Outcomes of ilium and iliosacral Ewing's sarcoma resection reconstructed with tibial strut allograft

a retrospective analysis

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Aims

Ilium is the most common site of pelvic Ewing's sarcoma (ES). Resection of the ilium and iliosacral joint causes pelvic disruption. However, the outcomes of resection and reconstruction are not well described. In this study, we report patients' outcomes after resection of the ilium and iliosacral ES and reconstruction with a tibial strut allograft.

Methods

Medical files of 43 patients with ilium and iliosacral ES who underwent surgical resection and reconstruction with a tibial strut allograft between January 2010 and October 2021 were reviewed. The lesions were classified into four resection zones: I_1, I_2, I_3, and I_4, based on the extent of resection. Functional outcomes, oncological outcomes, and surgical complications for each resection zone were of interest. Functional outcomes were assessed using a Musculoskeletal Tumor Society (MSTS) score and Toronto Extremity Salvage Score (TESS).

Results

The mean age of the patients was 17 years (SD 9.1). At a mean follow-up of 70.8 months (SD 50), the mean functional outcomes were 24.2 points (SD 6.3) for MSTS and 81 points (SD 11) for TESS. The mean MSTS and TESS scores were associated with the iliac resection zone (< 0.001). Nine patients (20.9%) had local recurrence. The recurrence was not associated with the zone of iliac resection ($p = 0.324$). The two-year disease-free survival of the patients was 69.4%. The mean time to graft union was longer in patients with the I_4 resection zone ($p < 0.001$). The complication rate was 34.9%, and nerve palsy (11.6%) was the most common. The rate of surgical complications was not associated with the resection zone.

Conclusion

Reconstruction using tibial strut allograft is an efficient procedure after the resection of the ilium and iliosacral ES. Functional outcomes and complications of iliac ES depend on the resection zone, and inferior outcomes could be generally expected when more segments of the pelvic ring are resected, even if it is reconstructed.

Take home message

- Functional outcomes and complications of iliac Ewing's sarcoma depend on the resection zone, and inferior outcomes could be generally expected when more segments of the pelvic ring are resected, even if it is reconstructed.

Introduction

Ewing's sarcoma (ES) is the second most common malignant bone tumour in patients before the age of 30 years and the most common before ten years.[1,2] It is generally detected in the second decade of life, with a median age at diagnosis ranging from 13 to 19 years.[3] Advances in diagnostic imaging and multimodality therapy over the past few decades have increased ES's overall five-year survival rate from 10% in the 1970s[4] to 55% to 75% at the turn of the century.[5] The pelvis is one of the most frequent locations of ES, accounting for almost 20% of all ES cases.[6]

Ilium is the most common site of pelvic ES, accounting for almost 62% of all pelvic ESs.[6] However, its optimal treatment and outcomes are less understood.[7,8] Ilium and iliosacral tumours, by nature of their location, large size at presentation, and proximity to neurovascular structures and visceral organs, offer a unique challenge to adequate oncological resection.[9-11]

Surgical resection is acknowledged as the standard choice of treatment for tumours of the pelvis, including the ilium.[12] The outcomes of the resection of iliac and iliosacral resection could be different depending on the defect size.[13] There is no agreement on the necessity of reconstruction after iliac resection due to the increased surgical time, blood loss, and postoperative complications associated with this reconstruction. Moreover, it is not clear which type of reconstruction is associated with fewer complications.[9,11,14,15]

Using a modification of the Campanacci classification of iliac resection,[13] we categorized iliac and iliosacral resection into four zones causing pelvic ring disruption. In this study, we report functional outcomes, oncological outcomes, and surgical complications of iliac and iliosacral ES based on this modified classification.

Methods

This study was approved by the ethics committee of our institution (Iran University of Medical Sciences). Medical profiles of patients with ilium and iliosacral ES who were treated in our referral hospital between January 2010 and October 2021 were retrospectively reviewed. The inclusion criteria were treatment with surgical resection causing pelvic ring disruption and reconstruction with a tibial strut allograft, with a minimum follow-up of two years. Patients for whom the defect was not reconstructed or reconstructed with autogenous fibula (tibial allograft was not available), patients who received adjuvant radiotherapy, patients who were lost to follow-up, and patients who were referred for the management of recurrence were excluded from the study. Patients with metastasis at presentation were also excluded. All patients received neoadjuvant chemotherapy with doxorubicin, vincristine, cyclophosphamide, and dactinomycin (VACA) for 12 weeks prior to surgery. Patients with less than 100% chemotherapy effect (n = 6) and a positive surgical margin (n = 2) received postoperative radiotherapy. Since radiotherapy adversely affects the outcomes of surgery, these patients were also excluded from the study.

