Radiation Therapy for Angiosarcoma
The 35-year University of Florida Experience

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Background and Purpose: We sought to identify prognostic factors and successful therapeutic approaches when treating angiosarcoma with radiotherapy.

Materials and Methods: From 1974 to 2009, 41 patients with angiosarcoma were treated with radiotherapy. The median patient age was 67 years. Sixteen angiosarcomas were radiation induced. Tumor sites included the head and the neck in 22 patients, breast in 14, and other sites in five. Thirty-one patients were treated with both surgery and radiotherapy (12 preoperatively and 19 postoperatively) and 10 patients were treated with radiotherapy alone. The median radiotherapy dose was 60 Gy (range, 37.5 to 76 Gy).

Results: The 5-year local control and overall survival rates were 64% and 54%, respectively. Median follow-up was 3.7 years. Of the 23 patients who relapsed, 15 had a local failure. Predictors of 5-year local control were nonscalp primary location, tumor size of $\leq$5 cm, radiation-induced tumors, and combined-modality local therapy. Predictors of 5-year overall survival were nonscalp location and a tumor size of $\leq$5 cm. The patients with the best outcomes were treated with surgery and radiotherapy 3 times daily for angiosarcoma that developed after breast-conserving therapy.

Conclusions: For angiosarcomas treated with radiotherapy, outcome varies widely and is impacted by tumor site, size, and resectability. In amenable sites, aggressive treatment with resection and hyperfractionated radiotherapy may offer the best prognosis.

Key Words: outcomes, radiotherapy, surgery, angiosarcoma

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Angiosarcoma is a rare malignant tumor of endovascular origin that comprises less than 2% of all soft tissue sarcomas.[1–9] Patients often present with an enlarging, painless, cutaneous red to purple color lesion (Fig. 1).[2,3,7,10–14] Common locations include the head and the neck, the extremities, and the breast.[2,5,6,8,10,15,16] De novo angiosarcoma typically occurs in older men,[2,7,8,10,11,13,15,17] whereas secondary angiosarcoma is seen in patients with a history of prior irradiation[15] or chronic lymphedema.[2,5,6,10,11,13,17,18] Regardless of origin, the histology of these tumors is usually intermediate to high grade, and the prognosis is poor.[2–6,11,13,17] The tumors are frequently multifocal and often spread transdermally to a greater extent than detectable on clinical examination.[4,8,11–13,15,19] For this reason, angiosarcomas tend to recur locally and metastasize early,[2–4,10,13,17,18] most frequently to the lungs and the liver.[3,5–8,10,11,16] Standard treatment has historically been wide-margin surgical resection alone,[2,8,13,17] although recognized poor outcomes and recent advances in radiation therapy have promoted more aggressive combined-modality treatment with surgery and radiation.

Most studies addressing the treatment of angiosarcoma have been limited by small patient populations and a therapeutic focus on surgery alone. Only the most recent series of angiosarcomas have explored the value of combined-modality local therapy with both surgery and radiation.[2,12,13,19] Studies reporting outcomes after definitive radiotherapy for unresectable tumors are even rarer. Furthermore, few studies[8,11,18] have addressed the potential biological differences and treatment outcomes of de novo versus radiation-induced angiosarcomas.

In this retrospective review, we update our experience treating patients with radiation therapy for angiosarcoma. The purpose of this study was to identify potential prognostic factors and to determine the optimal therapeutic approach.

MATERIALS AND METHODS

Patient and Tumor Characteristics

Patient information was retrospectively collected and evaluated for research purposes under the direction of a protocol approved by the University of Florida Institutional Review Board. Forty-six patients with histologically proven angiosarcoma treated with radiotherapy at the University of Florida between 1974 and 2009 were identified. Five patients treated with palliative intent were excluded from further analysis. The median patient age was 67 years (range, 21 to 87 y). Patient and tumor characteristics are summarized in Table 1. All but 1 scalp angiosarcoma were of cutaneous origin. All 14 tumors of the breast were radiation-induced angiosarcomas after breast-conserving therapy.

Depending on patient presentation and treatment era, workup included chest radiograph, computed tomography, magnetic resonance imaging, and/or angiograph. Tumor size was determined based on the largest documented size from physical examination, radiological studies, or pathologic specimen when available.

