the intramedullary type in proximal extremities\textsuperscript{14} at age 30 to 50 years\textsuperscript{16}; the most common presenting symptoms are pain and mass formation.\textsuperscript{14} Our patients usually presented at a late stage; most tumours were of grades 2 and 3, and the mean diameter of the tumours at presentation was 16.7 cm, which is >2 times larger than the mean diameter of 7.5 cm (volume, 567 cm\(^3\)) reported in other study.\textsuperscript{3}

The accuracy of core needle biopsy in diagnosing and grading of chondrosarcoma is 85.9\%, and the accuracy of fine needle aspiration biopsy is 67\% for primary chondrosarcoma and 86\% for metastatic chondrosarcoma.\textsuperscript{17}

Wide excision is the treatment of choice for grades 2 and 3 chondrosarcoma. For grade 1 chondrosarcoma, intralesional curettage followed by local adjuvant
therapy (phenol, liquid nitrogen) and filling the cavity with bone grafts achieves satisfactory outcome. As chondrosarcoma contains only a few actively proliferating cells, it is relatively radio-resistant and requires doses of >60 Gy to achieve local control after incomplete resection. Chemotherapy is only effective in high-grade chondrosarcoma and mesenchymal chondrosarcoma. In our study, radiotherapy and chemotherapy were performed in patients with local recurrence or metastasis or in whom a tumour-free margin could not be achieved because of proximity to vital structures such as the spinal cord.

In our study, the rate of local recurrence was 11%, which was similar to 14.8% reported in other study, but the rates of metastasis (43% vs. 8%) and extracompartmental extension (78% vs. 23%) in our study were higher. The higher degree of malignancy is associated with higher tendency to metastasise. The 5-year survival rate of 43% in our study was lower than the 59% or 64% reported in other studies. Early treatment before extracompartmental spread and metastasis would achieve a better outcome. The survival rate for grade 3 tumours is lower than that for grades 1 and 2 tumours. The survival rate decreases in

| Parameter                                | No. (%) of patients | Median (95% CI) survival (months) | p Value (log rank test) |
|-------------------------------------------|---------------------|-----------------------------------|-------------------------|
| No. (% of men: women                      | 15:8 (65:35)        |                                   |                         |
| Mean±SD (range) age (years)               | 37±12 (14–66)       |                                   |                         |
| Presenting symptom                        |                     |                                   |                         |
| Mass                                      | 20 (87)             |                                   |                         |
| Pain                                      | 3 (13)              |                                   |                         |
| Tumour diameter (cm)                      |                     |                                   |                         |
| <10                                       | 4 (17)              | 83 (41–125)                       | 0.0578                  |
| 10–19                                     | 12 (52)             | 14 (0–28)                         |                         |
| 20–30                                     | 7 (30)              | 22 (7–37)                         |                         |
| Tumour location                           |                     |                                   |                         |
| Axial skeleton                            | 8 (35)              | 10 (5–15)                         | 0.2155                  |
| Proximal extremity                        | 9 (39)              | 20 (14–26)                        |                         |
| Distal extremity                          | 6 (26)              | 84 (0–173)                        |                         |
| Origin                                    |                     |                                   |                         |
| Primary                                   | 19 (83)             | 16 (5–27)                         | 0.2448                  |
| Secondary                                 | 4 (17)              | 68 (44–92)                        |                         |
| Radiologic findings                       |                     |                                   |                         |
| Intramedullary involvement                | 17 (74)             | 14 (7–21)                         | 0.1949                  |
| Periosteal involvement                    | 6 (26)              | 72 (53–91)                        |                         |
| Biopsy                                    |                     |                                   |                         |
| Open biopsy                               | 12 (52)             | 68 (0–160)                        | 0.4502                  |
| Fine-needle aspiration biopsy             | 11 (48)             | 16 (5–27)                         |                         |
| Evans histological classification         |                     |                                   |                         |
| Grade 1                                   | 6 (26)              | 84 (36–132)                       | 0.0042                  |
| Grade 2                                   | 10 (43)             | 47 (23–71)                        |                         |
| Grade 3                                   | 7 (30)              | 16 (0–44)                         |                         |
| Tumour extension                          |                     |                                   |                         |
| Intracompartmental                        | 5 (22)              | 72 (0–97)                         | 0.4763                  |
| Extracompartmental                        | 18 (78)             | 18 (10–26)                        |                         |
| Metastasis                                |                     |                                   |                         |
| Yes (lung)                                | 10 (43)             | 10 (0–21)                         | 0.0264                  |
| No                                        | 13 (57)             | 72 (45–99)                        | 0.8014                  |
| Treatment                                 |                     |                                   |                         |
| Wide resection                            | 17 (74)             | 22 (0–78)                         | 0.0039                  |
| Adjuvant treatment only                   | 1 (4)               | 7 (7–7)                           |                         |
| Declined treatment                        | 5 (22)              | 10 (0–21)                         |                         |
| Local recurrence                          |                     |                                   |                         |
| Yes                                       | 2 (11)              | 8 (5–10)                          |                         |
| No                                        | 16 (89)             | 22 (0–100)                        |                         |
Figure Kaplan-Meier survival analysis for the 23 patients with chondrosarcoma showing (a) the 5-year survival rate of 43%, and correlation between survival and (b) Evans histological grading, (c) the presence of metastasis at presentation, and (d) the presence of local recurrence.
patients with metastasis or local recurrence compared with those without (18% vs. 64%).\textsuperscript{15,19}

CONCLUSION

The survival rate was lower in patients with higher Evans histological grading, metastasis, or local recurrence.

