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Low Dose Radiotherapy is Associated with Local Complications but Not Disease Control in Sacral Chordoma

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Abstract

Background: We reviewed the disease control and complications of the treatment of sacrococcygeal chordoma from 4 tertiary cancer centers with emphasis on the effects of radiotherapy in surgically treated patients.

Methods: 193 patients with primary sacrococcygeal chordoma from 1990 to 2015 were reviewed. There were 124 males, with a mean age of 59±15 years and a mean follow-up of 7±4 years. 89 patients received radiotherapy with a mean total dose of 61.8±10.9 Gy.

Results: The 10-year disease-free and disease-specific survival was 58% and 72%. Radiation was not associated with local recurrence (HR 1.13, 95% CI 0.59 – 2.17, P=0.71), metastases (HR 0.93, 95% CI 0.45 – 1.91, P=0.85) or disease-specific survival (HR 0.96, 95% CI 0.46 – 2.00, P=0.91). Higher doses (> 70 Gy, HR 0.52, 95% CI 0.20–1.32, P=0.17) may be associated with

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reduced local recurrence. Radiotherapy was associated with wound complications (HR 2.76, 95% CI 1.64–4.82, $P<0.001$) and sacral stress fractures (HR 4.73, 95% CI 1.88–14.38, $P<0.001$).

Conclusion: In this multicenter review radiotherapy was not associated with tumor outcome but associated with complications. Routine use of radiotherapy with en-bloc resection of sacrococcygeal chordomas should be reconsidered in favor of a selective, individualized approach with a radiation dose of 70 Gy.

Keywords

Chordoma; surgical resection; radiotherapy; sacrum; outcome

Introduction

Surgery has been the standard treatment for sacrococcygeal chordoma, but has high complication and local recurrence rates.[1–14] Some institutions have added radiotherapy to improve local control and reduce morbidity.[15–21] Centers which advocate for the routine use of radiotherapy combined with surgery in the treatment of chordoma typically use doses ranging between 50 and 72 Gy. [15–21] The purpose of this study was to combine the prospectively collected data from four tertiary-care sarcoma centers to evaluate factors which are associated with recurrence free and disease-specific survival, and postoperative complications with a focus on the influence of the addition of radiotherapy to the treatment of patients with sacrococcygeal chordomas.

Methods

Following approval from all centers' Institutional Review Boards (IRB), we performed a retrospective chart review of patients ($n=235$) identified from our prospectively collected sarcoma databases undergoing en-bloc resection of a histologically confirmed primary sacrococcygeal chordoma from 1990–2015. Twenty-nine patients were excluded as they received an unknown ($n=8$) or low doses of radiation ($n=21$, total dose <50 Gy). Thirteen patients were excluded for having less than 2 years of follow-up. The excluded patients consisted of patients with subtherapeutic radiotherapy doses at different schedules: preoperative radiotherapy ($n=21$, mean dose 26.5 ± 10.7 Gy), pre- and postoperative radiotherapy ($n=9$, mean dose 63.3 ± 21.7 Gy), postoperative radiotherapy ($n=5$, mean dose 19 ± 6.2 Gy) or no radiotherapy ($n=7$).

The remaining patients ($n=193$) included 124 males and 69 females (Table 1) with a mean age of 59 ± 15 years at the time of surgery. The most cephalad extent of the osteotomy was used to define the level of sacral resection: most commonly at the S2 body ($n=58$, 30%) with resections at or above S2 considered high resections ($n=93$, 48%). The mean follow-up was 7 ± 4 years.

All patients were treated with an en-bloc resection with the goal of achieving negative margins. Seven patients had evidence of metastatic disease at the time of surgical resection (lung, $n=6$; liver, $n=1$) which was deemed resectable. These patients were removed from the metastatic disease recurrence outcome analysis. The resection margin was considered to be

negative (n=162, 84%) or positive (n=31, 16%). There were no planned intralesional resections.