All but 2 patients with radiation-induced angiosarcomas were previously treated with breast-conserving surgery and radiation. One developed a 2-cm angiosarcoma of the neck after 10 radiation treatments of unknown dose to the entire head and neck for impetigo in 1941, 64 years before developing angiosarcoma. The other patient developed a 1-cm

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TABLE 1. Patient and Tumor Characteristics

Characteristic	No. Patients (N = 41)
Sex	
Male	18
Female	23
Tumor site	
Scalp	9
Other head and neck	13
Breast	14
Extremity/other*	5
Tumor size (cm)	
≤5	29
>5	12
Tumor type	
De novo	25
Radiation-induced	16
Tumor grade	
High/intermediate	30
Low	11

*Deep shoulder, abdomen, bone, and retroperitoneum (deep soft tissues of the pelvis).

angiosarcoma of the neck 4 years after receiving a dose of 68.4 Gy to the bilateral neck and mediastinum for metastatic papillary thyroid cancer.

Treatment Characteristics

Treatment was individualized based on tumor size, site, resectability, grade, patient performance status, and prior therapy. Treatment characteristics are summarized in Table 2.

The median radiation dose for all patients was 60 Gy (range, 37.5 to 76 Gy) given at 1.8 to 2.0 Gy once a day (N = 16), 1.2 to 1.5 Gy 2 times a day (N = 7), or 1.0 Gy 3 times a day (N = 18). Eleven of the 13 patients treated to a dose of 60 Gy had radiation-induced angiosarcoma of the breast. The patient treated to only 37.5 Gy received preoperative radiotherapy before a left hip disarticulation to facilitate wide surgical margins. Ten patients with unresectable tumors were treated with radiotherapy alone. Two patients received doxorubicin-based chemotherapy. Thirteen of 16 patients with radiation-induced angiosarcoma were treated with hyperfractionated and accelerated radiotherapy (HART) of 1 Gy given 3 times a day to a total dose of 60 Gy and surgery, as previously described.[20] If feasible, the treatment was preoperative and the reirradiated tissue was subsequently resected to theoretically minimize the risk of late fibrotic skin complications. The two patients with secondary angiosarcomas of the neck mentioned above were treated to 72 Gy at 1.8 Gy per fraction once daily and to 67.2 Gy at 1.2 Gy per fraction twice daily, respectively.

TABLE 2. Treatment Characteristics

Characteristic	No. Patients (N = 41)
Treatment Modality	
Surgery + RT	31
RT alone	10
RT dose	
<60 Gy	10
≥ 60 Gy	31
RT fractionation	
QD	16
BID	7
TID	18
Margin status (n = 31)	
Marginal/biopsy	13
Wide	18

BID indicates twice daily; QD, once daily; RT, radiotherapy; TID, three times daily.

Statistics

SAS and JMP software were used for all statistical calculations (SAS Institute, Cary, NC). Estimates of freedom from selected endpoints were achieved with the Kaplan-Meier product limit method.[21] The log-rank test statistic provided evidence of statistical significance between the strata of selected prognostic factors. The event for overall survival was defined as death from any cause. The event for local control was failure at the primary site. Although confounding factors are likely to be present, a valid multivariate analysis could not be performed due to the small sample size. Complications were retrospectively graded using the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) grading system, version 4.0.[22]

RESULTS

Overall Survival

The 5-year actuarial overall survival rate was 54% (Fig. 2). The median follow-up for all patients was 3.7 years calculated from the date of diagnosis (range, 0.2 to 28.6 y). The median follow-up among survivors was 5.1 years (range, 3 to 21.6 y). A univariate analysis showed that nonscalp tumor site (Fig. 3) and tumor size ≤5 cm (Fig. 4) were associated with a statistically significant improvement in overall survival (Table 3). All but 1 of the patients with angiosarcoma of the scalp ultimately died of the disease. Of the 31 patients treated surgically in combination with radiotherapy, resection with wide surgical margins was also a statistically significant predictor of 5-year overall survival ($P = 0.0238$). Patients with radiation-induced tumor types had a trend toward an improved overall survival rate at 5 years when compared with those with de novo angiosarcoma ($P = 0.0668$).