DISCLOSURE

No conflicts of interest were declared by the authors.

REFERENCES

1. van Loon CJ, Veth RP, Pruszczynski M, Wobbes T, Lemmens JA, van Horn J. Chondrosarcoma of bone: oncologic and functional results. J Surg Oncol 1994;57:214–21.
2. Healey JH, Lane JM. Chondrosarcoma. Clin Orthop Relat Res 1986;204:119–29.
3. Rizzo M, Ghert MA, Harrelson JM, Scully SP. Chondrosarcoma of bone: analysis of 108 cases and evaluation for predictors of outcome. Clin Orthop Relat Res 2001;391:224–33.
4. Fiorenza F, Abudu A, Grimer RJ, Carter SR, Tillman RM, Ayoub K, et al. Risk factors for survival and local control in chondrosarcoma of bone. J Bone Joint Surg Br 2002;84:93–9.
5. Unni KK. Chondrosarcoma. Dahlin's bone tumors. General aspects and data on 11,087 cases. 5th edition. Philadelphia: Lippincott Raven; 1996:71–108.
6. Merchan EC, Sanchez-Herrera S, Gonzalez JM. Secondary chondrosarcoma. Four cases and review of the literature. Acta Orthop Belg 1993;59:76–80.
7. Evans HL, Ayala AG, Romsdahl MM. Prognostic factors in chondrosarcoma of bone: a clinicopathologic analysis with emphasis on histologic grading. Cancer 1977;40:818–31.
8. Lee FY, Mankin HJ, Fondren G, Gebhardt MC, Springfield DS, Rosenberg AE, et al. Chondrosarcoma of bone: an assessment of outcome. J Bone Joint Surg Am 1999;81:326–38.
9. Cesari M, Bertoni F, Bacchini P, Mercuri M, Palmerini E, Ferrari S. Mesenchymal chondrosarcoma. An analysis of patients treated at a single institution. Tumori 2007;93:423–7.
10. Tsuchiya H, Ueda Y, Morishita H, Nonomura A, Kawashima A, Fellinger EJ, et al. Borderline chondrosarcoma of long and flat bones. J Cancer Res Clin Oncol 1993;119:363–8.
11. Gellerstam H, Hogendoorn PC, Dijkstra SD, van Rijswijk CS, Krol AD, Taminiau AH, et al. The clinical approach towards chondrosarcoma. Oncologist 2008;13:320–9.
12. McNaney D, Lindberg RD, Ayala AG, Barkley HT Jr, Hussey DH. Fifteen year radiotherapy experience with chondrosarcoma of bone. Int J Radiat Oncol Biol Phys 1982;8:187–90.
13. Patel SR, Burgess MA, Papadopoulos NE, Linke KA, Benjamin RS. Extraskeletal myxoid chondrosarcoma. Long-term experience with chemotherapy. Am J Clin Oncol 1993;18:161–3.
14. Pritchard DJ, Lunke R, Taylor WF, Dahlin DC, Medley BE. Chondrosarcoma: a clinicopathologic and statistical analysis. Cancer 1980;45:149–57.
15. Bruns J, Elbracht M, Niggemeyer O. Chondrosarcoma of bone: an oncological and functional follow-up study. Ann Oncol 2001;12:859–64.
16. Daugaard S, Myhre-Jensen O, Schiodt T, Jurik AG, Keller J, Mouridsen HT, et al. Clinical and histopathological prognostic factors in chondrosarcomas. Sarcoma 1997;1:47–54.
17. Jennings R, Riley N, Rose B, Rossi R, Skinner JA, Cannon SR, et al. An evaluation of the diagnostic accuracy of the grade of preoperative biopsy compared to surgical excision in chondrosarcoma of the long bones. Int J Surg Oncol 2010;2010:270195.
18. Mermerkaya MU, Bekmez S, Karaaslan F, Danisman M, Kosemehmetoglu K, Gedioglu G, et al. Intralresional curettage and cementation for low-grade chondrosarcoma of long bones: retrospective study and literature review. World J Surg Oncol 2014;12:336.
19. Frezza AM, Cesari M, Baumhoer D, Biad A, Bielack S, Campanacci D, et al. Mesenchymal chondrosarcoma: prognostic factors and outcome in 113 patients. A European Musculoskeletal Oncology Society study. Eur J Cancer 2015;51:374–81.