Radiotherapy was given to 89 patients (46%) following discussion at a multidisciplinary tumor board. Radiotherapy was used commonly in combination with surgery in two of the centers (25/29 patients (86%) and 53/60 (88%)) and rarely in the two (1/56 patients (2%) and 10/48 patients (21%)) other institutions. The decision to deliver radiotherapy preoperatively was made when there was a concern for a potentially close surgical margin, or postoperatively if there was a positive or close negative surgical margin on final pathology. Radiotherapy was delivered preoperative (n=30, dose 50 Gy), postoperative (n=17, mean dose 60.2±9.9 Gy), or pre- and postoperative (n=42, mean total dose 70.9±5.7 Gy) fashion.

Patients were followed for recurrence every 3 to 4 months for the first 2 years, every 6 months for years 2 to 5, and then annually for years 5 to 10. Follow-up involved a clinical examination and MRI of the pelvis and a CT scan or plain radiograph of the chest. Patients were censored at their last follow-up. Nineteen (9.8%) have not been seen for more than 5 years. Of these patients five had reached 10-years of clinical follow-up, with an additional 9 patients reaching at least 5-years of follow-up. The additional 5 patients had between 2 and 5-years of follow-up.

Patient Group Comparison

When comparing patients who received radiotherapy and those who did not (Table 1), there was no difference in the mean age (59±16 vs. 59±14 years, $P=0.97$), proportion of males (n=59, 66% vs. n=65, 63%, $P=0.65$), mean tumor maximal dimension (9±5 vs. 9±6 cm, $P=0.29$), mean tumor volume based on the final resected specimen (660±1111 vs. 551±1075 cm³, $P=0.54$), or proportion of high sacral resections (n=44, 49% vs. n=49, 47%, $P=0.77$). More patients with a positive margin received radiotherapy (n=21, 24% vs. n=10, 10%, $P=0.01$). The radiotherapy was planned in 15 patients (6 preoperative only, 9 pre- and postoperative radiotherapy); however in 6 patients radiotherapy was given postoperative due to a positive margin. There was no difference in the proportion of patients who received planned radiotherapy and those who did not receive radiotherapy (n=15, 17% vs. n=10, 10%, $P=0.19$) with a positive margin.

Statistical Analysis

Continuous variables were compared using the unpaired Student's t-test and categorical variables were compared with the Fisher's Exact test. Survival estimates were calculated using the Kaplan-Meier method. We employed competing risks as the method of analysis in our multivariable model, where death from other diseases was considered as a competing risk to local recurrence and distant recurrence. Fine and Gray proportional hazards were used to adjust for covariates. Each radiotherapy factor (i.e. preoperative radiotherapy only, postoperative therapy only, pre- and postoperative therapy) was adjusted for all variables determined to have univariate predictive value for death due to disease, local- or distant disease free survival in a competing risk analysis accounting for patients lost due to death.

All tests were two-sided. P-values < 0.05 were considered statistically significant. Analysis was performed using R 3.4.3 (R Core Team, Vienna, Austria).

Results

Disease Free Survival

Disease recurred in 58 (31%) patients at a mean of 4±3 years postoperatively. The overall 2-, 5-, 10-, and 15-year disease free survival following surgical excision of a sacral chordoma was 88%, 71%, 58%, and 47%. Disease recurrence was defined as metastatic (n=22, 11%), local recurrence (n=20, 10%) and combined metastatic and local recurrence (n=16, 8%).

Local tumor recurrence occurred in 36 (19%) patients at a mean of 4±3 years postoperatively. The overall 2-, 5-, 10-, and 15-year local-recurrence free survival rates following surgical excision of a sacral chordoma were 93%, 80%, 74%, and 67%. There was no difference (73% vs. 74%, $P=0.85$) in the 10-year local recurrence free survival between patients who received radiotherapy and those who did not. A positive surgical margin was associated with local recurrence (HR 2.25, 95% CI 1.03–4.52, $P=0.04$). The use of preoperative (HR 1.25, 95% CI 0.49–3.21, $P=0.65$), postoperative (HR 1.82, 95% CI 0.74–4.48, $P=0.19$) or pre- and postoperative radiotherapy (HR 0.56, 95% CI 0.22–1.44, $P=0.23$) was not associated with local recurrence (Table 2). Higher total dose (70 Gy (HR 0.52, 95% CI 0.20–1.32, $P=0.17$)) or proton therapy (HR 0.55, 95% CI 0.22–1.40, $P=0.21$) may be associated with a reduction in local recurrence. When only considering patients with a positive surgical resection margin (n=31), a total radiation dose of 70 Gy (HR 0.40, 95% CI 0.16–1.00, $P=0.051$) or proton therapy (HR 0.56, 95% CI 0.22–1.43, $P=0.23$) may be associated with improved local control.