Local Control

The 5-year actuarial local control rate was 64% (Fig. 2). A univariate analysis of local control indicated that patients with nonscalp tumors ($P = 0.0246$), tumor size ≤5 cm ($P = 0.0159$), radiation-induced tumor type ($P = 0.0033$), and

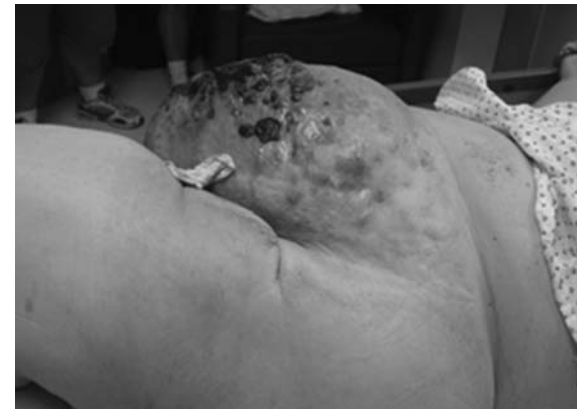

FIGURE 1. An example of cutaneous angiosarcoma of the abdomen in a patient treated at our institution.

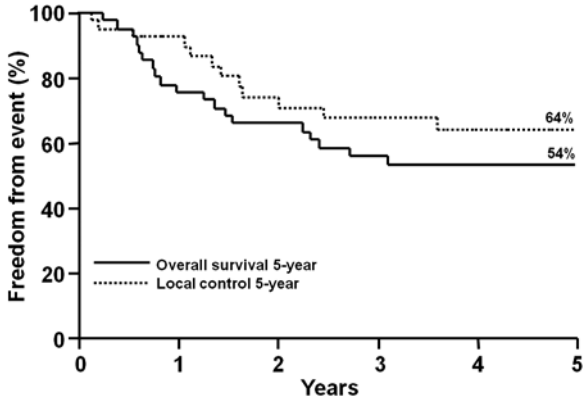

FIGURE 2. Local control and overall survival rates at 5 years after radiotherapy for 41 patients treated with curative intent.

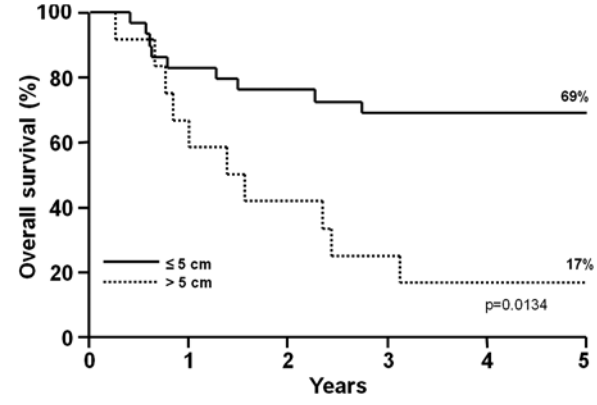

FIGURE 4. Overall survival rates by tumor size at 5 years after radiotherapy in 41 patients treated with curative intent.

combined-modality treatment with surgery and radiotherapy ($P = 0.0011$) had superior local control at 5 years (Table 3).

Tumor Site

All but 1 patient with angiosarcoma of the scalp experienced disease recurrence, including 5 patients with local recurrences (Table 4). Four of these 5 local recurrences were located within the radiation field despite aggressive high-dose radiotherapy ($\geq$ 70 Gy).

Tumor Size

All but 1 patient with a head and neck tumor >5 cm in diameter experienced a local recurrence, regardless of the treatment approach. The patient with durable local control at 5 years had a 10-cm tumor of the right maxillary region of the face with penetration into the bone and was treated to 70 Gy at 1.8 Gy per fraction once daily after subtotal right maxillectomy with wide margins.

Tumor Type

Nine of the 14 patients with radiation-induced angiosarcoma after breast-conserving therapy remain free of recurrence at a median of 5.1 years (range, 3 to 10.6 y; Table 4). Eight of these 9 patients were treated with HART and surgery. The ninth patient with local control received a total dose of 49.5 Gy at 1.5 Gy per fraction twice daily for 17 days followed by surgery with positive microscopic margins. In total, 7 of the 9 patients with local control received an R0 resection. One patient had a nodal recurrence in the contralateral axilla 18 months after preoperative HART and modified radical mastectomy with positive microscopic margins. The recurrence was successfully salvaged by means of HART to the contralateral axillary lymph nodes and axillary lymph node dissection, and the patient has remained disease free for the past 7.5 years.