A total of 43 patients were included in the final analysis, including 24 (55.8%) males and 19 (44.2%) females with a mean age of 17 years (standard deviation (SD) 9.1, 1 to 40). The mean follow-up of the patients was 70.8 months (SD 50, 24 to 216). According to the ilium and iliosacral zone of resections, eight patients (18.6%) were in I_1, 15 (34.9%) in I_2, 12 (27.9%) in I_3, and eight (18.6%) in I_4. Baseline characteristics of the patients are demonstrated in Table I. The flow diagram of the patients' inclusion and exclusion is demonstrated in Figure 1. Sonography-guided core needle biopsy was done for all patients, which was inconclusive in three. Open incisional biopsy was done for these three patients.

The resections were categorized using a modified Campanacci classification,[13] including four iliac and iliosacral resection zones with disruption of the pelvic ring, as demonstrated in Table II and Figure 2.

Surgical procedure and postoperative protocol

Under general anaesthesia and the insertion of a Foley catheter, the patient was placed in the semi-lateral position. The incision encompassing the elliptical biopsy tract started from the posterior superior iliac spine and followed the curve of the iliac crest towards the anterior superior iliac spine. The fascia lata was divided into line with the skin incision, and the gluteal muscles were detached from the iliac crest. A large flap, including the origin of the gluteal muscles, was moved posterolaterally. The sciatic notch was exposed posteriorly. The sciatic nerve and gluteal vessels were exposed. We tried to preserve the superior gluteal artery and superior gluteal nerve to provide primary vasculature and innervation to this flap. The abdominal muscles were detached to give access to the internal aspect of the ilium. The iliopsoas muscle covering the lesion was divided above the level of the iliac resection and below the lesser trochanter as a margin. The origins of sartorius and rectus femoris were divided if necessary. The iliac and femoral vessels were identified, explored, and retracted medially. The osteotomy of the ilium was made at the desired level, and the distal cut was performed with an oscillating bone saw anteriorly and completed with a Gigli saw at the ischial notch. In case of tumour expansion over the sacral body, after exposing the anterior of the sacrum and haemostasis of the presacral venous plexus, sacral laminectomy was performed, and the nerve roots were identified, ligated, and sectioned as required. Our goal was to achieve at least 1 cm surgical margins, except in cases where we were limited by vital structures, in which case we removed as much as possible in a safe manner. The specimen removed during surgery was sent to the pathology for evaluation of the surgical margins, as well as to assess the effectiveness of chemotherapy.

All patients underwent a pelvic reconstruction using a fresh frozen tibial strut allograft that was cut 5 mm longer than the defect to provide stability. It was anchored into a hole created in the sacrum and the remaining ilium (Figures 3 and 4). The stability of the reconstruction was ensured by screw fixation if needed, which allows modularity in three dimensions, as well as graft compression. Generally, screws were implanted from the graft to the anterolateral side of the sacral body. If needed, another screw was positioned from the graft to the anterior column of the acetabulum.

All allografts were obtained from our university bone bank and were harvested within 12 hours post-mortem from the bodies of young adults who had died in traffic accidents. Recommended procedures to make sure that the donors were healthy were carried out according to standard tissue banking

Table I. Demographic and surgical characteristics of the patients.

Variable	Value
Mean age, yrs (SD)	17 (9.1)
Sex, n (%)	
Male	24 (55.8)
Female	19 (44.2)
Laterality, n (%)	
Right	29 (67.4)
Left	14 (32.6)
Mean tumour size, cm (SD)	14 (4.3)
Zone of resection, n (%)	
I_1	8 (18.6)
I_2	15 (34.9)
I_3	12 (27.9)
I_4	8 (18.6)
Necrosis, n (%)	84.6 (19.3)
Mean follow-up, mths (SD)	70.8 (50)

SD, standard deviation.

protocol.[16] The allografts were stored at -85°C temperature for at least two weeks before their use. All patients completed postoperative chemotherapy.

The pelvis was protected in a hip abduction brace and kept on non-weightbearing ambulation for the first six weeks after the surgery. Partial weightbearing ambulation was initiated thereafter. Full weightbearing ambulation was allowed after radiological evidence of the union of the graft to the host bone was observed.

Assessments

The largest dimension in the resected specimen determined the size of the tumour. The histological effect of the neoadjuvant therapy was extracted from the pathology records, which were assessed by the Response Evaluation Criteria in Solid Tumours (RECIST).[17] Union of the graft to the host bone was considered if there was no visible osteotomy line at the allograft junctions, or if greater than or equal to 75% of cortical thickness was fused on follow-up radiographs, according to the International Society of Limb Salvage (ISOLS) radiological implants evaluation system.[18] The evaluation of union/nonunion at the junction was done every three months after the operation. All patients were followed continuously in the outpatient clinic. The limb function was assessed objectively with the Musculoskeletal Tumor Society (MSTS)[19] score and subjectively with the Toronto Extremity Salvage Score (TESS).[20] According to the MSTS score, each patient received a score between 0 and 30, with a higher score indicating a better function.[19] TESS ranged from 0 to a maximum score of 100, and higher scores were indicative of better function reported by the patients.[20] Postoperative complications were extracted from the patients' medical records. Functional scores were calculated by an orthopaedic oncologist (BTG) who was not involved in the patients' care.

