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Research Article

Adjuvant Radiotherapy for the Multimodal Treatment of Pediatric Ewing Sarcoma

Pediatrik Ewing Sarkoma Hastalarının Multimodal Tedavisinde Adjuvan Radyoterapi

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Abstract

Aim: This study aimed to report the adjuvant radiotherapy results of pediatric patients with Ewing sarcoma who received multimodal treatment for this rare disease using modern radiotherapy (RT) techniques.
Material and Methods: Pediatric patients with Ewing Sarcoma (ES) who received adjuvant radiotherapy were evaluated retrospectively. The study's primary endpoint was overall survival (OS) and disease-free survival (DFS). The secondary endpoint was local relapse-free survival after RT (LRFS- RT) and overall survival after RT (OS-RT).
Results: The results of 18 pediatric patients diagnosed with Ewing Sarcoma in our clinic between 09.12.2013-04.04.2021 and underwent RT for adjuvant were evaluated retrospectively. The three patients were excluded since they did not meet the inclusion criteria. The median age of the patients at the time of diagnosis was 10.5 (range 3-17). The time from diagnosis to the onset of RT was 8.6 (range 2-20) months. The median fraction dose was 180 cGy, and the median total RT dose was 50.4 (range 45-55.80) Gy. The median follow-up period of the study was 27 (range 11-86) months. The 12 (80%) patients survived, and 3 (20%) died. The median OS diagnosis of the patients was 27.3 (range 11 to 86.5) months. The overall survival of the patients after RT was median 17.3 (range 4.4-83.9) months. Recurrence (local+distant) was observed in 7 patients (46.7%); 2 (13.3%) local, 3 (20%) distant and 2 (13.3%) both. The median DFS was 24 months (range 1-86.5). Median LRFS-RT is 14.2 (range 1-83.9) months. The relationship between LRFS-RT and age (<10 vs. ≥10 years old) (p=0.050; HR:2.30; %95 CI 0.70-3.17) was significant. Significantly higher LRFS-RT was observed in the older age.
Conclusion: In patients with Ewing's sarcoma who are at high risk of local failure after surgery, adjuvant radiotherapy could be applied to increase local control rate, with reasonable side effects.

Keywords: Adjuvant radiotherapy, ewing sarcoma, pediatric oncology

Öz

Amaç: Bu çalışmada Ewing sarkomu nedeniyle multimodal tedavi uygulanan çocuk hastaların adjuvan radyoterapi sonuçlarını bildirmeyi amaçladık.
Materyal Metot: Adjuvan radyoterapi (RT) alan Ewing Sarkomlu pediatrik hastalar geriye dönük olarak değerlendirildi. Çalışmanın birincil sonlanım noktası, Genel Sağkalım (GS) ve hastalıksız sağkalım (HS) idi. İkincil sonlanım noktaları, RT den sonra lokal nükssüz sağkalım (LRFS-RT) ve RT'den sonra genel sağkalım (GS-RT)'di.
Bulgular: Kliniğimizde 09.12.2013-04.04.2021 tarihleri arasında Ewing Sarkomu tanısıyla adjuvan RT uygulanan 18 çocuk hastanın sonuçları retrospektif olarak değerlendirildi. Üç hasta dahil edilme kriterlerini karşılamadıkları için çalışma dışı bırakıldı. Hastaların tanı anındaki ortanca yaşı 10.5 (dağılım 3-17) idi. Tanıdan RT başlangıcına kadar geçen süre 8.6 (2-20) aydı. Ortanca fraksiyon dozu 180 cGy ve ortanca toplam RT dozu 50.4 (aralık 45-55.80) Gy idi. Çalışmanın ortanca takip süresi 27 (dağılım 11-86) aydı. Oniki (%80) hasta sağ ve 3 (%20) hasta ölü idi. Hastaların ortanca GS değeri 27.3 (dağılım 11 ila 86,5) aydı. Hastaların RT sonrası GS ortanca 17.3 (aralık 4.4-83.9) aydı. Yedi hastada (%46.7) nüks (lokal+uzak) vardı; 2 (%13.3) lokal, 3 (%20) uzak ve 2 (%13.3) lokal+uzak met vardı. Ortanca HS 24 aydı (aralık 1-86.5). Ortanca LRFS-RT 14.2 (aralık 1-83.9) aydı. LRFS-RT ile yaş (<10 ve ≥yaş üstü) arasındaki ilişki (p=0.050; HR:2.30; %95 GA 0.70-3.17) anlamlıydı. İleri yaşta anlamlı olarak daha yüksek LRFS-RT gözlendi.
Sonuç: Ameliyat sonrası lokal başarısızlık riski yüksek olan Ewing sarkomlu hastalarda adjuvan radyoterapi ile lokal kontrol şansı arttırılmaya çalışılmaktadır.

Anahtar Kelimeler: Adjuvan radyoterapi, ewing sarkomu, pediatrik onkoloji

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INTRODUCTION

Ewing Sarcoma is a rare type of cancer that affects bones and soft tissues. It accounts for 10-15% of all primary malignant bone tumors. It mainly occurs in children and young adults in the first and second decades of their lives. It has a high propensity to metastasize to the lung, bone, and bone marrow (1). Ewing sarcoma was first described by James Ewing, an American pathologist, as diffuse endothelioma, a highly radiosensitive tumor, in 1921 (2). Today, the standard of care is systemic treatment with surgery and/or radiotherapy. Tumors amenable to resection are treated primarily with surgery; otherwise, radiation therapy is the treatment of choice. Adjuvant Radiotherapy (RT) is generally considered if surgical margins are compromised or give poor response to chemotherapy.

In selecting the local treatment, function loss due to surgery, secondary malignancies, and other complications due to radiotherapy factors are considered. Although there is no study with a high level of evidence comparing these treatment modalities, it is reported that surgical outcomes are more favorable in retrospective series. However, it should be kept in mind that the patients who received radiotherapy in retrospective series had a worse prognosis in terms of location and size in which surgical treatment could not be performed (3-5). Radiotherapy was applied with old techniques in previous studies. The radiotherapy doses and schemes used differ; on the other hand, the development of surgical procedures makes it very difficult to compare these two local treatment modalities. Most of the studies in the literature are based on the evaluation of chemotherapy agents, and studies evaluating local treatment are generally retrospective (4,6).