Metastasis occurred in 38 (20%) patients. The overall 2-, 5-, 10-, and 15-year metastasis-free survival was 92%, 84%, 73% and 64%. There was no difference in the 10-year (72% vs. 73%, $P=0.73$) metastasis-free survival between patients who received radiotherapy and those who did not. Tumors ≥ 9 cm in maximal dimension (HR 2.03, 95% CI 1.04–4.11, $P=0.04$) and a high sacral resection (HR 2.25, 95% CI 1.10–4.94, $P=0.02$) was associated with metastases (Table 2). The use of preoperative (HR 1.21, 95% CI 0.42–3.45, $P=0.72$), postoperative (HR 0.55, 95% CI 0.15–2.02, $P=0.37$), pre- and postoperative radiotherapy (HR 1.00, 95% CI 0.37–2.73, $P=1.0$), total dose (50 Gy (HR 0.93, 95% CI 0.45–1.91, $P=0.85$) or 70 Gy (HR 1.01 95% CI 0.37–2.77, $P=0.98$)) or the use of proton therapy (HR 1.46, 95% CI 0.62–3.45, $P=0.39$) was not associated with metastases.

Overall and Disease-Specific Survival

Over the course of the study 67 (35%) patients expired and in half of them (n=34, 51%) this was directly due to their disease or a complication of surgery. The mean time to death was 5±4 years.

The 2-, 5-, 10-, and 15-year overall survival rates following surgical excision of a sacral chordoma were 90%, 75%, 59%, and 41%. Tumor size ≥ 9 cm (HR 1.73, 95% CI 1.03–2.89, $P=0.03$) was associated with all-cause mortality (Table 3). The use of radiotherapy (HR 0.93, 95% CI 0.54–1.60, $P=0.80$) was not associated with overall survival.

The 2-, 5-, 10-, and 15-year disease specific survival rates following surgical excision of a sacral chordoma were 94%, 84%, 71%, and 61%. Local (HR 4.33, 95% CI 2.19–8.77, $P<0.001$) and distant recurrence (HR 3.25, 95% CI 1.59–6.71, $P<0.001$) and tumor size ≥ 9 cm (HR 2.04, 95% CI 1.04–4.14, $P=0.04$) was associated with death due to disease (Table 3). The total dose of radiotherapy (≥ 50 Gy (HR 0.56, 95% CI 0.21–1.50, $P=0.25$), ≥ 70 Gy (HR 0.96, 95% CI 0.46–2.00, $P=0.91$)) or proton therapy (HR 0.59, 95% CI 0.23–1.55, $P=0.28$) was not associated with death due to disease.

In patients with a local tumor recurrence and a total dose of ≥ 70 Gy was not associated with improved overall survival (HR: 0.61, 95% CI 0.28–1.31, $P=0.20$) or death due to disease (HR 0.59, 95% CI 0.23 – 1.55, $P=0.28$); in addition proton therapy was not associated with improved overall survival (HR 0.94, 95% CI 0.47–1.87) or death due to disease (HR 0.72, 95% CI 0.30–1.76, $P=0.47$).

Postoperative Complications

Following surgical resection, complications occurred in 94 (49%) patients, with 15 patients having multiple complications (Table 4). The most common complications were wound complications including dehiscence, delayed wound healing or infection ($n=61$, 32%) and sacral stress fractures ($n=23$, 12%). For patients with wound complications, 45 (23%) had operative irrigation and debridement. Of the patients with a sacral stress fracture, 2 (1%) had lumbosacral fusion for pain. In addition a radiation-associated sarcoma developed in 3 (3%) patients who received radiotherapy. All these patients received at least 70 Gy of radiation.