Statistical analysis

Statistical analysis was conducted using SPSS for Windows, version 16 (SPSS, USA). Descriptive statistics were demonstrated by mean and SD or numbers with percentages. A comparison of mean values between different groups of resection was done with Kruskal-Wallis one-way analysis of variance (ANOVA). Recurrence-free survival was estimated using the Kaplan-Meier method, which used intervals between the dates of surgery and the time of each endpoint. In all analyses, a p-value < 0.05 was considered statistically significant.

Results

Functional outcomes

The mean MSTS score of the patients was 24.2 points (SD 6.3, 16 to 29). The mean TESS of the patients was 81 points (SD 11; 55 to 98). The mean MSTS score was 26.5 points (SD 2.9) for I_1 iliac resection, 24.9 points (SD 3.4) for I_2 iliac resection, 23.8 points (SD 4.1) for I_3 iliac resection, and 21.5 points (SD 4.2) for I_4 iliac resection. The difference in MSTS between different iliac resection groups was statistically significant ($p < 0.001$). The mean TESS was 86.1 (SD 6.3) for I_1 iliac resection, 82.8 (SD 7.3) for I_2 iliac resection, 79.2 (SD 6.9) for I_3 iliac resection, and 75.1 (SD 7.8) for I_4 iliac resection ($p < 0.001$, Kruskal-Wallis one-way ANOVA).

Eight patients (18.6%) had a leg-length discrepancy. The mean length of discrepancy was 3.1 cm (SD 1.6; 1 to 4), which was compensated with lift.

Oncological outcomes

Nine patients had local recurrence during the follow-up period. Of these patients, five had concurrent distant metastasis. The mean time to local recurrence was 18.7 months (SD 5.8; 12 to 36). The rate of local recurrence was not significantly associated with the zone of iliac resection ($p = 0.324$). Four other patients had metastasis without local recurrence. The mean time to metastasis was 10.5 months (SD 4.1; 6 to 18). Patients with local recurrence were referred for chemotherapy and radiation therapy. The two-year disease-free survival of the patients was 69.4% (Figure 5). In the last follow-up, 35 of 43 patients (81.4%) were still alive.

Complications

The overall complication rate was 34.9%. Infection occurred in two (4.6%) patients, one of which was superficial and managed with antibiotic therapy, while the other one required surgical debridement and graft removal. Nerve palsies were observed in five (11.6%) patients, including one femoral nerve palsy and four instances of peroneal nerve palsy. Four patients with neural damage had spontaneous recovery, and one patient had persistent neural damage. No vascular complication (thrombosis of the iliac artery) was recorded. Abdominal hernia was observed in two (4.6%) patients, for which no intervention was performed. The mean time to radiological union was 7.8 months (SD 2.4, 6 to 9) in the I_1 resection zone. The mean time to radiological union was 9.5 months (SD 3.1, 6 to 12) in the I_2 resection zone. The mean time to union was 9.8 months (SD 3, 6 to 12) in the I_3 resection zone. The mean time