This study aimed to report the adjuvant radiotherapy results of pediatric patients with Ewing Sarcoma who received multimodal treatment using modern radiotherapy techniques.

MATERIAL AND METHOD

For the study, pediatric patients with Ewing Sarcoma who received adjuvant RT in the Radiation Oncology Clinic of Ankara City Hospital were evaluated retrospectively. Patient interview information, patient files, and electronic system data were used for the study. Demographic status of the patients, tumor localization, clinical and pathological stage of the disease, chemotherapy, radiotherapy and surgery details, treatment response, and final status were noted. Ethics committee approval for the study was obtained from ethics committee no. 1 of Ankara City Hospital Hospital.

Patient Selection

Pediatric patients diagnosed with Ewing's Sarcoma, whose treatment details and follow-up information are available, were included in the study. Patients > 18 years old and those with the second malignancy were excluded. The statistical analyses were based on the following variables: gender (female vs. male), age at diagnosis <10 years vs ≥10 (7), recurrences (present vs. absent), tumor size (<8cm vs. ≥8cm) (8), RT total dose (under the 50 Gy and over the 50Gy), the margin status for patients undergoing surgery (R0 vs. R+) and tumor size (the longest axis measured on Magnetic Resonance Imaging (MRI)).

Treatment Details

The multidisciplinary tumor board evaluated patients after the pathological diagnosis. Patients were treated according to international multimodal protocols. The patients were assessed before the treatment, one and three months after the end of CT (chemotherapy), and every three months before and after the operation, and their examinations were carried out. Patients were treated using the Eclipse (Varian Oncology System Inc. CA, USA). External RT was applied to the patients five days a week.

Primary and Secondary Endpoints

The study's primary endpoints were Overall Survival (OS) and disease-free survival (DFS). The date of pathological diagnosis was accepted as the starting date for OS and DFS. The end date for OS was the last control date for surviving patients and the exitus date for ex-patients. The endpoint for DFS was the date of relapse for patients with relapse, the date of last check for patients without relapse. The secondary endpoint was local relapse-free survival after RT (LRFS-RT) and overall survival after RT (OS-RT). The last day of RT was taken as the starting date for OS-RT and LFS-RT values, which are the survival evaluation parameters after RT. The end date for OS-RT was the last check date for surviving patients and the exitus date for ex-patients. The end date for LRFS- RT was the date of relapse for patients with relapse, the date of last control for patients without relapse after RT.

Statical Analysis

Descriptive statistics for continuous (quantitative) variables were expressed as mean, standard deviation, minimum-maximum, and median values; categorical variables were expressed as number (n) and ratio (%). The categorical demographic characteristics of the patients were calculated with Chi-square with Fisher's exact test. Kaplan Meier was used in univariate survey analyses and compared with the log-rank test. Cox regression test was used in multivariate analysis. Analyses were performed with IBM SPSS Package Program version 23.0 (IBM Corporation, Armonk, NY, USA). The statistical significance level was set as $p<0.05$. The hazard ratio (HR) and 95% Confidence Interval (CI) values were noted for significant results.

RESULTS

The results of 18 pediatric patients diagnosed with Ewing Sarcoma in our clinic between 09.12.2013- 04.04.2021 and who underwent RT for adjuvant were evaluated retrospectively. The three patients were excluded since they did not meet the inclusion criteria.

The median age of the patients at the time of diagnosis

was 10.5 (range 3-17). The age of the patients was divided into two groups as under ten years old and above (7); 6 (%40) patients were younger than ten years, and 9 (60%) patients were ten years or older. In terms of gender, 8 (53.3%) patients were male, and 7 (46.7%) were female. The tumor size (long axis of the tumor) was median 106 mm (range 40-200), smaller than 8 cm in five patients (33.3%); 8 cm or larger in 10 patients (66.7%). Localization was lower extremity 3 (20%), upper extremity 3 (20%), costal 5 (33.3%), pelvic 3 (20%), head and skull base 1 (6.7%).

Patient and disease characteristics are summarized in Table 1.

Table 1. Patient and disease characteristics

Age	**Median**	**10.5 (range 3-17)**
	<10 y	6(40%)
	≥10 y	9(60%)
Gender	Male	8(53.3%)
	Female	7(46.7%)
Tumor size (Long axis of tumor)	Median	106mm(range 40-200)
	<8 cm	5 (33.3%)
	≥ 8 cm	10 (66.7%)
Localization	Lower extremity	3 (20%)
	Upper extremity	3 (20%)
	Costal	5 (33.3%)
	Pelvic	3 (20%)
	Head and skull base	1 (6.7%)
Surgical Margin Status	R0	7 (46.7 %)
	R1	4 (26.7%)
	R2	4 (26.7%)
Chemotherapy prior to RT	Median course number	6 (range 4-8)
Chemotherapy prior to RT -protocols	VIDE	10 (66.7%)
	VIDE + VAI	4 (26.7%)
	VIAE	1 (6.7%)
Concurrent CT	Yes	13 (86.7%)
	No	2 (13.3%)
Concurrent CT course	Median	2 (range 0-3)
Concurrent CT protocols	IE	4 (26.7%)
	VI	2 (13.3%)
	VIE	5 (33.3%)
	VCR	2 (13.3%)
Chemotherapy after RT	Yes	14 (93.3%)
	No	1 (6.7%)
Chemotherapy after RT course	Median	6 (range 1-14)
Post RT Local Recurrence	No	11 (73.3%)
	Yes	4 (26.7%)
Recurrence	No	8(53.3%)
	Yes	7(46,7%)
Recurrence Site	Local	2 (13.3%)
	Distance	3 (20%)
	Local+Distance	2 (13.3%)
Last Status	Alive	12 (80%)
	Ex	3 (20%)

