Outcomes of Pediatric Patients with metastatic Ewing sarcoma treated with interval compression

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Abstract

Background: Interval compression (IC), defined as 2 week-long cycles of alternating vincristine/doxorubicin/cyclophosphamide and ifosfamide/etoposide, improves survival for localized Ewing sarcoma. The outcomes of patients with metastatic disease treated with IC are uncertain. Methods: We retrospectively reviewed the charts of pediatric patients with metastatic Ewing sarcoma treated with IC at our center between January-2013 and March-2020. We calculated event-free survival and overall survival and used log rank tests for univariate comparisons. Results: We identified 34 patients aged 2.7–17.1 years (median,11.6 years). Twenty-six patients (76%) had pulmonary metastases, and 14 (41%) had extra-pulmonary metastases in the bone (n = 11), lymph nodes (n = 2), and intraspinal tissue (n = 1). All patients received local control therapy: surgery only (n = 7, 21%), radiotherapy only (n = 18, 53%), or both (n = 9, 26%). The estimated 3-year OS and EFS were 62%±9% and 39%±9%, respectively. Patients with pulmonary only metastasis had a 3-year OS of 88%±8% in comparison to those with extra-pulmonary metastasis of 27%±13% (P=0.0074). Survival did not differ according to age group (> vs < 12 years), metastasis site, or primary tumor site, but 3-year event-free survival significantly differed according to local control therapy (surgery only, 83% ± 15%; combined surgery and radiation, 30% ± 18%; radiation only, 15% ± 10%; P = .048). Conclusion: IC yielded similar outcomes for patients with metastatic Ewing sarcoma to that reported in the literature using other regimens. We suggest including this approach to other blocks of therapy

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Abbreviations:

CR	Complete response
ES	Ewing sarcoma
IE	Ifosfamide/etoposide
KM	Kaplan–Meier
PD	Progressive disease
PR	Partial response
VDC	Vincristine/doxorubicin/cyclophosphamide
WLI	Whole-lung irradiation

ABSTRACT

Background: Interval compression (IC), defined as 2 week-long cycles of alternating vincristine/doxorubicin/cyclophosphamide and ifosfamide/etoposide, improves survival for localized Ewing sarcoma. The outcomes of patients with metastatic disease treated with IC are uncertain.

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Conclusion: IC yielded similar outcomes for patients with metastatic Ewing sarcoma to that reported in the literature using other regimens. We suggest including this approach to other blocks of therapy

1 — INTRODUCTION

Ewing sarcoma (ES) is the second most common bone tumor in children, with an annual incidence of 2 to 3 cases per million.[1–3] Metastases at presentation occur in 25% of cases and typically involve the lung (50%), bone (25%), and bone marrow (20%).[4] The survival rates of patients with localized ES have increased over time, which is primarily due to the addition of cycles of ifosfamide/etoposide (IE) to a regimen of

vincristine/doxorubicin/cyclophosphamide (VDC).[5] The recent introduction of interval compression therapy further improved the outcomes of patients with localized ES tumors to yield 5-year event-free survival rates of 70%.[6,7]However, novel treatment regimens have only marginally improved the outcomes of patients with metastatic ES, with survival rates of approximately 30%.[8]Indeed, the presence of metastases at diagnosis constitutes the main adverse prognostic factor for ES.[9] Thus, the management of metastatic ES remains challenging because no standard treatment approach exists.[10] Many studies have reported different treatment approaches for metastatic ES, including chemotherapy intensification, local control, and autologous stem cell transplant, but a consensus is lacking.[11–15]Therefore, we report the outcomes of pediatric patients with metastatic ES who were treated with an interval compression regimen at the King Hussein Cancer Center. We also investigated various prognostic indicators, including tumor characteristics and local control modalities.

2 — METHODS

2.1 — Patients and treatment regimens

We conducted a retrospective chart review of pediatric patients (aged < 18 years at diagnosis) with metastatic ES who were treated at our facility from January 2013 (i.e., when interval compression was first used to treat ES) until March 2020. We excluded patients with incomplete records, those who received part of their therapy outside of our facility, and those who were treated with other protocols. We identified 47 pediatric patients with metastatic ES treated at our center during the study period. We excluded 13 patients because seven were treated with other protocols, four received part of their treatment at other facilities, and two received palliative care only because of terminal disease. Among the patients who were treated with other protocols, three were treated with the Euro-EWING-99 trial (NCT00020566) protocol, and three were treated without interval compression. These treatment regimen decisions were based on multidisciplinary discussions that favored other therapies according to patient status.