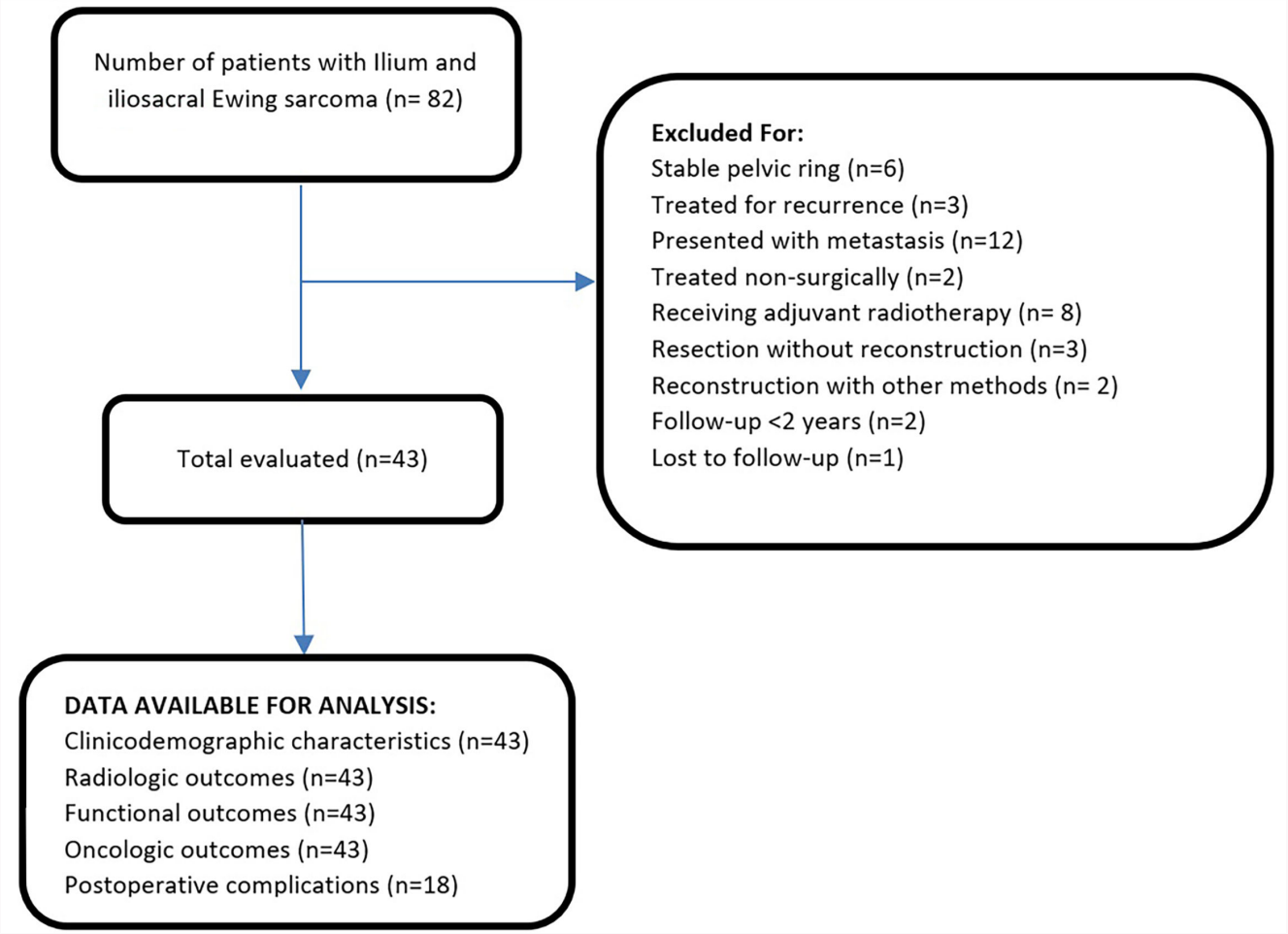

Fig. 1
Flow diagram of the study.

Table II. Classification for ilium and iliosacral resection zones.

Zone of resection	Description
I_1	Iliac wing resection with intact sciatic notch and unstable pelvic ring (resection ≥ 50% of sacroiliac joint)
I_2	Iliac resection from the neck of the ilium to the sacroiliac joint
I_3	En bloc resection of the iliac wing with the sacroiliac joint as margin
I_4	En bloc resection the iliac wing with half of the sacrum as margin

to union was 11 months (SD 6.1, 9 to 18) in the I_4 resection zone. Two partial graft absorptions occurred in the I_3 resection zone. One graft fracture and one partial absorption of graft occurred in the I_4 resection zone. Graft displacement was seen in two patients (4.6%). Considering the stability of the pelvis, no intervention was required for this patient. The total and resection zone-specific complications are summarized in Table III.

Discussion

Adequate reconstruction is an essential part of limb salvage surgeries to obtain enough stability after tumour resection.[21–24] In this study, we evaluated the outcomes of the ilium and iliosacral reconstructed with a minimally aggressive method (tibial strut allograft) in patients with pelvic ring disruption following the ES resection. We included patients with ≥ 50 sacroiliac joint resection, as it has been associated with chronic instability of the pelvic ring.[25,26]

The mean functional outcomes were 24.2 points (SD 6.3) for MSTS and 81.1 points (SD 11) for TESS. The functional outcomes were significantly associated with the zone of resection, as it was poorer in higher zones of resection. Nine patients (20.9%) had local recurrence during the average follow-up of 70.8 months, which was not associated with the zone of iliac resection. The time to union of the allograft was

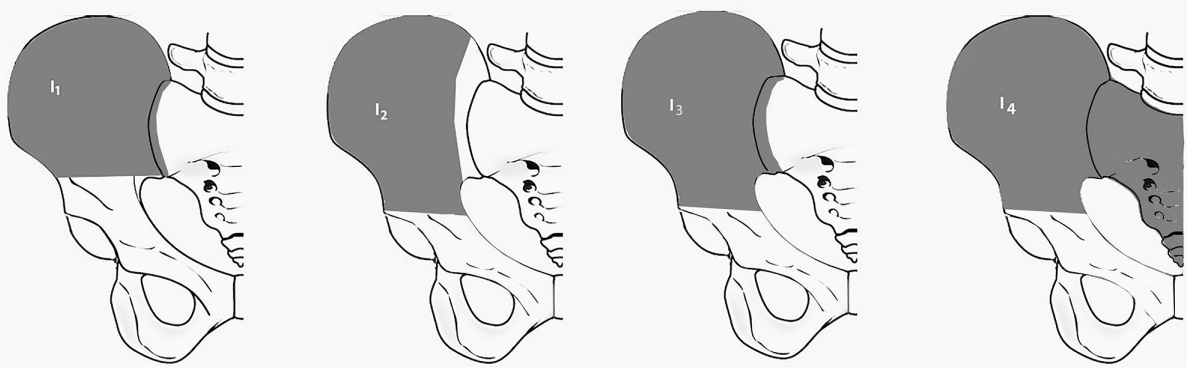

Fig. 2
Pictorial image of the modified Campanacci classification for iliac resections.

