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Comparison of preoperative chemoradiation with radiation or chemotherapy alone in patients with non-metastatic, resectable retroperitoneal sarcoma

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Abstract

Aim: Optimal preoperative therapy regimen in the treatment of resectable retroperitoneal sarcoma (RPS) remains unclear. This study compares the impact of preoperative radiation, chemoradiation and chemotherapy on overall survival (OS) in RPS patients.
Materials and Methods: The National Cancer Database (NCDB) was queried for patients with non-metastatic, resectable RPS (2006–15). The primary endpoint was OS, evaluated by Kaplan–Meier method, log-rank test, Cox multivariable analysis and propensity score matching.
Results: A total of 1,253 patients met the inclusion criteria, with 210 patients (17%) receiving chemoradiation, 850 patients (68%) receiving radiation and 193 patients (15%) receiving chemotherapy. On Cox multivariable analysis, when compared to preoperative chemoradiation, preoperative radiation was not associated with improved OS (hazards ratio [HR] 0·98, 95% CI 0·76–1·25, $p = 0·84$), while preoperative chemotherapy was associated with worse OS (HR 1·64, 95% CI 1·24–2·18, $p < 0·001$). Similar findings were observed in 199 and 128 matched pairs for preoperative radiation and chemotherapy, respectively, when compared to preoperative chemoradiation.
Findings: Our study suggested an OS benefit in using preoperative chemoradiation compared to chemotherapy alone, but OS outcomes were comparable between preoperative chemoradiation and radiation alone.

Background

Soft tissue sarcomas are a rare, heterogeneous group of malignancies, accounting for only 1% of all cancer types.[1] Up to 15–20% of sarcomas arise from the retroperitoneum.[1,2] The most common recurrence pattern is locoregional failure and occurs in 25–50% of patients, despite complete surgical resection.[3–5] Although a previous prospective trial showed no survival benefit with preoperative radiation therapy,[6] prior retrospective studies showed that those receiving preoperative radiation therapy were more likely to have negative surgical margin and improved survival.[7,8] The National Comprehensive Cancer Network (NCCN) guidelines currently recommend the consideration of neoadjuvant therapies, such as chemotherapy (doxorubicin and ifosfamide among others) and radiation (external beam radiation therapy with 50 Gy, with consideration of intraoperative radiation therapy [IORT] or simultaneous integrated boost in select cases), at the discretion of clinicians.[9] However, given the rare incidence of retroperitoneal sarcoma, the comparison of various neoadjuvant therapies has not been evaluated prospectively. To address this knowledge gap, we performed a retrospective, observational cohort study to compare preoperative chemotherapy, radiation and chemoradiation using a nationwide clinical oncology database.

Methods

Our study was approved by institutional review board at the Roswell Park Comprehensive Cancer Center (BDR-131220). It also follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.[10]

The National Cancer Database (NCDB)[11] is a nationwide clinical oncology database that captures more than 70% of newly diagnosed cancer cases in the United States and is jointly

sponsored by the American College of Surgeons and the American Cancer Society. The NCDB is accessible to investigators from the Commission of Cancer-accredited institutions after obtaining an approval from the American College of Surgeons and the American Cancer Society. The database was queried for patients diagnosed between 2006 and 2015 with non-metastatic, resectable retroperitoneal sarcoma (RPS) treated with neoadjuvant therapies followed by surgery. Follow-up was until the end of 2017. Variables of interest included facility type (academic versus non-academic), facility volume (low, intermediate or high volume), age, gender, Charlson-Deyo comorbidity score (CDS), income, insurance, histology, tumour grade, year of diagnosis, T and N staging, surgery types, surgical margin, postoperative readmission, and postoperative inpatient duration. Income levels and insurance status were included for analysis since they were previously shown to be associated with survival outcomes.[12] Those with metastatic disease, surgery alone and unknown receipt of neoadjuvant therapy were excluded.

The primary endpoint was overall survival (OS), defined as the time interval between diagnosis and the last follow-up or death. OS was evaluated using Kaplan–Meier method, log-rank test and Cox regression multivariable analysis. Interaction term analysis was performed to evaluate differences in treatment effects with respect to facility type, facility volume and histology.[13] Logistic regression multivariable analysis was also performed to evaluate the association of variables with surgical margin status.