The interval compression protocol consisted of alternating cycles of VDC and IE every 2 weeks. Mesna was administered with cyclophosphamide and ifosfamide at a ratio of 0.6:1, with close monitoring of hydration, urine output, and urine color. Granulocyte colony-stimulating factor was administered at a dose of 5 µg/kg until neutrophil count recovery, beginning at the end of each cycle. These regimens were administered on an outpatient basis for most of the cycles, as previously reported.[16] Details of the treatment regimens are described in Supplemental Table S1.

2.2 — Patient outcomes

Metastatic site responses were evaluated according to the Response Evaluation Criteria in Solid Tumors criteria.[17] We defined complete response (CR) as the complete disappearance of lesions, partial response (PR) as [?] 30% decreased sum of the diameters of the target lesions, progressive disease (PD) as [?] 20% increased sum of the diameters of the target lesions, and stable disease as all lesions that did meet the criteria to qualify as CR, PR, or PD.

2.3 — Ethical review and statistical analysis

Our study was approved by the King Hussein Cancer Center Institutional Review Board and was conducted in accordance with human subject research ethics. We used descriptive analyses to evaluate the data and Kaplan–Meier (KM) estimates to calculate event-free (EFS) and overall survival (OS) rates. We subsequently used log-rank tests for univariate comparisons of the KM estimates. All statistical analyses were performed with R software (v4.0.4.).

3 — RESULTS

3.1 — Patient characteristics

The study participants consisted of 34 patients (14 female and 20 male; female-to-male ratio, 1:1.4) aged 2.7 to 17 years (median, 11.6 years). The most common site of primary tumors was the axial skeleton (n = 20, 59%), followed by bones of the extremities (n = 11, 32%) and soft tissue extra-skeletal sites (n = 3, 9%). Twenty-six (76%) patients had pulmonary metastases at diagnosis, and 14 (41%) had extra-pulmonary

metastases that were distributed among the bone (n = 11, 79%), lymph nodes (n = 2, 14%), and intraspinal tissue (n = 1, 7%). Six patients (18%) had both pulmonary and extra-pulmonary metastases. The patient characteristics are detailed in Table 1.

All patients received chemotherapy according to the interval compression protocol defined above. Twenty-nine patients completed all of the assigned 14 cycles, whereas five patients did not complete their planned regimen because of disease progression. All patients received the following local control treatments: radiation only (n = 18, 53%), surgery only (n = 7, 21%), or both radiation and surgery (n = 9, 26%). Pulmonary metastases were specifically treated with chest radiotherapy (n = 19, 73%) or thoracotomy (n = 1, 4%).

3.2 — Outcomes

We evaluated the metastatic tumor responses after five to six cycles of chemotherapy. For patients with pulmonary metastases, CRs occurred in 20 (77%) patients; PRs occurred in four (15%) patients; and SD and PD were present in one (3%) patient each. For patients with extra-pulmonary metastases, CRs occurred in six (43%) patients; PRs occurred in seven (50%) patients; and SD was present in one (7%) patient.

After a median follow-up period of 2.6 years, 19 (56%) patients experienced an event, including progression during therapy and relapse in 9 and 10 patients, respectively. Fourteen (41%) patients died of their disease during the follow-up period. No treatment-related mortality was observed. The estimated 3-year EFS and OS rates were 39% ± 9% and 62% ± 9%, respectively (Fig. 1). When we compared survival rates according to the sites of metastases, we found that the patients with pulmonary-only metastases had significantly higher estimated 3-year OS (88% ± 8%) than did those with extra-pulmonary metastases (27% ± 13%) ($P = 0.0074$; Fig. 2). In contrast, the primary tumor site and patient age did not significantly affect survival.

We also analyzed patient outcomes according to the local control modality. The patients who received surgery-only local control had a 3-year OS rate of 100%. In contrast, patients who were treated with combined surgery and radiation and those who were treated with radiotherapy only had similar outcomes - OS, 45% ± 19% and 46% ± 14% , respectively ($P = .051$). Likewise, the 3-year EFS rate was 83% ± 15% for patients who received surgery only, 30% ± 18% for those who received combined surgery and radiation, and 15% ± 10% for those who received radiation only ($P = .048$; Fig. 3).

4 — DISCUSSION

We report the outcomes of 34 pediatric patients with metastatic ES who received interval compression therapy with alternating cycles of VDC and IE. Despite improved outcomes for patients with nonmetastatic disease, few studies have reported the efficacy of interval compression therapy for patients with metastatic ES. We found an OS rate of 62% and an EFS rate of 39% at 3 years for the patients with metastatic ES treated at our institution during the study period, which is similar to the findings of other published studies.