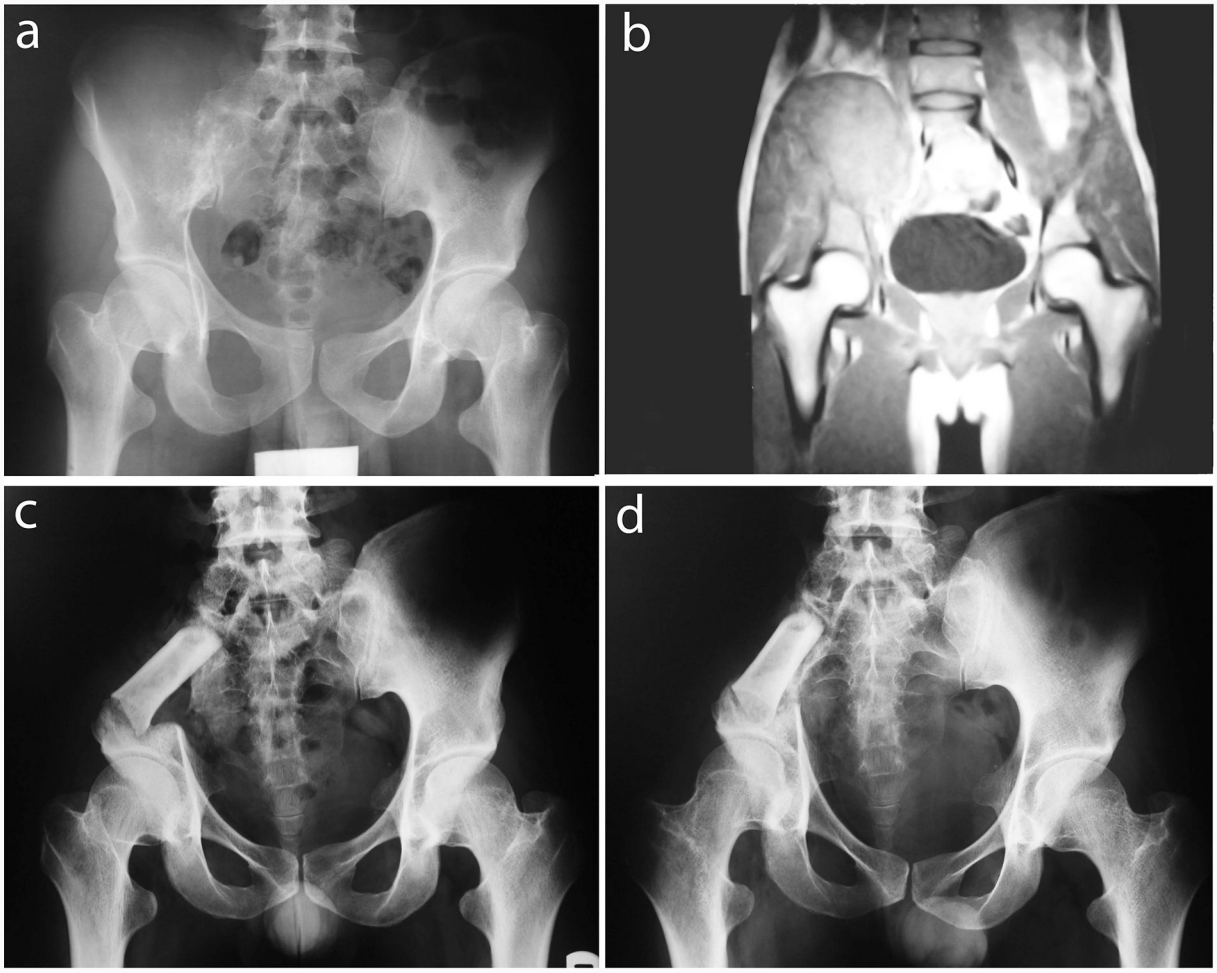

Fig. 4
a) Anteroposterior radiograph of the hip showing pre-chemotherapy Ewing's sarcoma of the ilium in a 23-year-old male. b) T1-weighted MRI of the hip showing the tumour extension close to the sacroiliac joint (Zone I_3 resection). c) Anteroposterior radiograph of the hip six months after surgical resection and reconstruction with tibial strut graft. d) Anteroposterior radiograph of the hip three years after surgical resection and reconstruction, showing the complete incorporation of the graft into the host bone.

longer in higher zones of iliac resection, and the number of postoperative complications was higher.