Abbreviations: VIDE: vincristine, ifosfamide, doxorubicin and etoposide; VIE: vincristine, ifosfamide, and etoposide; VAI: vincristine, actinomycin-D and ifosfamide BVIT: bevacizumab, vincristine, irinotecan and temozolamide

Chemotherapy

All the patients received pre-RT chemotherapy. All but one patient were treated with the European Ewing tumor Working Initiative of National Groups Ewing Tumor Studies 1999 (EURO-EWING 99) Chemotherapy protocol. Only 1 (6.7%) patient was treated with the EICESS (European Intergroup Cooperative Ewing's Sarcoma Study) protocol. As induction CT, median six courses of vincristine, ifosfamide, doxorubicin, and etoposide (VIDE) (range 4 to 8 courses) were given to 14 patients treated according to the EURO-EWING 99 protocol. After induction, surgical excision was performed in all patients, except for one. All but one patient received concurrent chemotherapy (median two courses, range 1-3) during adjuvant RT. Anthracyclines or actinomycin-D were avoided as concomitant chemotherapies. After RT, patients completed 14 cycles of chemotherapy according to the protocol. After RT, CT consisted of vincristine, actinomycin-D, and ifosfamide in 11 patients median five courses (range, 4-8). One patient underwent autologous stem cell transplantation, then RT. Three patients developed progressive disease or relapse; second-line CT containing irinotecan and temozolomide was given. After RT, patients received a median of 7 (range 4-17) cycles of CT.

Surgery

All patients were operated. Of the patients, 7 (46.7 %) were R0, 4 (26.7%) patients were R1 and 4 (26.7%) patients were R2.

Radiotherapy

RT was administered to patients for adjuvant purposes. The period from diagnosis to the onset of RT was 8.6 (range 2-20) months. The median fraction dose was 180cGy. The median total fraction number was 28 (range 25-31), and the median total RT dose was 50.4 (range 45-55.8) Gy.

Radiotherapy was examined in terms of the total dose, and 3 (20%) patients received less than 50 Gy, and 12 (80%) patients received 50 Gy or more. Radiotherapy technique was applied with IMRT in 6 patients and with 3D-CRT technique in 9 patients.

Overall Survival Analyses

Two different OS analyses were performed, namely overall survival from diagnosis and overall survival after RT. The median follow-up period of the study was 27 (range 11-86) months. 12 (80%) patients survived, and 3 (20%) died. The median OS of the patients was 27.3 (range 11 to 86.5) months. The overall survival of the patients after RT was median 17.3 (range 4.4-83.9) months (Figure 1).

There was no significant relationship between overall survival and gender (female vs. male) (p=0.350), age at diagnosis (10y and under vs. older than 10y) (p=0.757), margin status (R0 vs. R+) (p=0,579), tumor size (<8cm vs. ≥8cm) (p=0.619), total RT doses (under the 50 Gy and over the 50 Gy) (p=0.411) (Figure 2).