The R2Pulm trial (NCT00987636), part of Euro-EWING-99 (NCT00020566) study, randomized 287 patients with metastatic ES after induction with 4–6 cycles of vincristine/ ifosfamide/doxorubicin/etoposide to either one course of vincristine/actinomycin D/ifosfamide and subsequent whole-lung irradiation (WLI) or high-dose busulfan-melphalan and autologous stem cell transplant. No significant difference was found between the two arms. The 8-year EFS rates were 43.1% and 52.9%, respectively, and the 8-year OS rates were 54.2% and 55.3%, respectively. Treatment-related toxicity was more frequent in the busulfan-melphalan treatment group and led to four deaths due to toxicity.[18]

Bernstein et al. studied the addition of a window of topotecan monotherapy or topotecan/cyclophosphamide combination before the classical five-drug regimen. However, this regimen did not improve survival over other regimens, with 2-year EFS and OS rates of 24% and 46%, respectively. Nevertheless, they noted that patients with pulmonary-only metastases experience better outcomes than do those with widespread metastases, with 2-year EFS rates of 31% and 20%, respectively.[15]

In the Italian Sarcoma Group–Scandinavian Sarcoma Group study, patients with primary metastatic ES were treated with the standard five-drug induction and maintenance therapy, with local control by surgery

or radiotherapy. This regimen was followed by consolidation with high-dose busulfan-melphalan, stem cell rescue, and WLI. They reported 5-year EFS and OS rates of 43% and 52%, respectively, with one death due to toxicity and one secondary acute myeloid leukemia occurrence. Their multivariate analysis identified poor tumor histologic response and poor metastatic tumor radiologic response as poor prognostic factors.[19]

Primary tumor site did not significantly affect survival in our study. Although older studies suggest that axial and pelvic locations are associated with inferior outcomes, more recent studies have found that primary tumor site is not a significant prognostic factor, most likely because newer protocols employ surgical local control.[21,22]Likewise, we found that patients treated with surgical resection alone had the best outcomes, whereas those treated with radiotherapy alone had the worst outcomes. However, this may be due to selection bias because patients who were more likely to experience superior responses were also more likely to receive definitive surgery. Indeed, all patients who received definitive surgical control of their primary tumors experienced CRs for their metastatic tumors. Therefore, aggressive local control is important because primary tumor recurrence occurred in only three of the 18 patients who did not receive definitive surgery.

Thorpe et al. conducted a retrospective review to determine whether local control affects survival of patients with primary metastatic ES tumors and found that the survival rate of patients who experienced local relapses was significantly lower than that of those without local relapse (5-year OS 34% vs 83% for those with and without recurrence, respectively). The rate of local recurrence itself was associated with treating the primary tumors with radiation rather than surgery.[22] Twenty-six patients in our cohort had lung metastases, 19 of whom received WLI, including 14 patients who experienced lung CRs at their interim evaluations.

The EICESS-92 (NCT00002516) trial followed 99 patients with ES lung metastases who were treated with or without WLI. The OS and EFS rates of patients treated with WLI was 61% and 39%, respectively, whereas the OS and EFS rates for those who did not receive WLI was 49% and 37%, respectively. Mild, moderate, or severe pulmonary function abnormalities occurred in 8 (29%), 6 (21%), and 2 (7%) patients who received WLI, respectively.[23]

Using radiotherapy to treat extra-pulmonary ES metastases improves patient outcomes.[26]Grewal et al. found that the median time to relapse is longer in patients who receive metastatic site irradiation than in those who do not (19.5 vs 12.3 months) and that most relapses occur in non-irradiated areas (15% irradiated sites vs 31% non-irradiated sites).[25] Of the 14 patients with extra-pulmonary metastases in our cohort, four received radiation to metastatic bony sites. Recurrences occurred in two of these patients, one of which occurred at a site of previous irradiation and the other three at new metastatic sites.

Our study is limited by its small sample size and retrospective nature. Tumor volumes were also not measured consistently and therefore were not included in our analyses. Furthermore, a uniform approach was not used to address control of distant metastases, which prevented us from making definitive conclusions.

5 — CONCLUSION

Interval compression therapy has improved the outcomes of patients with localized ES, yet the effect of interval compression on the outcomes of patients with metastatic disease has not been extensively studied. Therefore, we investigated the outcomes of patients with metastatic ES who were treated with interval compression at our institution. Our findings were comparable with those of previous studies using other regimens, which all reported inferior survival rates for patients with metastatic ES. We also found that the pattern of metastasis and modality of local control imparted a significant effect on survival.