The outcomes of iliac resection have been reported in a limited number of earlier studies. Gupta et al[27] reported the functional outcomes of 32 patients with ilium and iliosacral resection without reconstruction. The mean MSTS score and TESS of the patients were 21.1 and 76.2, respectively, which was inferior compared to the present series of patients. There were 18 complications (50%) in the study by Gupta et al,[27] including 13 wound-healing complications/infections, three

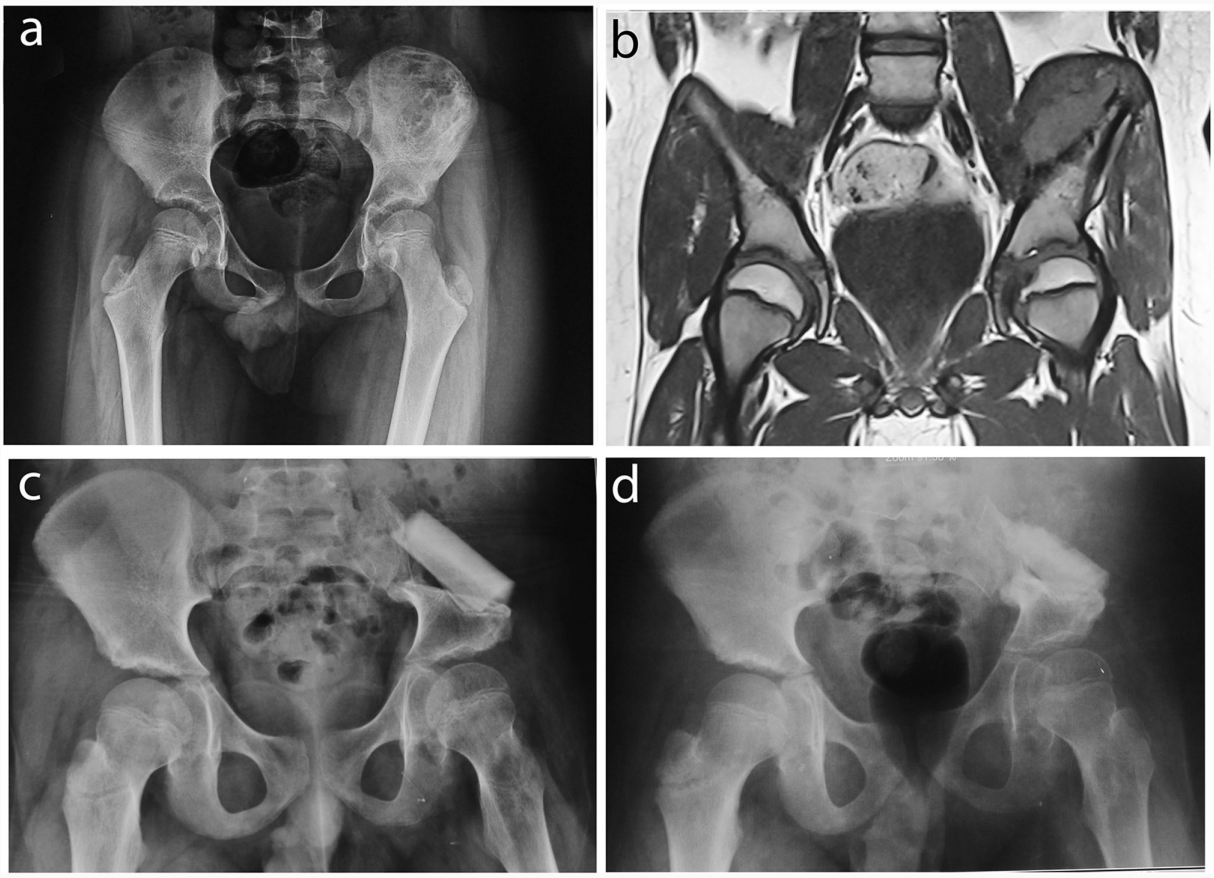

Fig. 3
a) Anteroposterior radiograph of the hip showing post-chemotherapy Ewing's sarcoma of the ilium in a ten-year-old male. b) T1-weighted MRI of the hip showing the intact sciatic notch (Zone I_1 resection). c) Anteroposterior radiograph of the hip three months after surgical resection and reconstruction with tibial strut graft. d) Anteroposterior radiograph of the hip five years after surgical resection and reconstruction, showing a limb shortening of 2 cm.

fractures, one pulmonary embolism, and one dislocation of the hip. The rate of complications was 34.9% in the present study. The high rate of wound complications of the Gupta et al[27] series could be attributed to sacrificing gluteal arteries.