To reduce selection bias, propensity score matching was performed based on the nearest neighbour method in a 1:1 ratio without a replacement and with a caliper distance of 0·1 of the standard deviation of the logit of the propensity score.[14] The standardised differences of variables were less than 0·1, indicating adequate match.[15] To address immortal time bias, those who survived less than 6 months after diagnosis were excluded as a conditional landmark. Analyses were performed with R-software version 3.6.1 (R Project for Statistical Computing). Drs Ma and Singh had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Results

A total of 1,253 patients with a median age of 60 years (interquartile range [IQR] 51–69) met our inclusion criteria. Of those, 210 patients (17%) received chemoradiation, 850 patients (68%) received radiation and 193 patients (15%) received chemotherapy. The median follow-up was 36·1 months (IQR 19·9–63·9). For those who underwent radiation therapy, its median total dose was 50·0 Gy (IQR 48·8–50·4). When compared between those treated with chemoradiation or radiation therapy, they both received comparable radiation doses ($p = 0·40$). On multivariable analysis, when compared to preoperative chemoradiation, preoperative radiation was not associated with improved OS (hazards ratio [HR] 0·98, 95% CI 0·76–1·25, $p = 0·84$), while preoperative chemotherapy was associated with worse OS (HR 1·64, 95% CI 1·24–2·18, $p < 0·001$).

On Cox multivariable analysis, other factors associated with worse OS were recent years of diagnosis (2011–15 versus 2006–10; HR 1·30, 95% CI 1·08-1·58, $p = 0·007$), elderly age (≥ 65 versus <65; HR 1·32, 95% CI 1·10-1·59, $p = 0·003$), male gender (HR 1·20, 95% CI 1·00-1·43, $p = 0·047$), lower income (HR 1·19, 95% CI 1·00-1·43, $p = 0·049$), poorly differentiated (HR 2·53, 95% CI 1·84-3·48, $p < 0·001$) or other tumour grade (HR 2·44, 95% CI 1·75-3·40, $p < 0·001$), and positive surgical margin (HR 1·37, 95% CI 1·12-1·68, $p = 0·002$). No interaction of preoperative therapy was observed with facility type (interaction $p = 0·08$), facility volume (interaction $p = 0·89$) or histology (interaction $p = 0·49$). On logistic multivariable analysis, histology was the only factor associated with surgical margin status (low grade liposarcoma, not otherwise specified: odds ratio [OR] 2·93, 95% CI 1·93-4·46, $p < 0·001$; intermediate grade liposarcoma: OR 0·37, 95% CI 0·15-0·78, $p = 0·02$; high-grade liposarcoma: OR 2·62, 95% CI 1·82-3·78, $p < 0·001$) when compared to leiomyosarcoma. After propensity score matching, all baseline characteristics were well balanced (Table 1). Similar findings were observed in 199 matched pairs for preoperative radiation (HR 1·00, 95% CI 0·74-1·36, $p = 0·98$; Figure 1) and 128 matched pairs for preoperative chemotherapy (HR 1·51, 95% CI 1·04-2·19, $p = 0·03$; Figure 2) when compared to preoperative chemoradiation.

Discussion

This is the first report to compare preoperative chemotherapy, radiation and chemoradiation using a national oncology database. While preoperative radiation and chemoradiation had comparable survival outcomes, preoperative chemotherapy was associated with worse survival outcomes compared to chemoradiation.

Several single-arm prospective trials involving approximately 30–80 patients have investigated chemotherapy as a radiosensitiser and showed preoperative chemoradiation (up to 50·4 Gy with either ifosfamide or doxorubicin) to be feasible in select patients with the majority of patients receiving grossly complete surgical resection.[16,17] However, although survival outcomes from the prospective trial were consistent with our study, up to one-third of patients from the trial could not complete preoperative chemoradiation due to toxicity and local failure still occurred in over 40% of cases.[18] Significant locoregional failure despite the use of chemoradiation may explain a lack of OS benefits seen with preoperative chemoradiation in our study.