Conflicts of interest statement : None

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REFERENCES

1. Hesla AC, Papakonstantinou A, Tsagkozis P. Current status of management and outcome for patients with Ewing sarcoma. *Cancers* . 2021;13(6). Epub 2021/04/04.

2. Werier J, Yao X, Caudrelier JM, Di Primio G, Ghert M, Gupta AA, et al. A systematic review of optimal treatment strategies for localized Ewing's sarcoma of bone after neo-adjuvant chemotherapy. *Surg Oncol.* 2016;25(1):16-23. Epub 2016/03/17.

3. Spector LG, Hubbard AK, Diessner BJ, Machiela MJ, Webber BR, Schiffman JD. Comparative international incidence of Ewing sarcoma 1988 to 2012. *Int J Cancer.*2021;149(5):1054-1066. Epub 2021/05/08.

4. Esiashvili N, Goodman M, Marcus RB, Jr. Changes in incidence and survival of Ewing sarcoma patients over the past 3 decades: Surveillance Epidemiology and End Results data. *J Pediatr Hematol Oncol.* 2008;30(6):425-430. Epub 2008/06/06.

5. Grier HE, Krailo MD, Tarbell NJ, Link MP, Fryer CJ, Pritchard DJ, et al. Addition of ifosfamide and etoposide to standard chemotherapy for Ewing's sarcoma and primitive neuroectodermal tumor of bone. *N Engl J Med.* 2003;348(8):694-701. Epub 2003/02/21.

6. Eaton BR, Claude L, Indelicato DJ, Vatner R, Yeh B, Schwarz R, et al. Ewing sarcoma. *Pediatr Blood Cancer.* 2021;68 Suppl 2:e28355. Epub 2021/04/06.

7. Womer RB, West DC, Krailo MD, Dickman PS, Pawel BR, Grier HE, et al. Randomized controlled trial of interval-compressed chemotherapy for the treatment of localized Ewing sarcoma: a report from the Children's Oncology Group. *J Clin Oncol.* 2012;30(33):4148-4154. Epub 2012/10/24.

8. Ladenstein R, Potschger U, Le Deley MC, Whelan J, Paulussen M, Oberlin O, et al. Primary disseminated multifocal Ewing sarcoma: results of the Euro-EWING 99 trial. *J Clin Oncol.* 2010;28(20):3284-3291. Epub 2010/06/16.

9. Rodriguez-Galindo C, Liu T, Krasin MJ, Wu J, Billups CA, Daw NC, et al. Analysis of prognostic factors in ewing sarcoma family of tumors: review of St. Jude Children's Research Hospital studies. *Cancer.* 2007;110(2):375-384. Epub 2007/06/15.

10. Ozaki T. Diagnosis and treatment of Ewing sarcoma of the bone: a review article. *J Ortho Sci* . 2015;20(2):250-63. Epub 2015/02/19.

11. Meyers PA, Krailo MD, Ladanyi M, Chan KW, Sailer SL, Dickman PS, et al. High-dose melphalan, etoposide, total-body irradiation, and autologous stem-cell reconstitution as consolidation therapy for high-risk Ewing's sarcoma does not improve prognosis. *J Clin Oncol* . 2001;19(11):2812-2820. Epub 2001/06/02.

12. Oberlin O, Rey A, Desfachelles AS, Philip T, Plantaz D, Schmitt C, et al. Impact of high-dose busulfan plus melphalan as consolidation in metastatic Ewing tumors: a study by the Societe Francaise des Cancers de l'Enfant. *J Clin Oncol.*2006;24(24):3997-4002. Epub 2006/08/22.

13. Kushner BH, Meyers PA. How effective is dose-intensive/myeloablative therapy against Ewing's sarcoma/primitive neuroectodermal tumor metastatic to bone or bone marrow? The Memorial Sloan-Kettering experience and a literature review.*J Clin Oncol.* 2001;19(3):870-880. Epub 2001/02/07.

14. Loschi S, Dufour C, Oberlin O, Goma G, Valteau-Couanet D, Gaspar N. Tandem high-dose chemotherapy strategy as first-line treatment of primary disseminated multifocal Ewing sarcomas in children, adolescents and young adults. *Bone Marrow Transplant* . 2015;50(8):1083-1088. Epub 2015/06/02.

15. Bernstein ML, Devidas M, Lafreniere D, Souid AK, Meyers PA, Gebhardt M, et al. Intensive therapy with growth factor support for patients with Ewing tumor metastatic at diagnosis: Pediatric Oncology Group/Children's Cancer Group Phase II Study 9457–a report from the Children's Oncology Group. *J Clin Oncol.* 2006;24(1):152-159. Epub 2005/12/31.