Laitinen et al[28] reported the outcomes of iliac resection in 64 patients with ilium sarcoma. Patients were divided into two groups, including complete resection of the ilium and disruption of the pelvic ring, with or without reconstruction (group 1), and partial resection of the ilium with preservation of the pelvic ring (group 2). The mean TESS was not significantly different between the two groups (72 vs 76.3). Six postoperative complications were recorded in each group. Although the number of complications was not significantly different, the type of complications differed between the two groups, so graft-related problems were the most common complication in group 1, and infection was the most common complication in group 2. In this study, we included patients who underwent reconstruction after resection. Including a control group of patients without reconstruction could have better demonstrated the efficiency of iliac reconstruction. However, the inclusion of this group was not possible due to the small number of patients.

Porsch et al[29] reported the outcomes of partial pelvic resection in seven patients with iliac ES. According to the Enneking classification of resection,[19] five patients had type IA; one patient had type I, and one patient had type IIA. In five of seven patients, the functional results were good to excellent. The good results were attributed to the reconstruction of the pelvic girdle and its mechanical stability. No surgery-related complications were reported. The present study also revealed satisfactory outcomes following the reconstruction of the ilium in patients with pelvic ring disruption.

Guo et al[12] reported the outcomes of iliac resection and reconstruction in 61 patients. According to the Enneking staging system, the majority of lesions were located in region I, while the remaining lesions were located in combined regions (I and II, or I and IV). All patients with the region I resection regained normal walking ability because the pelvic ring was not disrupted. The present study, in line with the study by Guo et al,[12] further supports the efficiency of reconstruction in patients with pelvic ring disruption.

A review of the literature highlights the need for a comprehensive iliac resection classification for a standardized reporting of the outcomes to allow comparison of the results between different studies. Currently, a comparison of the outcomes between different studies does not provide much information because the type of resection is not standardized.

In the study by Laitinen et al,[28] the rate of recurrence was 42.2%, and patients with partial resection of ilium had significantly higher recurrence. They attributed this association to the amount of margin achieved at resection. In the study by Guo et al,[12] of 48 patients who were followed for

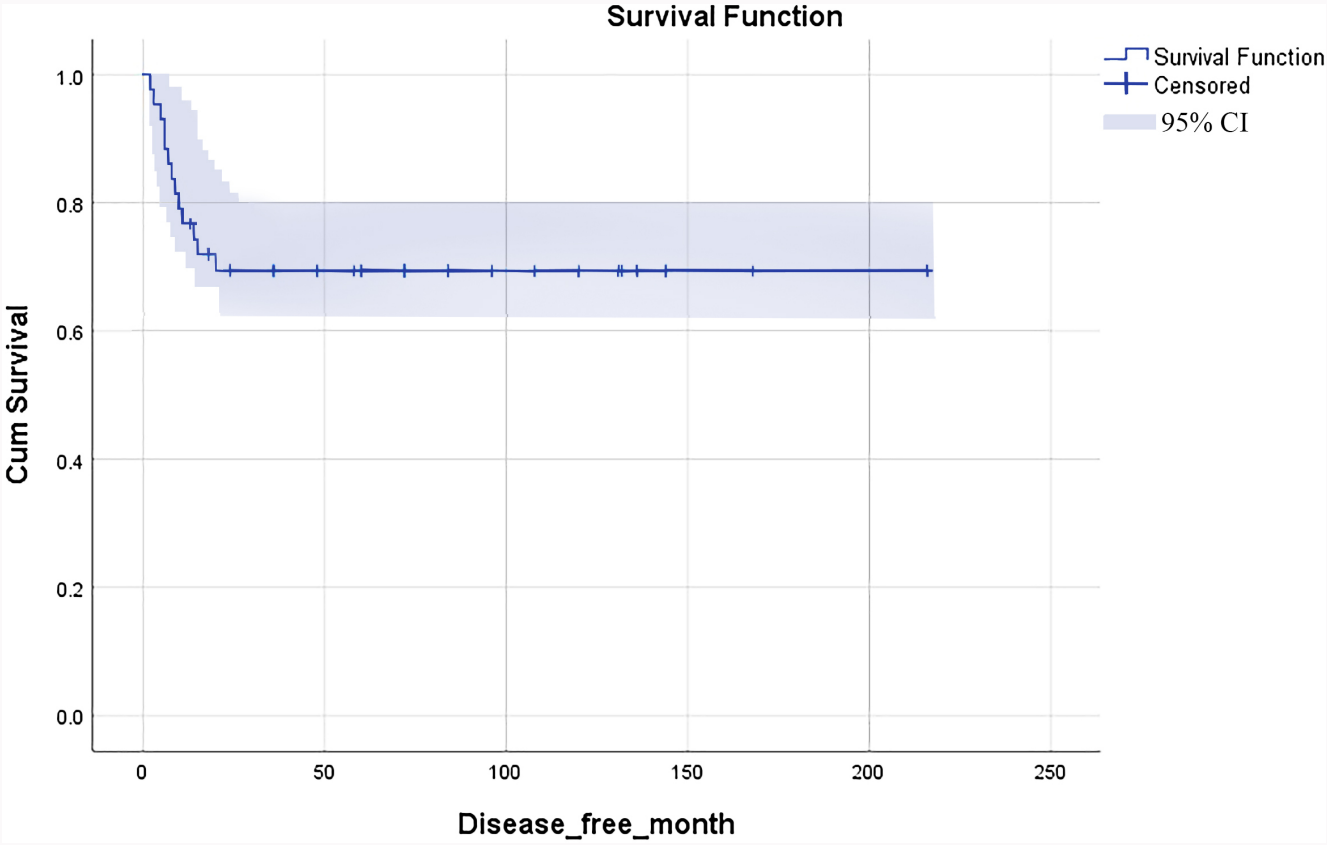

Fig. 5
Kaplan Meier curve showing a two-year disease-free survival of 69.4%. CI, confidence interval.