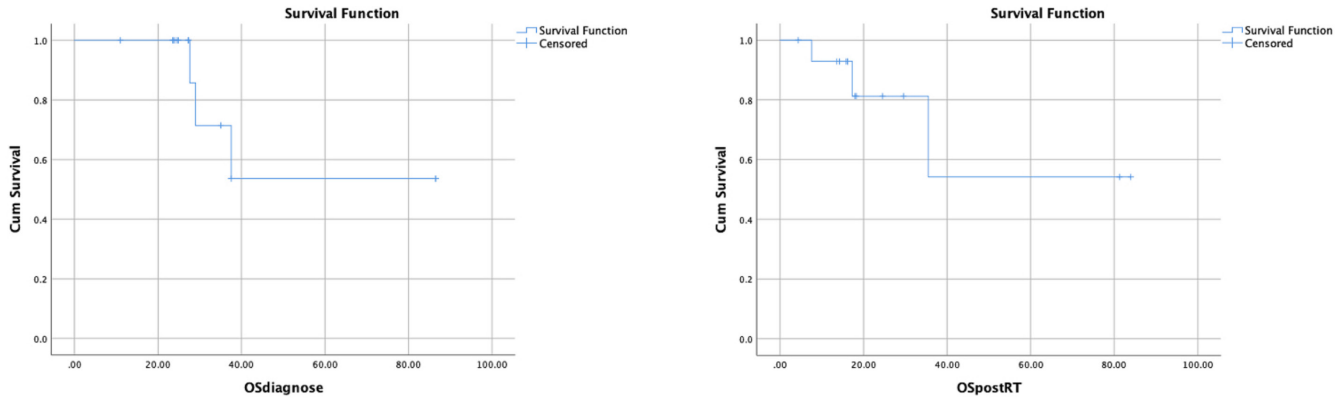


Figure 1. Kaplan Meier Analysis Results for Overall Survival

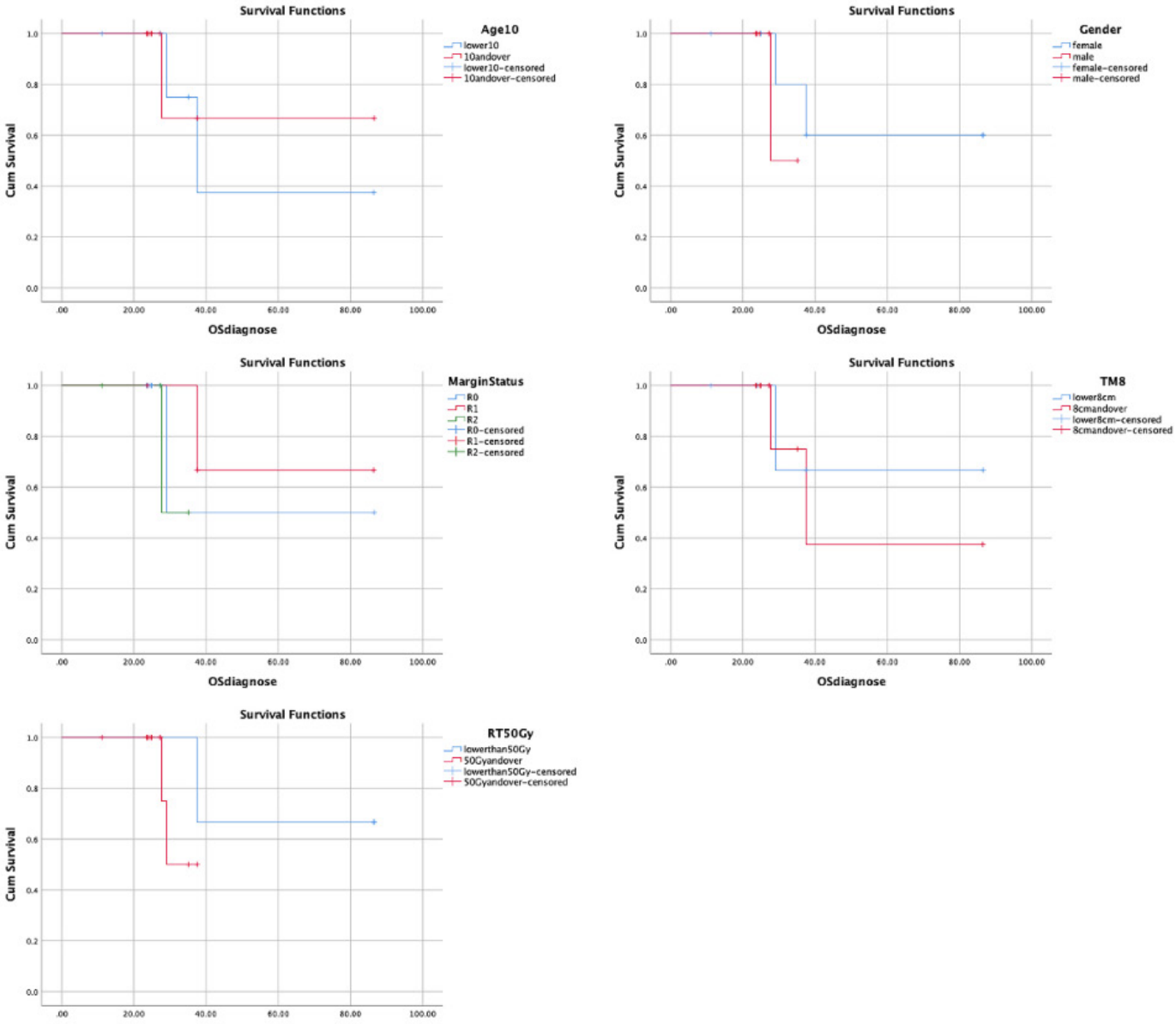


Figure 2. Kaplan Meier Analysis Results for Overall Survival from diagnosis

Similar results were also seen in the OS-RT analysis; gender (female vs. male) (p=0.938), age at diagnosis (<10 vs. over ≥ years old) (p=0.672), margin status (R0 vs. R+) (p=0.663), tumor size (<8cm vs. ≥8cm) (p=0.994), total RT doses (under the 50 Gy and over the 50 Gy) (p=0.353) (Figure 3).

Disease-Free Survival Analyses (From diagnosis)

The median DFS was 24 months (range 1-86.5). Recurrence (local+distant) was observed in 7 patients (46.7%); 2 (13.3%) local, 3 (20%) distant and 2 (13.3%) both. No significant relationship was found between DFS and the following variables: gender (female vs. male) (p=0.167), age at diagnosis <10 years vs ≥10 (p=0.813), tumor size (<8cm vs. ≥8cm) (p=0.610), margin status (p=0.945), RT total dose (under the 50 Gy and over the 50 Gy) (p=0.167) (Figure 4 and 5).