Worse mortality with preoperative chemotherapy in our study is consistent with a prior NCDB report that included 163 patients treated with chemotherapy.[19] This observation may be likely due to mortality secondary to locoregional, rather than distant recurrences.[5,20–22] Several multimodality approaches involving chemotherapy (ifosfamide, doxorubicin and etoposide) were investigated, such as regional hyperthermia with favourable local control and survival outcomes, in prospective trials, one of which was a phase III trial involving 341 patients.[23,24] However, the use of hyperthermia was not available in the NCDB for comparison. In our study, intermediate grade liposarcoma was associated with negative margin, which was consistent with literature suggesting that myxoid and round cell liposarcoma are sensitive to radiation and chemotherapy.[25–28] Ongoing trials, such as Surgery With Or Without Neoadjuvant Chemotherapy in High-Risk Retroperitoneal Sarcoma II trial (STRASS II; NCT04031677), are further investigating the role of preoperative chemotherapy.

Limitations of our study are related to the retrospective nature of the NCDB. In addition, clinically relevant factors, such as performance status, chemotherapy agents and toxicity profiles, were not captured in the NCDB. Unmeasured confounding and selection bias may be present despite propensity score matching. In our analysis, postoperative readmissions and duration of postoperative inpatient admission were also matched as proxy measures for postoperative performance status.[29] Our findings also may not be generalisable to other populations that were not included in the NCDB.

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Table 1. Baseline characteristics for cohorts after matching

	Chemoradiation		Radiation			Chemoradiation		Chemotherapy		
	N	%	*N*	%	*P*-value	*N*	%	*N*	%	*P*-value
Facility type					1					0·59
Non-academic	51	25·6	50	25·1		31	24·2	25	19·5	
Academic	123	61·8	124	62·3		78	60·9	85	66·4	
Not available	25	12·6	25	12·6		19	14·8	18	14·1	
Total	199	100·0	199	100·0		128	100·0	128	100·0	
Facility volume					0·94					0·66
Low	8	4·0	7	3·5		15	11·7	11	8·6	
Intermediate	16	8·0	15	7·5		23	18·0	21	16·4	
High	175	87·9	177	88·9		90	70·3	96	75·0	
Total	199	100·0	199	100·0		128	100·0	128	100·0	
Age					0·64					0·78
<65 years	153	76·9	148	74·4		96	75·0	93	72·7	
65 years or older	46	23·1	51	25·6		32	25·0	35	27·3	
Total	199	100·0	199	100·0		128	100·0	128	100·0	
Gender					0·84					0·80
Female	90	45·2	87	43·7		64	50·0	67	52·3	
Male	109	54·8	112	56·3		64	50·0	61	47·7	
Total	199	100·0	199	100·0		128	100·0	128	100·0	
CDS					0·88					1
0	164	82·4	162	81·4		107	83·6	107	83·6	
1	31	15·6	34	17·1		17	13·3	18	14·1	
2 or higher	4	2·0	3	1·5		4	3·1	3	2·3	
Total	199	100·0	199	100·0		128	100·0	128	100·0	
Income					0·81					0·80
Above median	123	61·8	129	64·8		72	56·3	76	59·4	
Below median	70	35·2	64	32·2		52	40·6	47	36·7	
Not available	6	3·0	6	3·0		4	3·1	5	3·9	
Total	199	100·0	199	100·0		128	100·0	128	100·0	
Insurance					0·78					0·65
Uninsured	8	4·0	5	2·5		3	2·3	4	3·1	
Private	131	65·8	127	63·8		83	64·8	79	61·7	
Government	59	29·6	66	33·2		42	32·8	43	33·6	
Not available	1	0·5	1	0·5		0	0·0	2	1·6	
Total	199	100·0	199	100·0		128	100·0	128	100·0	
Histology					1					1
Leiomyosarcoma	69	34·7	68	34·2		45	35·2	45	35·2	
Sarcoma, NOS	20	10·1	17	8·5		9	7·0	12	9·4	
Spindle cell sarcoma	19	9·5	20	10·1		7	5·5	7	5·5	
Giant cell sarcoma	22	11·1	23	11·6		19	14·8	14	10·9	
Fibrosarcoma	3	1·5	2	1·0		1	0·8	1	0·8	
Malignant fibrous histiocytoma	7	3·5	8	4·0		6	4·7	5	3·9	
Low-grade liposarcoma	4	2·0	4	2·0		4	3·1	3	2·3	