Larger tumors (dimension ≥ 9 cm (HR 2.44, 95% CI 1.43–4.22, $P<0.001$) and volume ≥ 500 cm³ (HR 1.74, 95% CI 1.02–3.06, $P=0.04$)) were associated with wound complications (Table 5). With regards to the use of radiotherapy, any radiotherapy (HR 2.76, 95% CI 1.64–4.82, $P<0.001$), only preoperative radiotherapy (HR 2.10, 95% CI 1.15–3.64, $P=0.01$) or pre- and postoperative radiotherapy (HR 2.28, 95% CI 1.15–3.64, $P=0.01$), a total dose (≥ 50 Gy (HR 2.76, 95% CI 1.64–4.82, $P<0.001$) or ≥ 70 Gy (HR 2.01, 95% CI 1.15–3.40, $P=0.01$)) and the use of proton therapy (HR 2.37, 95% CI 1.39–3.96, $P<0.001$) was associated with wound complications.

Tumor size ≥ 9 cm (HR 3.15, 95% CI 1.29–8.40, $P=0.01$)) was associated with the development of a stress fracture (Table 5). The use of any radiotherapy (HR 4.73, 95% CI 1.88–14.38, $P<0.001$), pre- and postoperative radiotherapy (HR 14.42, 95% CI 5.82–41.04, $P<0.001$), total dose of radiotherapy (≥ 50 Gy (HR 4.73, 95% CI 1.88–14.38, $P<0.001$) or ≥ 70 Gy (HR 12.11, 95% CI 5.00–33.78, $P<0.001$) and proton therapy (HR 5.67, 95% CI 2.44–13.61, $P<0.001$) were associated with a sacral stress fracture.

When comparing the increased rate of complications observed in the radiotherapy group, the number of patients treated with radiotherapy needed to generate one additional wound dehiscence / delayed healing compared to no radiotherapy (number needed to harm) was 3.6 patients and the number of patients needed to generate one additional stress fracture was 6.7.

Discussion

Sacrococcygeal chordomas remain a therapeutic challenge. The primary treatment for these tumors is wide surgical excision; however radiotherapy as an adjunct to surgery has been used due to the difficulty obtaining wide margins in tumors which are often large and abutting critical structures. The results of this multicenter series of patients who underwent en-bloc sacrectomy for chordoma, suggests that the addition of radiotherapy, either in pre- or post-operative setting was not associated with improved local tumor control, metastatic disease or survival. However, certain radiation therapy techniques may be associated with improved local control, especially in the setting of a positive margin. The potential protective benefits of radiation must be weighed against its increased morbidity.

Surgical treatment of sacrococcygeal chordomas had resulted in a 5-year overall-survival rate ranging from 50–97%, [2–4,9–11,22–31] and a local recurrence rate with wide margins, of 0–60%. [2,4,22,24,25,27,30,31] Due to the high rates of local recurrence following surgery alone, radiotherapy has been used in addition to surgery to assist with local tumor control. [15–20] In the setting of a negative margin, and the addition of pre- and postoperative radiotherapy, Delaney et al. [17] noted a local control rate of 100% in 7 patients at 5- and 8-years postoperatively. When reviewing all chordomas treated at the same institution, the rate of local control at 5-years with radiotherapy and surgical excision combined was 72%, [20] which is similar to the 5-year local control rate of 80% for all patients in the current series. The results of the current study indicate in the setting of a positive surgical margin, a total radiotherapy dose 70 Gy and use of protons may be associated with improved local control. As such in cases where the surgical margin maybe unreliably close, or in the setting of a planned-positive margin along a critical structure, [32,33] the addition of radiotherapy to a total dose 70 Gy and protons should be considered.

The minimum total radiotherapy dose which effectively improves local control following sacrectomy for chordoma remains unknown. In the current series, the typical doses of radiotherapy were either a preoperative total dose of 50 Gy or a pre- and postoperative dose totaling 70.2 Gy. In a series by Catton et al. [18] the authors noted no survival benefit between patients who received greater or less than 50 Gy of radiation, however indicated that response needed to influence survival may require doses greater than 60 Gy. This is further seen in data from skull base chordoma which suggests doses 64 Gy are inadequate. [34] The results from the current series indicate a dose 70 Gy is likely needed to impact outcome of sacrococcygeal chordoma.