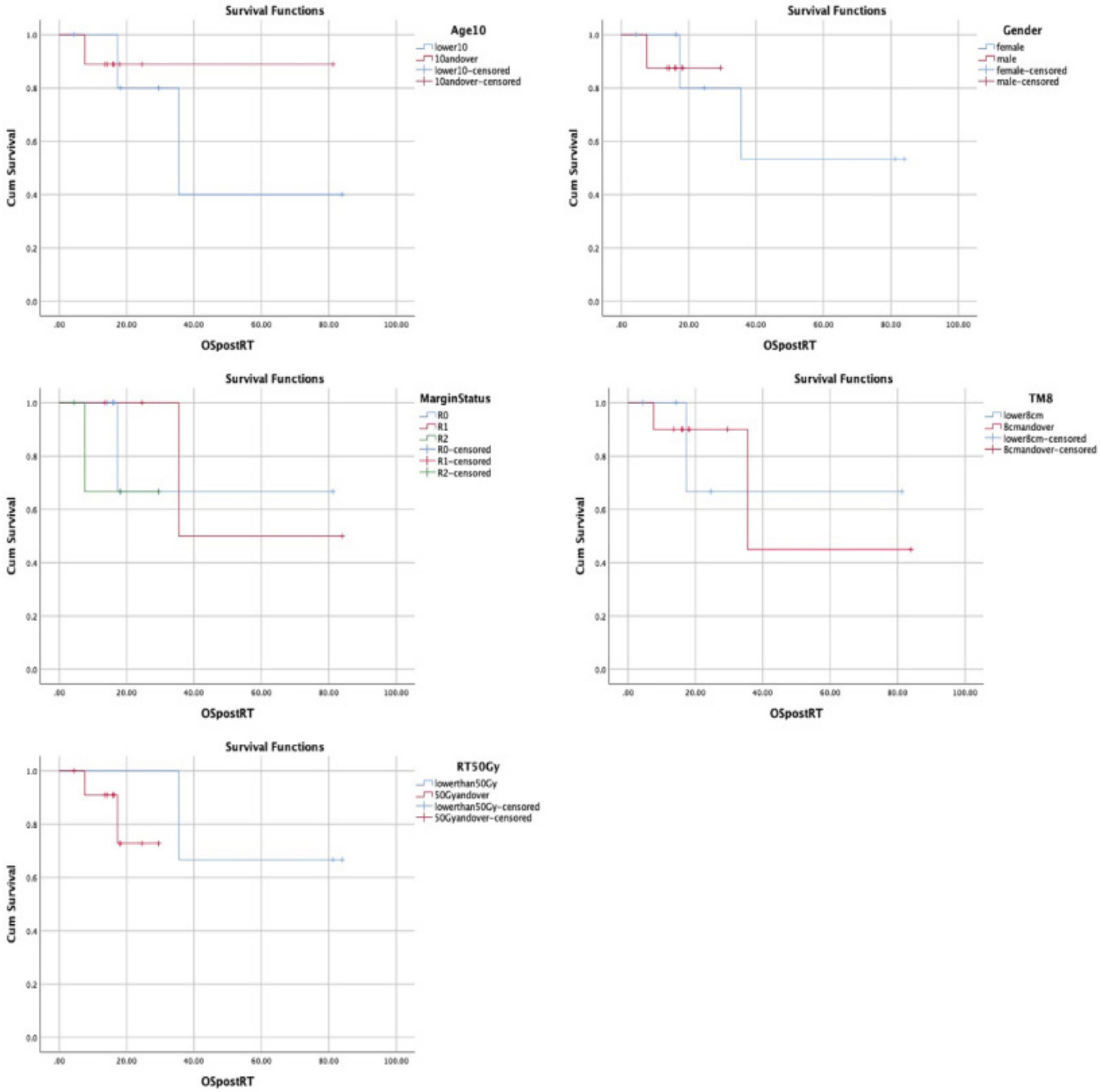


Figure 3. Kaplan Meier Analysis Results for Overall Survival from RT

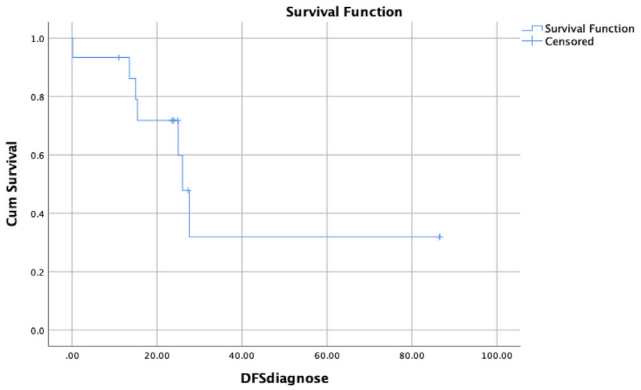


Figure 4. Kaplan Meier Analysis Results for DFS and LRFS-RT

Local Recurrence Free Survey from RT

Median LRFS-RT is 14.2 (range 1-83.9). The relationship between LRFS-RT and age (<10 vs. over ≥ years old) (p=0.050; HR:2.30; 95% CI 0.70-3.17) was significant. Significantly higher LRFS-RT was observed at the older ages (Figure 6 and 7).

There was no significant relationship between LRFS-RT and other variables; gender (male vs female) (p=0.253), tumor size (<8 cm vs. ≥8 cm) (p=0.416), RT total dose (under the 50 Gy and over the 50 Gy) (p=0.977), margin status (R0 vs. R+) (p=0.317) (Figure 8).