(*Continued*)

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Table 1. (*Continued*)

	Chemoradiation		Radiation			Chemoradiation		Chemotherapy		
	N	%	*N*	%	*P*-value	*N*	%	*N*	%	*P*-value
Intermediate-grade liposarcoma	14	7·0	13	6·5		7	5·5	8	6·3	
High-grade liposarcoma	33	16·6	35	17·6		26	20·3	28	21·9	
Hemangiosarcoma	2	1·0	2	1·0		3	2·3	4	3·1	
Malignant peripheral nerve sheath tumour	6	3·0	7	3·5		1	0·8	1	0·8	
Total	199	100·0	199	100·0		128	100·0	128	100·0	
Grade					0·85					0·94
Well differentiated	10	5·0	11	5·5		7	5·5	6	4·7	
Moderately differentiated	15	7·5	14	7·0		9	7·0	11	8·6	
Poorly differentiated	80	40·2	74	37·2		44	34·4	46	35·9	
Others	53	26·6	63	31·7		38	29·7	40	31·3	
Not available	41	20·6	37	18·6		30	23·4	25	19·5	
Total	199	100·0	199	100·0		128	100·0	128	100·0	
Year					0·92					0·61
2006–10	81	40·7	79	39·7		52	40·6	57	44·5	
2011–15	118	59·3	120	60·3		76	59·4	71	55·5	
Total	199	100·0	199	100·0		128	100·0	128	100·0	
T staging					0·95					0·68
1	12	6·0	15	7·5		11	8·6	8	6·3	
2	50	25·1	45	22·6		28	21·9	37	28·9	
3	70	35·2	73	36·7		33	25·8	33	25·8	
4	60	30·2	58	29·1		51	39·8	44	34·4	
Not available	7	3·5	8	4·0		5	3·9	6	4·7	
Total	199	100·0	199	100·0		128	100·0	128	100·0	
N staging					0·76					1
0	153	76·9	152	76·4		98	76·6	97	75·8	
1	15	7·5	12	6·0		5	3·9	5	3·9	
Not available	31	15·6	35	17·6		25	19·5	26	20·3	
Total	199	100·0	199	100·0		128	100·0	128	100·0	
Surgery					0·91					0·90
Local excision	39	19·6	35	17·6		19	14·8	19	14·8	
Simple resection	113	56·8	116	58·3		75	58·6	80	62·5	
Radical resection	35	17·6	38	19·1		25	19·5	22	17·2	
Other	12	6·0	10	5·0		9	7·0	7	5·5	
Total	199	100·0	199	100·0		128	100·0	128	100·0	
Margin					0·83					1
Negative	134	67·3	136	68·3		83	64·8	82	64·1	
Positive	39	19·6	41	20·6		28	21·9	29	22·7	
Not available	26	13·1	22	11·1		17	13·3	17	13·3	
Total	199	100·0	199	100·0		128	100·0	128	100·0	
Readmission within 30 days					0·44					0·14
None	184	92·5	180	90·5		119	93·0	112	87·5	
Unplanned	9	4·5	10	5·0		3	2·3	8	6·3	

(*Continued*)

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Table 1. (*Continued*)

	Chemoradiation		Radiation			Chemoradiation		Chemotherapy		
	N	%	*N*	%	*P*-value	*N*	%	*N*	%	*P*-value
Planned	0	0·0	3	1·5		0	0·0	3	2·3	
Others	1	0·5	0	0·0		1	0·8	0	0·0	
Not available	5	2·5	6	3·0		5	3·9	5	3·9	
Total	199	100·0	199	100·0		128	100·0	128	100·0	
Postoperative inpatient duration (day)					1					0·97
<6	53	26·6	54	27·1		31	24·2	32	25·0	
6 or longer	116	58·3	116	58·3		80	62·5	81	63·3	
Not available	30	15·1	29	14·6		17	13·3	15	11·7	
Total	199	100·0	199	100·0		128	100·0	128	100·0	

Abbreviations: NOS, Not otherwise specified.