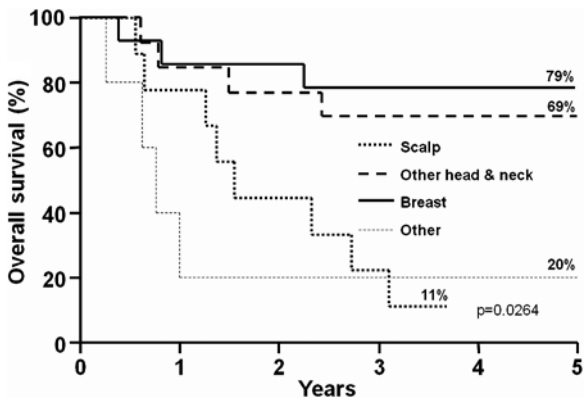

FIGURE 3. Overall survival rates by primary site at 5 years after radiotherapy in 41 patients treated with curative intent.

The patient with secondary angiosarcoma after radiotherapy to the entire head and neck 64 years earlier remained disease free for more than 9 years before passing away of intercurrent disease. The other patient with a 1-cm angiosarcoma of the neck 4 years after prior radiotherapy experienced distant recurrence to the L4 spine and died of complications 6 months after the initial diagnosis of angiosarcoma. Using our approach, no patients treated for radiation-induced angiosarcoma developed CTCAE grade 3 or worse complications despite a high cumulative life dose of radiation.

Treatment Modality

Of the 10 patients treated with radiotherapy alone, 8 experienced local progression at a median of 16 months and eventually died of their disease. One survivor had angiosarcoma of the nose treated to 50.4 Gy at 1.8 Gy per fraction once daily followed by a 20 Gy implant boost for a total dose of 70.4 Gy. The second patient with ongoing local control after treatment with radiotherapy alone had angiosarcoma of the right shoulder treated to 70 Gy at 1.8 Gy per fraction once daily. Overall, 2 of the 4 patients treated with radiotherapy alone to a dose $\geq$ 70 Gy had local control, whereas all 6 patients treated with radiotherapy alone to a dose <70 Gy experienced local progression (Table 4).

Patterns of Failure

The first site of treatment failure was isolated local recurrence in 11 patients, whereas 4 patients had local or regional recurrence in conjunction with distant metastases (Table 4). One patient had a regional recurrence alone and 7 patients had distant metastases alone. Local or regional recurrence was not routinely evaluated after the development of distant disease due to rapid patient decline.

Of the 23 recurrences, 2 patients were successfully salvaged. One was the patient with a contralateral axillary nodal recurrence whose salvage treatment was described above. The other patient experienced a distant recurrence alone and remains disease free 4 years after stereotactic body radiosurgery for lung and adrenal metastases.

TABLE 3. Univariate Analysis for Patients Treated With Curative Intent

Variable Group	No. Patients (N = 41)	5- Year Overall Survival (%)	*P*	5- Year Local Control (%)	*P*
Tumor Site			0.0264		0.0246
Scalp	9	11		18	
Other head and neck	13	69		60	
Breast	14	79		92	
Extremity, other	5	20		80	
Tumor Size			0.0134		0.0159
≤5 cm	29	69		76	
>5 cm	12	17		26	
Tumor Type			0.0668		0.0033
RT-induced	16	75		92	
De novo	25	40		44	
Tumor Grade			0.3265		0.4459
High/ intermediate	30	50		61	
Low	11	64		70	
Treatment Modality			0.7687		0.0011
Surgery + RT	31	55		78	
RT Alone	10	50		30	
RT Dose			0.1766		0.7037
<60 Gy	10	50		72	
≥ 60 Gy	31	55		63	
RT Fractionation			0.1800		0.4906
QD	16	56		60	
BID	7	29		43	
TID	18	61		74	
Margin Status (n = 31)			0.0238		0.3095
Marginal / Biopsy	13	31		59	
Wide	18	72		87	

BID indicates twice daily; QD, once daily; RT, radiotherapy; TID, three times daily.

Acute Treatment Toxicity and Complications

All 3 patients who experienced complications of CTCAE grade 3 or worse had angiosarcoma of the head and the neck. The male patient with angiosarcoma involving the floor of the mouth and right base of the tongue experienced grade 4 mucositis of the oral mucous membranes, resulting in pain that interfered with oral intake and requiring admission for fluids and hyperalimentation therapy. This acute toxicity resolved but he developed severe trismus and fibrosis in the long term. A 65-year-old woman with angiosarcoma located on the left upper eyelid received 50 Gy at 2 Gy per fraction once daily and suffered from grade 3 radiation dermatitis of the periorbital skin. A 79-year-old male patient with a large tumor on the left parietal scalp received 70 Gy at 2 Gy per fraction once daily and suffered from grade 3 tissue necrosis of the scalp area surrounding the tumor bed, which eventually resolved.