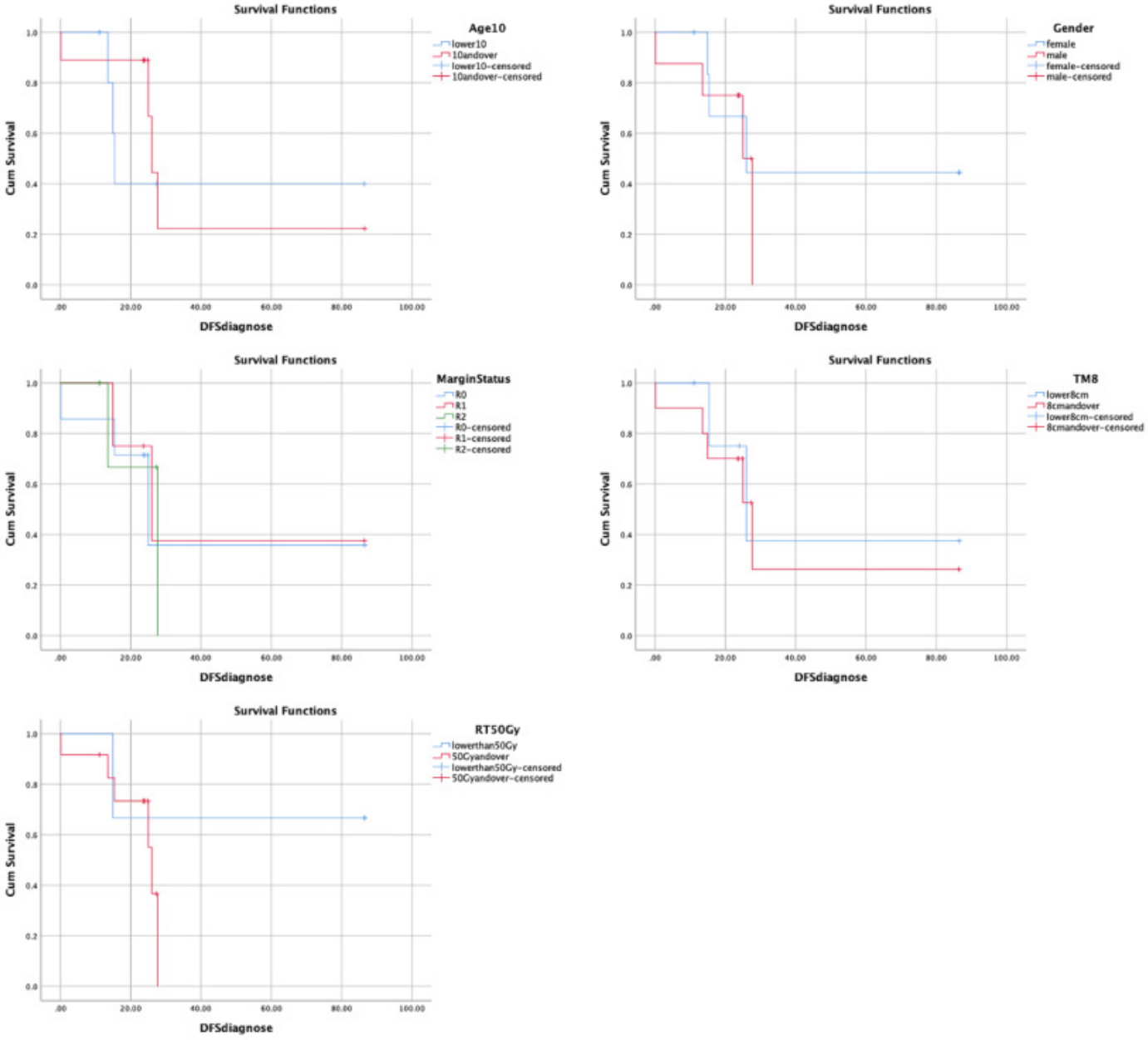


Figure 5. Detailed Kaplan Meier Analysis Results for DFS

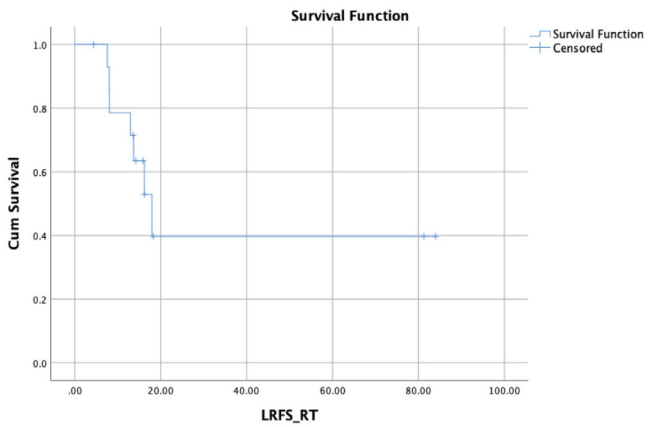


Figure 6. Kaplan Meier Analysis for LRFS-RT

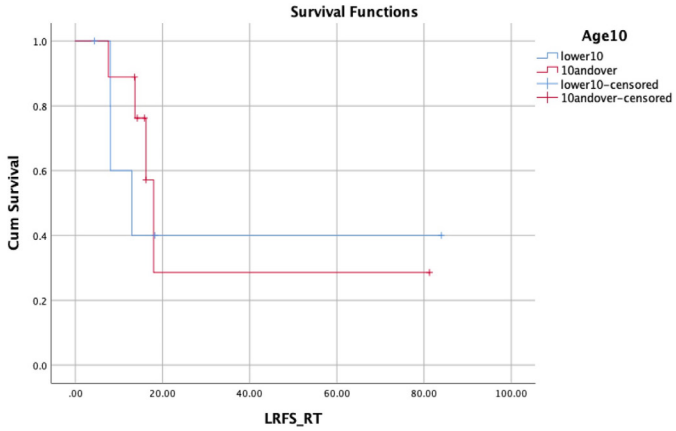
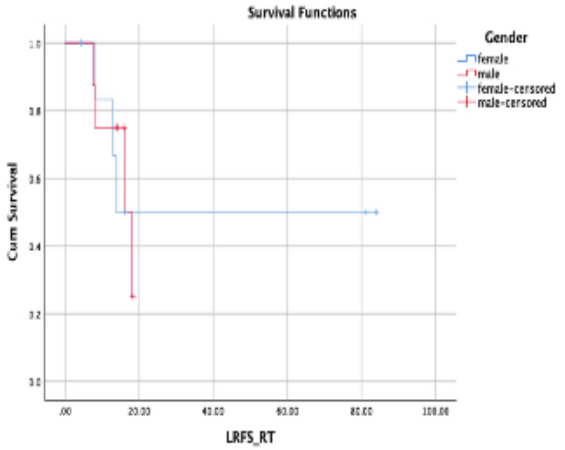
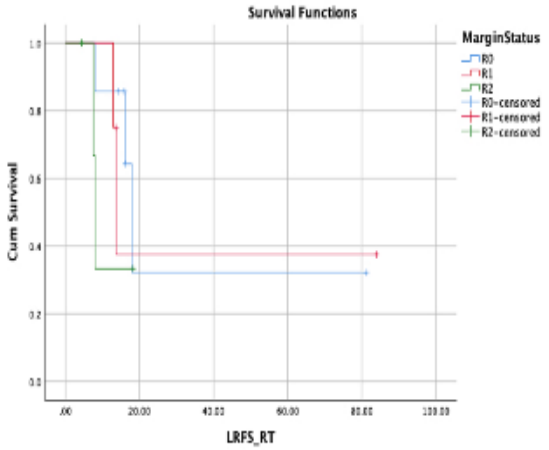
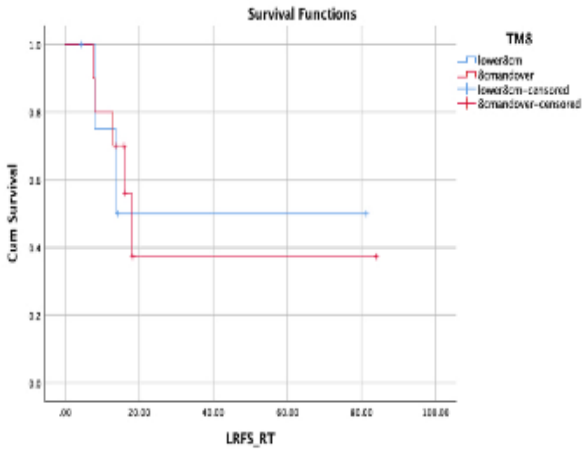