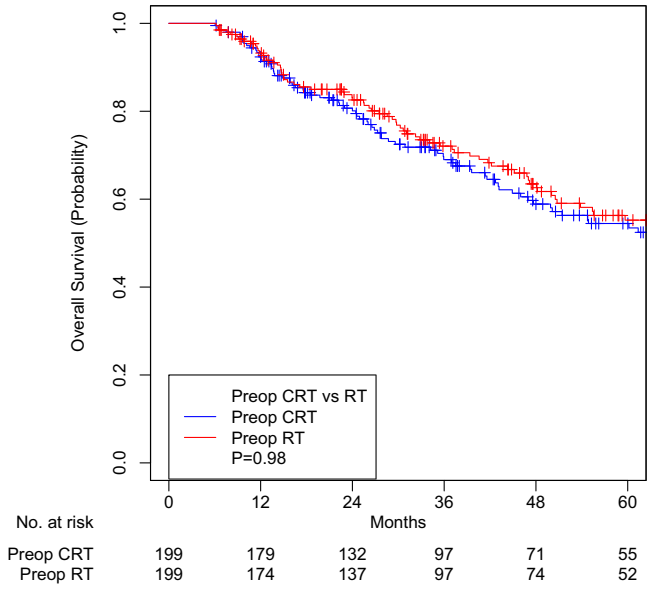

Figure 1. Kaplan–Meier survival curves for preoperative chemoradiation versus radiation.
Preop: preoperative; CRT: chemoradiation; RT: radiation.

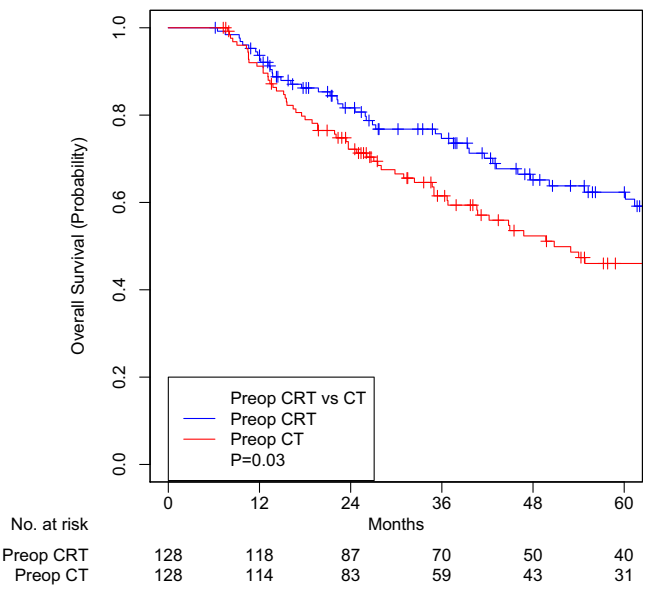

Figure 2. Kaplan–Meier survival curves for preoperative chemoradiation versus chemotherapy
Preop: preoperative; CRT: chemoradiation; CT: chemotherapy.

While our report suggests radiation may be an integral part of preoperative modalities, further studies are warranted to optimise preoperative therapies to improve local control and survival outcomes among patients with retroperitoneal sarcoma. For example, the role of intensity-modulated proton therapy and simultaneous integrated boost to high-risk tumour regions is being currently investigated in an ongoing trial.[30] In addition, given favourable outcomes from incorporating IORT,[17,31,32] the European Society of Radiotherapy and Oncology (ESTRO)[33] and the NCCN[9] guidelines both recommend the consideration of IORT in select patients. Ultimately, systematic multidisciplinary discussions are important to tailor treatment options based on individual patient and tumour characteristics, institutional areas of expertise, and shared decision-making with patients in the context of their treatment goals.[34]

Conclusion

Our study suggested an OS benefit in using preoperative chemoradiation compared to chemotherapy alone, but OS outcomes were comparable between preoperative chemoradiation and radiation alone.

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Conflicts of Interest. The authors declare none.

Ethical Standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008, and have been approved by Clinical Research Services and Office and Office of Research Subject Protection at Roswell Park Cancer Institute. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guides on the care and have been approved by Clinical Research Services and Office and Office of Research Subject Protection at Roswell Park Cancer Institute under the study number STUDY00000621/BDR 099918.