Recently radiotherapy treatment using only photons has shifted towards the use of combined photon/proton or proton alone therapy delivered in a pre- and postoperative setting. [15,17,19,20] Although the results from these series are promising, the results of the current study show that there was no association in local control based on pre- or postoperative radiation treatment at a mean dose of 61.8 Gy, but could be related to insufficient numbers in the subset of patients with high dose proton beam therapy. That being said, the smaller population of patients who received high doses (70 Gy) typically with both pre- and postoperative treatment and proton beam therapy have lower hazard ratios and smaller

confidence interval ranges, suggesting the need for very aggressive treatment to potentially impact local control. Review of a larger population of patients with this approach is warranted given the high recurrence rate.

Although radiotherapy was not associated with local control and survival in the current series, radiotherapy, either in the form of combined photon/proton or carbon ion, still plays a role in unresected chordomas. [15,21,35] Typically patients referred for primary radiation are considered unresectable due to medical comorbidities, tumor location and size, age, or may refuse surgery due to concerns related to morbidity of surgery. Recent data suggests that definitive high dose radiotherapy of 77.4 Gy can achieve local control rates of 85% at 5-years of follow-up.[15] There remains substantial risk of complications following definitive high dose radiation, including late tumor progression, radiation associated sarcoma, late neurological toxicity and sacral stress fractures.[15,36,37]

At the given sample size of 193 patients with a relatively even distribution between radiotherapy (46%) and no radiotherapy (54%), no analyzed radiotherapy factor was associated with local recurrence, distant recurrence, and overall survival, whether performed in univariate or multivariable analysis. The data suggest that certain radiation techniques (pre- and postoperative radiation with protons) and doses ≥ 70 Gy may reduce local recurrence. Since these techniques were routinely used in only 1 of the 4 centers contributing patient data, the power to detect a significant decrease in local recurrence could be insufficient. While it is possible that an association of radiotherapy on oncologic outcomes, especially local recurrence, might be seen with a larger sample size, and more patients treated with protons and/or doses ≥ 70 Gy, it is noteworthy that radiotherapy was associated with increased morbidity compared to patients treated without radiotherapy.

Preoperative radiotherapy and tumor size have been shown in several studies to be associated with postoperative wound complications in patients with soft tissue sarcoma.[38–45] The results of this study show that radiotherapy has a similar association on patients undergoing surgical treatment for sacrococcygeal chordoma. Likewise sacral stress fractures have been associated with radiotherapy, especially for patients with high sacral resections. [36] In order to potentially reduce stress fractures, sacropelvic fixation should be considered for patients with high sacral resections, especially if the osteotomy is above the level of the S1 neural foramen.[46] In order to reduce the risk of postoperative infection and wound complications, we recommend the use of a vertical rectus abdominus (VRAM) flap to reconstruct the posterior soft-tissue defect in the pelvic floor.[47–49]

There are several limitations to this study. The retrospective nature of the study limits the data we were able to collect and contains constraints on the analysis presented. Since this study was performed at multiple institutions, there was no standardized treatment paradigm. We are unable to comment on the outcome of patients who were surgical candidates, however elected for non-operative treatment. The use of radiotherapy was not standardized according to the field design, pre- or postoperative, external beam technique (protons versus photons) and dose; with many patients being treated with doses of radiation < 70 Gy. Just as en-bloc resection is considered the appropriate surgical approach, it is important to use radiation techniques and effective doses.[15,17,19,20]

Conclusion

The routine use of radiotherapy either in a pre-, post- or combined pre- and postoperative setting was not associated with improved rates of local recurrence, metastatic disease or disease-specific survival following surgical resection of sacrococcygeal chordoma. Radiotherapy was associated with morbidity. As a result, we would recommend the use of radiotherapy for sacrococcygeal chordomas only in selected patients such as those with unresectable tumors or when the treating surgeon feels the margin of resection will be unreliably close or planned positive to allow preservation of an adjacent critical structure, because there remains a high risk of local failure. In such situations efforts that allow for radiation dose escalation in addition to the use of protons may be preferred to maximize local tumor control.

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Synopsis:

In this multicenter review, the addition of radiotherapy at a mean dose of 61.8 Gy to en-bloc sacral resection was not associated with improved tumor outcome but resulted in higher complication rates. Routine use of radiotherapy with en-bloc resection of sacrococcygeal chordomas should be reconsidered in favor of a selective, individualized approach with a radiation dose of 70 Gy and use of protons.