DISCUSSION

Angiosarcomas are rare, aggressive tumors of vascular origin that often present in the head and the neck, and carry a poor prognosis, particularly when located on the scalp. Five-year survival rates in the literature range from 12% to 35%.[2,11,13,17,18,23] The distinction between benign vascular proliferation and low-grade angiosarcoma may be difficult and diagnosis may be delayed until the clinical course displays an abrupt acceleration of the disease process.[2] The mainstay of the therapy has been surgery, but outcomes are poor after resection alone. For the past three decades, our institutional policy has advocated both aggressive surgery and radiation for angiosarcomas whenever feasible. The 5-year survival rate for patients treated with curative intent was 54%. In particular, we have experienced notable success in treating radiation-induced angiosarcomas after breast-conserving therapy with HART with or without surgery.[20,24] The predominant pattern of failure in our study and that of others[2,3,13,18,25] was local failure, followed by distant metastases.

Tumor Site

In our series, patients with tumors originating on the scalp had a particularly poor prognosis. Tumor site has been shown in numerous other studies to be prognostically significant. In one series,[2] patients with tumors of the extremity had the best prognosis, possibly related to an increased likelihood of complete resection. Morrison et al,[12] Pawlik et al,[13] and Sasaki et al[3] have all shown significant reduction in overall survival for patients with angiosarcoma of the scalp when compared with other tumor locations.

Tumor Type

Radiation-induced angiosarcomas can develop in various sites and have been reported to occur from 2 to 44 years after

TABLE 4. Outcomes for Patients Treated With Definitive Radiotherapy With or Without Surgery (N = 41)

Patient	Decade of Treatment	Tumor Site	Tumor Size (cm)	Tumor Type	Treatment	Total Dose (Gy)	Fractionation	Years to Disease Recurrence (Site)	Status at Last Follow-up
1	1970s	H&N (face)	2	P	RT alone	65.2	QD	0.2 (L)	DWD at 0.8 y
2	1970s	Extremity (deep shoulder)	4	P	RT alone	70	QD	N/A	DID at 28.6 y
3	1980s	Other (deep pelvis)	5	P	Post-op	47	QD	0.6 (D)	DWD at 0.6 y
4	1980s	H&N (scalp)	3	P	Post-op	66.15	BID	0.6 (R+D)	DWD at 1.3 y