Availability of Data and Materials. The data that support the findings of this study are available from the Commission on Cancer of the American College of Surgeons and the American Cancer Society. The data are publicly accessible by any investigator affiliated with the Fellow of the American College of Surgeons applying to gain access. More information can be found at http://ncdbpuf.facs.org/.

References

1. Clark MA, Fisher C, Judson I, Thomas JM. Soft-tissue sarcomas in adults. N Engl J Med 2005; 353 (7): 701–711.
2. Brennan MF, Antonescu CR, Moraco N, Singer S. Lessons learned from the study of 10,000 patients with soft tissue sarcoma. Ann Surg 2014; 260 (3): 416–421; discussion 21–22.
3. Chouliaras K, Senehi R, Ethun CG, et al. Recurrence patterns after resection of retroperitoneal sarcomas: an eight-institution study from the US Sarcoma Collaborative. J Surg Oncol 2019; 120 (3): 340–347.
4. MacNeill AJ, Miceli R, Strauss DC, et al. Post-relapse outcomes after primary extended resection of retroperitoneal sarcoma: a report from the Trans-Atlantic RPS Working Group. Cancer 2017; 123 (11): 1971–1978.
5. Singer S, Antonescu CR, Riedel E, Brennan MF. Histologic subtype and margin of resection predict pattern of recurrence and survival for retroperitoneal liposarcoma. Ann Surg 2003; 238 (3): 358–370; discussion 70–71.
6. Bonvalot S, Gronchi A, Le Pechoux C, et al. Preoperative radiotherapy plus surgery versus surgery alone for patients with primary retroperitoneal sarcoma (EORTC-62092: STRASS): a multicentre, open-label, randomised, phase 3 trial. Lancet Oncol 2020; 21 (10): 1366–1377.
7. Ma SJ, Oladeru OT, Farrugia MK, Shekher R, Iovoli AJ, Singh AK. Evaluation of Preoperative Chemotherapy or Radiation and Overall Survival in Patients With Nonmetastatic, Resectable Retroperitoneal Sarcoma. J Am Med Assoc Netw Open 2020; 3 (11): e2025529.
8. Nussbaum DP, Speicher PJ, Gulack BC, Ganapathi AM, Englum BR, Kirsch DG, et al. Long-term Oncologic Outcomes After Neoadjuvant Radiation Therapy for Retroperitoneal Sarcomas. Ann Surg 2015; 262 (1): 163–170.
9. National Comprehensive Cancer Network. Soft Tissue Sarcoma (Version 1.2021). Available from: https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf.
10. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet 2007; 370 (9596): 1453–1457.
11. Bilimoria KY, Stewart AK, Winchester DP, Ko CY. The National Cancer Data Base: a powerful initiative to improve cancer care in the United States. Ann Surg Oncol 2008; 15 (3): 683–690.
12. Penumarthy NL, Goldsby RE, Shiboski SC, Wustrack R, Murphy P, Winestone LE. Insurance impacts survival for children, adolescents, and young adults with bone and soft tissue sarcomas. Cancer Med 2020; 9 (3): 951–958.
13. Barraclough H, Govindan R. Biostatistics primer: what a clinician ought to know: subgroup analyses. J Thorac Oncol 2010; 5 (5): 741–746.
14. Austin PC. Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies. Pharm Stat 2011; 10 (2): 150–161.
15. Haukoos JS, Lewis RJ. The propensity score. J Am Med Assoc. 2015; 314 (15): 1637–1638.
16. Gronchi A, De Paoli A, Dani C, et al. Preoperative chemo-radiation therapy for localised retroperitoneal sarcoma: a phase I-II study from the Italian Sarcoma Group. Eur J Cancer. 2014; 50 (4): 784–792.
17. Pisters PW, Ballo MT, Fenstermacher MJ, et al. Phase I trial of preoperative concurrent doxorubicin and radiation therapy, surgical resection, and intraoperative electron-beam radiation therapy for patients with localized retroperitoneal sarcoma. J Clin Oncol 2003; 21 (16): 3092–3097.