Figure 7. LRFS-RT and Age Relationship with Kaplan Meier Analysis







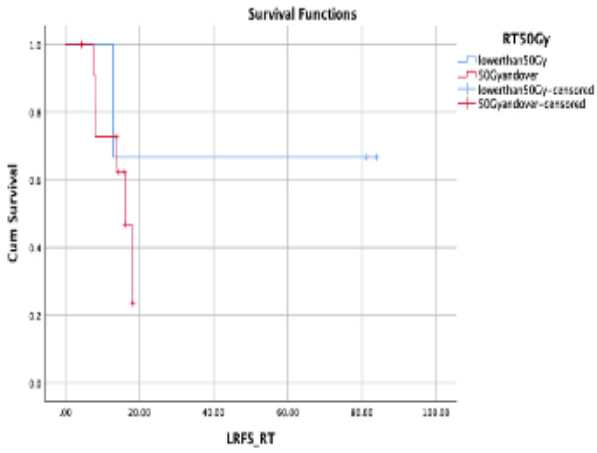


Figure 8. Detailed Kaplan Meier Analysis for LRFS-RT

	Age	Younger than 10	10 and older	p	HR
LRFS-RT	Median	10.5 (4.4-83.9)	15.8 (7-81)	0.050	0.14 (0.014-1.36)

Table 2. Patient Detail

Pt	Age, Gender	Localization	Size (mm)	Pre-RT CT	CCT	Post RT CT	MS	RT Details	Last Status	OS mo	DFS
1	11, M	UE	184	6c VIDE	VIE	Beva +8c VAI	R0	50 Gy/1.8 AE: Grade 1 RD	Alive LR:-	OSdiagnosis: 23.4 OSRT:15.8	DFSdiagnosis:23.4LRFS-RT:15.8
2	11,F	LE	200	6c VIDE+ 1cVAİ	3c VIE	Beva +4c VAI	R0	55.8 Gy/1.8 AE: NS	Alive LR:-	OSdiagnosis: 24.9 OS RT:16.2	DFSdiagnosis:24.9LRFS-RT:16.2
3	8,F	Pelvic	180	6cVIDE+ 1cVAİ	2c VI	OKIT ICE BIT	R1	45 Gy /1.8 AE: Grade 1 Diarre	Ex LR:+CT + for recurrence	OSdiagnosis: 37.5 OSRT:35	DFSdiagnosis: 14.9LRFS-RT:12.9
4	8,F	Head, Skull	40	4c VİAE	-	-	R2	54Gy/1.8Gy AE: Grade 1 RD	Alive LR:-	OSdiagnosis: 11 OSRT:4.4	DFSdiagnosis:11LRFS-RT:4.4
5	13, F	LE	35	6c VIDE+1c VAİ	3c VCR	12BVIT	R1	50.4 Gy/ 1.8 Gy AE: NS	Alive LR+ Distant Met:+	OSdiagnosis: 37.5 OSRT:24.5	DFSdiagnosis: 26LRFS-RT:13.7
6	6, F	Costa	110	5c VIDE	-	Beva 1c VIDE 1c VAI 7c VAC	R1	39 Gy71.5 Gy AE: NS	Alive LR:-	OSdiagnosis: 86.4 OSRT:83.9	DFSdiagnosis:86.4LRFS-RT:83.9
7	7, M	Pelvic	90	4c VIDE	2c IE	5cVAC12c VIT	R2	55.8 Gy /1.8Gy AE: NS	Alive LR:+	diagnosis: 35 OSRT:29.5	DFSdiagnosis:13.5LRFS-RT:8
8	17, M	Costa	101	8c VIDE	2c VIE	Beva 4c VAI	R1	50.4 Gy / 1.8 Gy AE: Grade 2 RD	Alive LR:-	OSdiagnosis: 23.6 OSRT: 13.6	DFSdiagnosis:23.6LRFS-RT:13.6
9	15, M	UE	90	6c VIDE	2c VIE	Beva 5c VAI	R2	54 Gy / 1.8 Gy AE: NS	Ex LR:-DM:+ Palliative RT for DM	OSdiagnosis: 27.6 OSRT: 7.5	DFSdiagnosis:27.6LRFS-RT:7.5
10	15, M	LE	170	6c VIDE	2c IE	Beva5VAI	R0	50.4 Gy /1.8 Gy, AE: Grade 1 RD	AliveLR:-DM:+	OSdiagnosis: 24.5 OSRT:16.2	DFSdiagnosis: 1LRFS-RT:16.2
11	14, F	Costa	40	4c VIDE	VCRCY	Beva 6c VAC	R0	45Gy /1.8 Gy AE: Grade 1 RD	Alive LR:-	OSdiagnosis: 86.5 OSRT: 81.2	DFSdiagnosis:86.5LRFS-RT:81.2
12	16, M	pelvic	65	6c VIDE	3c VIE	Beva4c VAI	R0	54 Gy /1.8 Gy AE: NS	AliveLR:-	OSdiagnosis: 24 OSRT:14.2	DFSdiagnosis: 24LRFS-RT:14.2
13	3, M	UE	98	6c VIDE	2c VIE	Beva4c VAC	R2	55.8 Gy /1.8 Gy AE: Grade 2 RD	AliveLR:-	OSdiagnosis:27.3 OSRT:18.2	DFSdiagnosis:27.3LRFS-RT:18.2
14	10,M	Costa	110	6c VIDE+1c VAİ	VIE	Beva5c VAI	R0	50.4 Gy /1.8 Gy, AE: NS	AliveLR:-DM:+	OSdiagnosis: 27.2 OSRT:17.9	DFSdiagnosis:25LRFS-RT:17.9
15	4, F	Costa	51	6c VIDE	VI	Beva6c VAI	R0	50.4 Gy /1.8 Gy, AE: NS	Ex LR:+DM:+	OSdiagnosis:29 OSRT:17	DFSdiagnosis:15LRFS-RT:8