Table 1:

Patients Undergoing Sacrectomy for Chordoma

Demographic	All Patients (n=193)	No Radiotherapy (n=104, 54%)	Radiotherapy (n=89, 46%)	P Value
Males	124 (64%)	65 (63%)	59 (66%)	0.65
Females	69 (46%)	39 (37%)	30 (34%)	
Mean Age (SD)	59 (15) Years	59 (14) Years	59 (16) Years	0.97
High Sacral Resection	93 (48%)	49 (47%)	44 (49%)	0.77
Mean Tumor Volume (SD)	597 (1088) cm ³	551 (1075) cm ³	660 (1111) cm ³	0.54
Maximal Tumor Dimension (SD)	9 (6) cm	9 (6) cm	9 (5) cm	0.29
Positive Margin	31 (16%)	10 (10%)	21 (24%)	0.01

Table 2:

Univariate and Multivariate Analysis of Factors for Local- and Metastatic Free Survival Following Surgical Excision of a Sacral Chordoma (Hazard Ratios and 95% CI)

Patient and Tumor Factors	Local Disease Free Survival	P Value	Metastatic Disease Free Survival	P Value
Local Tumor Recurrence	-	-	2.67 (1.31–5.25)	0.008
Metastatic Disease	-	-	-	-
Positive Surgical Margin	2.25 (1.03–4.52)	0.04	1.08 (0.40–2.43)	0.85
Males	0.75 (0.39–1.48)	0.40	1.20 (0.61–2.51)	0.59
Age 55 Years	0.82 (0.39–1.61)	0.58	1.82 (0.93–3.58)	0.07
Tumor Dimension 9 cm	1.38 (0.69–2.71)	0.35	2.03 (1.01–4.11)	0.04
Tumor Volume 500 cm ³	0.84 (0.35–1.81)	0.67	1.03 (0.42–2.26)	0.93
High Sacral Resection	1.34 (0.68–2.71)	0.38	2.25 (1.10–4.94)	0.02
Univariate Radiotherapy Factors	Local Disease Free Survival	P Value	Metastatic Disease Free Survival	P Value
Any Radiotherapy	1.05 (0.54–2.04)	0.85	1.11 (0.56–2.18)	0.73
Only Preoperative Radiotherapy	1.00 (0.33–2.43)	0.98	1.59 (0.52–3.97)	0.37
Only Postoperative Radiotherapy	1.55 (0.57–3.56)	0.35	0.73 (0.17–2.10)	0.59
Pre- and Postoperative Radiotherapy	0.55 (0.18–1.30)	0.19	1.18 (0.50–2.49)	0.68
Total Dose 50 Gy	1.06 (0.54–2.04)	0.85	1.12 (0.56–2.18)	0.73
Total Dose 70 Gy	0.49 (0.16–1.16)	0.11	1.15 (0.51–2.37)	0.71
Proton Therapy	0.56 (0.19–1.33)	0.20	1.24 (0.52–2.63)	0.59
Multivariate Radiotherapy Factor	Local Disease Free Survival	P-value	Metastatic Disease Free Survival[†]	P-value
Any Radiotherapy	1.13 (0.59–2.17)	0.71	0.93 (0.45–1.91)	0.85
Only Preoperative Radiotherapy	1.25 (0.49–3.21)	0.65	1.21 (0.42–3.45)	0.72
Only Postoperative Radiotherapy	1.82 (0.74–4.48)	0.19	0.55 (0.15–2.02)	0.37
Pre- and Postoperative Radiotherapy	0.56 (0.22–1.44)	0.23	1.00 (0.37–2.73)	1.00
Total Dose 50 Gy	1.13 (0.59–2.17)	0.71	0.93 (0.45–1.91)	0.85
Total Dose 70 Gy	0.52 (0.20–1.32)	0.17	1.01 (0.37–2.77)	0.98
Proton Therapy	0.55 (0.22–1.40)	0.21	1.46 (0.62–3.45)	0.39

* Bold indicates statistical significance

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Adjusted for local tumor recurrence, tumor dimension 9 cm, and presence of high sacral resection