18. De Sanctis R, Giordano L, Colombo C, et al. Long-term Follow-up and post-relapse outcome of patients with localized retroperitoneal sarcoma treated in the Italian Sarcoma Group-Soft Tissue Sarcoma (ISG-STS) protocol 0303. Ann Surg Oncol. 2017; 24 (13): 3872–3879.
19. Miura JT, Charlson J, Gamblin TC, et al. Impact of chemotherapy on survival in surgically resected retroperitoneal sarcoma. Eur J Surg Oncol. 2015; 41 (10): 1386–1392.
20. Linehan DC, Lewis JJ, Leung D, Brennan MF. Influence of biologic factors and anatomic site in completely resected liposarcoma. J Clin Oncol 2000; 18 (8): 1637–1643.
21. Park JO, Qin LX, Prete FP, Antonescu C, Brennan MF, Singer S. Predicting outcome by growth rate of locally recurrent retroperitoneal liposarcoma: the one centimeter per month rule. Ann Surg 2009; 250 (6): 977–982.
22. Stojadinovic A, Yeh A, Brennan MF. Completely resected recurrent soft tissue sarcoma: primary anatomic site governs outcomes. J Am Coll Surg. 2002; 194 (4): 436–447.
23. Issels RD, Lindner LH, Verweij J, et al. Effect of neoadjuvant chemotherapy plus regional hyperthermia on long-term outcomes among patients with localized high-risk soft tissue sarcoma: the EORTC 62961-ESHO 95 randomized clinical trial. J Am Med Assoc Oncol 2018; 4 (4): 483–492.
24. Wendtner CM, Abdel-Rahman S, Krych M, et al. Response to neoadjuvant chemotherapy combined with regional hyperthermia predicts long-term survival for adult patients with retroperitoneal and visceral high-risk soft tissue sarcomas. J Clin Oncol 2002; 20 (14): 3156–3164.
25. Chowdhry V, Goldberg S, DeLaney TF, et al. Myxoid liposarcoma: treatment outcomes from chemotherapy and radiation therapy. Sarcoma 2018; 2018: 8029157.
26. Engstrom K, Bergh P, Cederlund CG, et al. Irradiation of myxoid/round cell liposarcoma induces volume reduction and lipoma-like morphology. Acta Oncol 2007; 46 (6): 838–845.
27. Jones RL, Fisher C, Al-Muderis O, Judson IR. Differential sensitivity of liposarcoma subtypes to chemotherapy. Eur J Cancer. 2005; 41 (18): 2853–2860.
28. Pitson G, Robinson P, Wilke D, et al. Radiation response: an additional unique signature of myxoid liposarcoma. Int J Radiat Oncol Biol Phys. 2004; 60 (2): 522–526.
29. Stitzenberg KB, Chang Y, Smith AB, Nielsen ME. Exploring the burden of inpatient readmissions after major cancer surgery. J Clin Oncol. 2015; 33 (5): 455–464.
30. DeLaney TF, Chen YL, Baldini EH, et al. Phase 1 trial of preoperative image guided intensity modulated proton radiation therapy with simultaneously integrated boost to the high risk margin for retroperitoneal sarcomas. Adv Radiat Oncol 2017; 2 (1): 85–93.
31. Alektiar KM, Hu K, Anderson L, Brennan MF, Harrison LB. High-dose-rate intraoperative radiation therapy (HDR-IORT) for retroperitoneal sarcomas. Int J Radiat Oncol Biol Phys 2000; 47 (1): 157–163.
32. Yoon SS, Chen YL, Kirsch DG, et al. Proton-beam, intensity-modulated, and/or intraoperative electron radiation therapy combined with aggressive anterior surgical resection for retroperitoneal sarcomas. Ann Surg Oncol. 2010; 17 (6): 1515–1529.
33. Roeder F, Morillo V, Saleh-Ebrahimi L, Calvo FA, Poortmans P, Ferrer Albiach C. Intraoperative radiation therapy (IORT) for soft tissue sarcoma - ESTRO IORT Task Force/ACROP recommendations. Radiother Oncol J Euro Soc Therap Radiol Oncol 2020; 150: 293–302.
34. Blay JY, Soibinet P, Penel N, et al. Improved survival using specialized multidisciplinary board in sarcoma patients. Ann Oncol 2017; 28 (11): 2852–2859.

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