5	1980s	H&N (floor of mouth)	4	P	RT alone	75.6	TID	8.6 (L), 16.5 (L)	DWD at 17.2 y
6	1980s	H&N (face)	10	P	Post-op	70	QD	N/A	ANED at 21.6 y
7	1980s	H&N (upper eyelid)	1.3	P	Pre-op	50	QD	N/A	DID at 20.0 y
8	1980s	H&N (scalp)	9	P	Post-op	76	TID	1.1 (L)	DWD at 3.1 y
9	1980s	H&N (scalp)	3.5	P	Pre-op	50	QD	0.4 (D)	DWD at 0.6 y
10	1980s	H&N	4	P	RT alone	45	QD	1.3 (L), 4.8 (D)	DWD at 6.3 y
11	1990s	H&N (scalp)	7	P	Post-op	70.2	QD	1.1 (L)	DWD at 1.37 y
12	1990s	H&N (face)	2	P	RT alone	63	QD	3.6 (L), 9.4 (L)	DWD at 10.3 y
13	1990s	H&N (scalp)	7.5	P	RT alone	70	QD	1.4 (L+D)	DWD at 1.6 y
14	1990s	H&N	2.5	P	Post-op	66	BID	10.2 (L)	DWD at 10.4 y
15	1990s	H&N (scalp)	7	P	Pre-op	60	QD	0.6 (D)	DWD at 0.7 y
16	1990s	H&N (scalp)	8	P	Post-op	60	BID	2.0 (L+D)	DWD at 2.3 y
17	1990s	H&N (neck)	2	RI	Post-op	72	QD	N/A	DID at 9.6 y
18	1990s	Breast	3.5	RI	Pre-op	50	BID	N/A	DID at 6.2 y
19	1990s	Breast	3	RI	Pre-op	60	TID	N/A	ANED at 10.6 y
20	1990s	H&N (scalp)	4	P	Post-op	72	BID	2.5 (L)	DWD at 2.7 y
21	1990s	Extremity (femur)	5.8	P	Pre-op	37.5	QD	N/A	DID at 0.8 y
22	1990s	Breast	2.4	RI	Post-op	60	TID	2.4 (R)	ANED at 9.3 y
23	2000s	Extremity (thigh)	22	P	RT alone	59	TID	0.1 (L), 0.4 (L)	DWD at 1.0 y
24	2000s	Breast	0.1	RI	Post-op	60	TID	N/A	ANED at 6.2 y
25	2000s	Breast	7	RI	Pre-op	60	TID	N/A	ANED at 5.5 y
26	2000s	H&N (nose)	0.5	P	RT alone	70.4	QD	N/A	ANED at 5.7 y
27	2000s	Breast	0.1	RI	Post-op	59	TID	N/A	ANED at 5.1 y
28	2000s	Breast	4	RI	Pre-op	60	TID	N/A	ANED at 4.7 y
29	2000s	Breast	3	RI	Post-op	60	TID	N/A	ANED at 4.3 y
30	2000s	H&N (nose)	0.5	P	Post-op	54.12	QD	N/A	ANED at 5.1 y
31	2000s	Breast	1	RI	Pre-op	60	TID	0.5 (D)	ANED at 3.9 y
32	2000s	Breast	5	RI	Post-op	60	TID	N/A	ANED at 4.0 y
33	2000s	Breast	10	RI	Pre-op	60	TID	0.8 (D)	DWD at 0.8 y
34	2000s	Breast	5	RI	Post-op	60	TID	0.1 (D)	DWD at 0.4 y
35	2000s	H&N (scalp)	1.2	P	Post-op	64	QD	N/A	ANED at 3.7 y
36	2000s	Breast	1.7	RI	Pre-op	60	TID	N/A	ANED at 3.0 y
37	2000s	Breast	0.1	RI	Post-op	75	TID	1.6 (L)	DWD at 2.3 y
38	2000s	H&N (face)	14.5	P	RT alone	69	TID	1.6 (L)	DWD at 2.4 y
39	2000s	H&N (nose)	0.5	P	RT alone	64	BID	0.5 (L)	DWD at 0.6 y
40	2000s	Other (abdomen)	23	P	Pre-op	44.5	TID	N/A	DID at 0.2 y
41	2000s	H&N (neck)	1	RI	Post-op	67.2	BID	0.9 (D)	DWD at 1.5 y