Table III. Outcomes of iliac Ewing's sarcoma based on the resection zone.

	Resection zone				p-value
Outcome measure	**I_1 (n = 8)**	**I_2 (n = 15)**	**I_3 (n = 12)**	**I_4 (n = 8)**	
Mean MSTS score (SD)	26.5 (2.9)	24.9 (3.4)	23.8 (4.1)	21.5 (4.2)	< 0.001
Mean TESS score (SD)	86.1 (6.3)	82.8 (7.3)	79.2 (6.9)	75.1 (7.8)	< 0.001
Recurrence, n (%)	1 (12.5)	3(20)	3 (25)	2 (25)	0.32
Metastasis, n (%)	1 (16.7)	1 (8.3)	2(16.7)	1 (16.7)	0.54
Mean time to graft union, mths (SD)	7.8 (2.4)	9.5 (3.1)	9.8 (3)	15 (6.1)	< 0.001
Nonunion, n (%)	0	0	0	1 (16.7)	0.89
Partial graft resorption, n (%)	0	0	2 (20)	1 (16.7)	0.59
Graft fracture, n (%)	0	1 (8.3)	0	1 (16.7)	0.76
Graft displacement, n (%)	0	1 (8.3)	1 (10)	0	0.81
Infection, n (%)	0	0	1 (10)	1 (16.7)	0.61
Nerve palsy, n (%)	0	1 (8.3)	2 (20)	2 (33.3)	0.21
Limb shortening, n (%)	1	2 (16.7)	3 (30)	2 (33.3)	0.28
Hernia, n (%)	0	0	1 (10)	1 (16.7)	0.61

MSTS, Musculoskeletal Tumor Society; SD, standard deviation; TESS, Toronto Extremity Salvage Score.

16 to 72 months, 33 patients (68.7%) remained disease-free until the last follow-up. Local recurrence occurred in 19.4% of patients with region I resection, 35.3% of patients with region I and II resections, and 50% of patients with region I and IV resections. In the study by Porsch et al,[29] six of seven patients (85.7%) remained disease-free until the last follow-up.

The rate of local recurrence was 20.9% in the present study, which was similar to that reported by Porsch et al.[29] We found no association between the rate of local recurrence and zone of resection, which could be attributed to achieving adequate margin in all patients, even with the increased risk of functional impairment. However, it should be noted that the oncological outcomes of the present study are not comparable to the study of Laitinen et al[28] and Guo et al[12] because we only included ES patients, while Laitinen et al[28] and Guo et al[12] included different tumour types.

Chemoradiation without surgical resection is considered another therapeutic option for ilium ES, particularly if the preoperative radiological investigations indicate that surgical excision would be difficult.[30] Although functional outcomes of the patients who are managed with non-surgical treatment seem to be superior to those treated with surgical treatment,[31] the addition of surgery significantly improves survival.[31–33] In addition, radiotherapy is associated with a variety of late effects, such as pneumonitis, radiation cystitis, second malignancy, and radiation-induced bone fracture.[34,35] For this reason, non-surgical treatment is mostly selected for inoperable tumours.[30]

The present study was not without limitations. The main limitation was its retrospective design, which predisposed several biases, such as selection bias and transfer bias. Misassessment might be regarded as the other source of bias; we used the MSTS score for the objective evaluation of functional outcomes and the TESS score for the subjective evaluation of functional outcomes, both of which were assessed through a chart review. In addition, we had no control group to demonstrate the advantage of reconstruction versus no reconstruction.

In summary, tibial strut allograft reconstruction of ilium and iliosacral in ES patients with pelvic ring disruption is a minimally aggressive method of reconstruction that provides acceptable functional outcomes and low rates of complications. Less promising results could be generally expected when the defect is larger, extending to the sacral region. Oncologic outcomes are less affected by the class of iliac resection if adequate margin is achieved.

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Data sharing

The data that support the findings for this study are available to other researchers from the corresponding author upon reasonable request.

Ethical review statement

This study has been performed in accordance with the ethical standards in the 1964 Declaration of Helsinki as well as relevant regulations of the US Health Insurance Portability and Accountability Act (HIPAA). The study protocol was approved by the ethics committee of the Iran University of Medical Sciences under the code of IR.IUMS.REC.1402.625.