Abr: PT= Patients; M=Male; F=Female; mm=millimeter; RT=Radiotherapy; CT=Chemotherapy; CCT=Concurrent Chemotherapy; MS=Margin Status; OS: Overall Survey; DFS=Disease Free Survey; mo=months; UE=Upper Extremity; LE=Lower Extremity; c=course; VIDE= vincristine, ifosfamide, doxorubicin, and etoposide; VIE= vincristine, ifosfamide, and etoposide; Beva=Bevacisumab; VAI=?; AE: Adverse Effect; RD=Radiodermatitis; LR=Locale Recurrence; NS=Not specified; OKIT=; ICE=; BIT=; VİAE=; VCR=; BVIT=;IE=; DM=Distant Metastasis

Table 3. Retrospective trials for Ewing Sarcoma

Study	Number of patients	Special characteristics	Chemotherapy	Radiotherapy	Follow-up	Results for radiotherapy
Choi et al. (7)	91	The localized disease of ESFT	All pts received VACA Etoposid± Ifospfamid (65 pts)	Local curative therapy for 15 pts Adjuvant therapy for 32 pts Neoadj therapy for 1 pt	Med 43.8 month	The 5-year PFS was 55.9% combined RT and surgery vs. 39.4% in those treated with RT without surgery
Esmati et (2016) (13)	75	ESFT (localized+metastatic)	ND	Definitive (46) Adjuvant (16) Palliative (10)	ND	5 y OS 24% met (+) 21±17m met (-) 75±10 m
Wan et al. (2017) (14)	397	ES of bone and joints 65% <18 y (SEER data)	ND	RT alone 102 pts RT+surgery 86 pts	ND	5 y OS Surgery only 78.4% Surgery+RT 66.9% RT only 47.8%
Sarı et al. (2009) (15)	13	Extraosseos ES (<18 y)	EVAIA (7) VAIA (3) Others (3)	10 pts received surgery	48m	5 y OS 67% (Results for RT not defined)
Kaçmaz et al. 2019 (16)	39	Neoadjuvant RT applied pts	VAIA	CT+RT 28 pts NeoCT±NeoRT 11 pts	37.95m	5 y OS surgery (+) pts 26.1% surgery (-) pts 35.4%
Goyal et al. 2019 (17)	21	Non-met EFSTarisnf from head and neck	VAC/IE St Jude's	Surgery+adj RT 5 pts Definitive RT 16 pts	26.7m	At last fu 12 pts were disease-free 6 pts were alive with disease
Sathamurthy et al. 2020 (18)	65	Extraosseous ES (met and non-met)	VAC/IE (40% of pts)	Adjuvant RT 22 pts Palliative RT 5 pts Definitive RT 2 pts	The follow-up ranged from 1 to 121 months.	36 m OS RT (+) 45% RT(-) 8% Med OS RT (+) 26m RT (-) 5m
Momin et al. 2021 (19)	49	ESFT (curative intent)	VIE+VAC	Neoadj RT+ surgery 5 pts Surgery+adj RT 9 pts Definitive RT 35 pts	18m	Local control with combined surgery and radiotherapy was better than definite radiotherapy, but the difference was statistically insignificant.

Abbreviations: ESFT; Ewing Sarcoma Family Tumors, ND; Not defined, NeoCT; neoadjuvant chemotherapy, NeoRT; neoadjuvant radiotherapy

DISCUSSION

This study evaluated a small group of patients receiving radiotherapy for Ewing sarcoma, primarily in an adjuvant setting. The results of 15 pediatric patients diagnosed with Ewing Sarcoma and who underwent adjuvant RT were evaluated retrospectively. The median follow-up period of the study was 27 (range 11-86) months and within this period, 12 (80%) patients survived. The recurrence observed five patients (33.3%) . The median OS diagnosis of the patients was 27.3 (range 11 to 86.5) months. The overall survival of the patients after RT was median 17.3 (range 4.4-83.9) months. Median LRFS-RT is 14.2 (range 1-83.9). The relationship between LRFS-RT and age (<10 vs. over 10≥ years old) was significant and significantly higher LRFS-RT was observed in the older age. However, the study was conducted in a few patients with a short follow-up period.

Ewing sarcoma is a disease group in which survival increases gradually, thanks to systemic therapy and the development of multimodal treatment schemes. Especially with the development of systemic therapy, the treatment of metastatic disease seems to be the primary factor in the increase in survival in this disease with early metastasis tendency (9,10). Five-year survival rates for patients with ES increased from 36% in 1975-1984 to 56% in 1985-1994. (11). This rate has increased up to 70% with multimodal treatment for non-metastatic cases (12).

No randomized trial evaluates the role of radiotherapy in the curative or adjuvant setting. Most of the data in the literature consist of radiotherapy results obtained from retrospective analyses (Table 1) (7,13-19). Although different chemotherapy schemes and different patient groups were evaluated in these studies, generally, local control and survival rates were reported to be higher in patients who received radiotherapy as a part of multimodal therapy. Our study calculated the median follow-up period as 19 months, and the median survival was 17.9 months.

Table 2. Retrospective Trials for Ewing Sarcoma

It has been shown in previous studies that local control is increased by adjuvant radiotherapy in the presence of microscopic tumors after surgery (20,21). Krasin et al. demonstrated that a negative margin is essential for local failure control. (21). It was shown that not only R0 resection but also the rate of necrosis after chemotherapy is critical for local tumor control (22). Although this factor is not accepted as a general indication for adjuvant radiotherapy, it is effective in different study groups. Although seven patients in this cohort were defined as R0 resection, adjuvant radiotherapy was indicated due to low necrosis rates and suspicion of possible tumor seeding during surgery.

Although the number of patients in this study is limited, it consisted of only patients who received adjuvant RT, making the study important. On the other hand, the patients must be treated with modern radiotherapy techniques.

CONCLUSION

Adjuvant radiotherapy indications and approaches to treating Ewing's sarcoma may differ between clinics. Using modern radiotherapy techniques, it should be determined which patients will benefit from adjuvant radiotherapy.

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