ANED indicates alive with no evidence of disease; BID, twice daily; D, distant; DID, died of intercurrent disease; DWD, died with disease; H&N, head and neck; L, local; P, primary; QD, once daily; R, regional; RI, radiation-induced; TID, three times daily.

prior irradiation.[8,14,16,26,27] These tumors most commonly present in women 5 to 10 years after irradiation of the breast as part of breast-conserving therapy.[8,14,16,26,27] However, the overall incidence of postirradiation angiosarcoma is quite low, ranging from 0.03% to 0.16%.[2,27]

This study is unique in that the radiation-induced angiosarcomas showed a trend toward better overall survival compared with de-novo tumors. Other studies contradict our findings. Abraham et al[6] observed that patients who developed angiosarcoma in radiation or lymphedema fields were far more prone to local and distant recurrence and death from the disease. Although radiotherapy was not used as treatment, Fury et al[8] also showed a modest trend toward inferior median survival in radiation-induced breast angiosarcoma treated with surgery with or without chemotherapy ($P = 0.35$). Our data suggest that treating radiation-induced angiosarcoma after breast-conserving therapy with a regimen of HART may offer a real advantage for secondary angiosarcomas of the breast. This may in fact be the key difference between our multisite overall survival outcomes and other reports in the literature.

Treatment Modality and Tumor Size

Our series highlights the importance of surgery whenever feasible, preferably with wide margins. Several studies have confirmed that resectability and the adequacy of surgical margins are important prognostic factors.[2,12,17,19,28] Mark et al[2] reported that only 9% of patients treated without surgery were rendered disease free. Maddox et al[18] suggested that lower recurrence rates in the postmastectomy group in their series was likely due to peripheral location, which increased the likelihood of uninvolved surgical resection. In our series, patients with tumors ≤ 5 cm had better rates of both local control and overall survival. Most studies have similarly shown tumor size to be important for prognosis.[2,3,13,15,18]

As mentioned above, the apparent prognostic significance of site and size may likely relate to the ability to achieve wide surgical margins.[10,19] Adequate surgical resection of the scalp is rarely possible. Owing to the extensive vascularity and lymphatic network of the scalp, angiosarcomas are frequently large by the time a diagnosis is made, and achieving wide surgical margins in these cases may be impossible. Therefore, radiation therapy is frequently indicated as an adjuvant to surgery.[13,17] Both Morrison et al[12] and Naka et al[19] have shown that patients who underwent surgery with wide margins combined with radiotherapy or chemotherapy had the best rates of survival. Although we found no significant improvement in overall survival with surgery and radiotherapy versus radiotherapy alone (55% vs. 50%; $P = 0.7687$) in this small series of patients, we continue to advocate for surgery whenever possible for scalp lesions.

Angiosarcomas are characterized by their diffuse radial spread, often clinically undetectable,[11,15] so adequate radiation margins are critical.[12,13] For example, our typical preoperative radiation treatment fields for radiation-induced breast angiosarcoma include a minimum of 8-cm to 10-cm margins around the gross tumor volume.[14] In addition, we advocate elective irradiation of regional lymph nodes for most sites, even if they are clinically uninvolved, due to an estimated 10% to 20% risk of lymph node metastasis.[7]

Radiotherapy Dose

Congruent with other reports,[3,13] we were unable to show a dose response in patients treated with a total radiation dose of ≥ 60 Gy. Mark et al[2] reported a local control rate of 25% at doses < 45 Gy versus 68% when doses exceeded 50 Gy ($P = 0.002$). As previously observed,[3] we primarily attribute this phenomenon to selection bias as our patients receiving high-dose radiation were far more likely to have de-novo, unresectable tumors located on the scalp. Analysis of our small subset of patients with unresectable tumors does provide preliminary evidence that doses >70 Gy may be associated with an improved local control when treating with radiotherapy alone.

Limitations

Although this study represents one of the largest single-institution experiences reporting outcomes after radiotherapy for angiosarcoma, it has clear limitations. It is meant to be a hypothesis-generating study. The observational nature of our findings prohibited direct causal interpretation of the results and the sample size limits the statistical validity of many desired subset analyses. In addition, an inherent selection bias is present in all retrospective studies, but with a relatively rare disease such as angiosarcoma there is little randomized data available. All of our patients had nonmetastatic disease and were treated at a single institution, but our experience spans decades during which imaging, chemotherapy, and RT methods changed significantly. In addition, our patient population included tumors of all locations, such as the head and the neck, breast, and extremities. This mixed population may result in difficulty in interpreting the prognostic factors as various tumors often display a distinct behavior and pattern of spread. The inability to perform a statistically valid multivariate analysis on this small number of patients has limited the detection of confounding factors such as site, size, or resectability that influence the outcomes, particularly for the subset of radiation-induced angiosarcomas.

Current Recommendations

In operable patients, we recommend aggressive surgical resection followed by radiotherapy. In borderline resectable cases, we advise preoperative radiation followed by resection. Our dose recommendations include 45 to 50 Gy for undissected subclinical disease, 60 to 65 Gy for a postoperative tumor bed with positive microscopic margins, and 70 to 75 Gy for gross disease. Patients irradiated for gross disease and those with radiation-induced tumors should be considered for altered fractionation. Given the favorable outcomes, we continue to offer HART to a total dose of 60 Gy when radiation is used alone or for patients with radiation-induced angiosarcoma after breast-conserving therapy.[23] We recommend 1.2 Gy given twice daily to 50.4 or 1.5 Gy given twice daily to 45 Gy when radiation is used preoperatively for nonbreast angiosarcoma. When feasible, large radiation margins (>5 to 8 cm expansion on macroscopic disease) are utilized to encompass the wide occult spread of disease. For large tumors (>5 cm) and all tumors located on the scalp, we also favor elective irradiation of regional lymph nodes due to the high risk of lymphatic progression.

CONCLUSIONS

Owing to the high risk of local recurrence, multimodality local therapy is critical to the management of most angiosarcomas. Our data illustrate that outcomes vary widely and are impacted by tumor site, size, and resectability. More research is needed to elucidate the biological differences between de-novo and radiation-induced angiosarcomas. Contrary to other studies, our data suggest that angiosarcomas secondary to prior radiation may have an improved prognosis, suggesting an inherently unique biologic response to treatment.

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