16. Elshahoubi A, Alnassan A, Sultan I. Safety and cost-effectiveness of outpatient administration of high-dose chemotherapy in children with Ewing sarcoma. *J Pediatr Hematol Oncol.* 2019;41(3):e152-e154. Epub

2019/01/05.

17. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer* . 2009;45(2):228-247. Epub 2008/12/23.

18. Dirksen U, Brennan B, Le Deley MC, Cozic N, van den Berg H, Bhadri V, et al. High-dose chemotherapy compared with standard chemotherapy and lung radiation in Ewing sarcoma with pulmonary metastases: Results of the European Ewing Tumour Working Initiative of National Groups, 99 Trial and EWING 2008. *J Clin Oncol* . 2019;37(34):3192-3202. Epub 2019/09/26.

19. Luksch R, Tienghi A, Hall KS, Fagioli F, Picci P, Barbieri E, et al. Primary metastatic Ewing's family tumors: results of the Italian Sarcoma Group and Scandinavian Sarcoma Group ISG/SSG IV Study including myeloablative chemotherapy and total-lung irradiation. *Ann Oncol.* 2012;23(11):2970-2976. Epub 2012/07/10.

20. Cotterill SJ, Ahrens S, Paulussen M, Jurgens HF, Voute PA, Gadner H, et al. Prognostic factors in Ewing's tumor of bone: analysis of 975 patients from the European Intergroup Cooperative Ewing's Sarcoma Study Group. *J Clin Oncol.*2000;18(17):3108-3114. Epub 2000/08/30.

21. Rodriguez-Galindo C, Navid F, Liu T, Billups CA, Rao BN, Krasin MJ. Prognostic factors for local and distant control in Ewing sarcoma family of tumors. *Ann Oncol.*2008;19(4):814-820. Epub 2007/11/14.

22. Thorpe SW, Weiss KR, Goodman MA, Heyl AE, McGough RL. Should aggressive surgical local control be attempted in all patients with metastatic or pelvic Ewing's sarcoma?*Sarcoma.* 2012;2012:953602. Epub 2012/05/03.

23. Bolling T, Schuck A, Paulussen M, Dirksen U, Ranft A, Konemann S, et al. Whole lung irradiation in patients with exclusively pulmonary metastases of Ewing tumors. Toxicity analysis and treatment results of the EICESS-92 trial.*Strahlenther Onkol* . 2008;184(4):193-197. Epub 2008/04/10.

24. Elghazawy H, Nasr A, Zaky I, Zamzam M, Elgammal A, Farid N, et al. Whole lung irradiation for completely responding pulmonary metastases in pediatric Ewing sarcoma.*Future Oncol.* 2020;16(15):1043-1051. Epub 2020/04/07.

25. Grewal AS, Li Y, Grewal SK, Bagatell R, Balamuth N, Womer R, et al. Role of metastatic site irradiation in pediatric patients with metastatic Ewing sarcoma. *J Pediatr Hematol Oncol* . 2020;42(5):e305-e309. Epub 2020/02/23.

26. Karimi AM, Campbell SR, Parsai S, Angelov L, Scott J, Qi P, et al. Aggressive local control with multisite stereotactic body radiation in metastatic Ewing sarcoma: A literature review and case report. *Anticancer Res* . 2020;40(2):951-955. Epub 2020/02/06.

27. Pinkerton CR, Bataillard A, Guillo S, Oberlin O, Fervers B, Philip T. Treatment strategies for metastatic Ewing's sarcoma. *Eur J Cancer* . 2001;37(11):1338-1344. Epub 2001/07/04.

FIGURE LEGENDS

FIGURE 1 Kaplan–Meier curves of the overall survival (A) and event-free survival (B) rates for patients with metastatic Ewing sarcoma who were treated with an interval compression therapy regimen.

FIGURE 2 Kaplan–Meier curves of the overall survival rates for patients with either none or at least one extra-pulmonary Ewing sarcoma metastatic tumors.

FIGURE 3 Kaplan–Meier curves of the event-free survival rates for patients with metastatic Ewing sarcoma who were treated with the following local control modalities: surgery only, radiotherapy only, and surgery and radiotherapy.

SUPPORTING INFORMATION LEGENDS

SUPPLEMENTAL TABLE S1 Interval compression treatment regimens for patients with metastatic Ewing sarcoma.

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`Table1.docx` available at https://authorea.com/users/450617/articles/549292-outcomes-of-pediatric-patients-with-metastatic-ewing-sarcoma-treated-with-interval-compression