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Univariate and Multivariate Analysis of Factors for Overall- and Disease Specific Survival Following Surgical Excision of a Sacral Chordoma (Hazard Ratios and 95% CI)

Table 3:

Patient and Tumor Factors	Overall Survival	P Value	Disease Specific Survival	P Value
Local Tumor Recurrence	1.55 (0.38–1.11)	0.11	4.33 (2.19–8.77)	<0.001
Metastatic Disease	1.21 (0.67–2.09)	0.49	3.25 (1.59–6.71)	<0.001
Positive Surgical Margin	1.19 (0.60–2.15)	0.58	0.97 (0.33–2.32)	0.96
Males	1.36 (0.82–2.31)	0.23	1.44 (0.71–3.10)	0.31
Age 55 Years	0.74 (0.43–1.23)	0.25	1.13 (0.55–2.19)	0.75
Tumor Dimension 9 cm	1.73 (1.03–2.89)	0.03	2.04 (1.01–4.14)	0.04
Tumor Volume 500 cm ³	1.49 (0.84–2.59)	0.16	1.59 (0.70–3.45)	0.25
High Sacral Resection	1.48 (0.87–2.57)	0.14	2.00 (0.22–1.03)	0.06
Univariate Radiotherapy Factors	Overall Survival	P Value	Disease Specific Survival	P Value
Any Radiotherapy	1.07 (0.65–1.74)	0.76	1.09 (0.53–2.18)	0.79
Only Preoperative Radiotherapy	1.49 (0.71–2.82)	0.26	2.32 (0.91–5.15)	0.07
Only Postoperative Radiotherapy	0.98 (0.43–1.94)	0.96	0.94 (0.22–2.66)	0.92
Pre- and Postoperative Radiotherapy	0.80 (0.39–1.48)	0.49	0.41 (0.09–1.18)	0.11
Total Dose 50 Gy	1.07 (0.65–1.74)	0.76	1.09 (0.53–2.18)	0.79
Total Dose 70 Gy	0.75 (0.38–1.37)	0.36	0.40 (0.09–1.16)	0.10
Proton Therapy	0.96 (0.48–1.76)	0.91	0.59 (0.17–1.53)	0.30
Multivariate Radiotherapy Factor	Overall Survival [/]	P-value	Disease Specific Survival [/]	P-value
Any Radiotherapy	0.93 (0.54 – 1.60)	0.80	0.96 (0.46 – 2.00)	0.91
Only Preoperative Radiotherapy	1.43 (0.74 – 2.76)	0.29	1.72 (0.65 – 4.56)	0.28
Only Postoperative Radiotherapy	0.88 (0.34 – 2.24)	0.78	0.74 (0.16–3.40)	0.70
Pre- and Postoperative Radiotherapy	0.68 (0.33 – 1.40)	0.30	0.56 (0.21 – 1.50)	0.25
Total Dose 50 Gy	0.93 (0.54 – 1.60)	0.80	0.96 (0.46 – 2.00)	0.91
Total Dose 70 Gy	0.61 (0.28 – 1.31)	0.20	0.59 (0.23 – 1.55)	0.28

* Bold indicates statistical significance

[/] Adjusted for local tumor recurrence, metastatic disease, and tumor dimension 9 cm

Postoperative Complications Following Surgical Excision of a Sacral Chordoma (Odds Ratios and 95% CI)

Table 4:

Complication	Radiotherapy (n=89)	No Radiotherapy (n=104)	Odds Ratio (95% CI)	P Value
Wound Dehiscence/Delayed Healing	35 (39%)	11 (11%)	5.47 (2.57–11.66)	<0.001
Sacral Stress Fracture	18 (20%)	5 (5%)	5.02 (1.78–14.15)	<0.001
Wound Infection	8 (9%)	7 (7%)	1.36 (0.47–3.93)	0.59
Hernia	3 (3%)	1 (1%)	3.59 (0.36–35.17)	0.33
Small Bowel Obstruction	3 (3%)	0 (0%)	N/A	0.09
Radiation Associated Sarcoma	3 (3%)	0 (0%)	N/A	0.09
DVT	2 (2%)	5 (5%)	0.45 (0.08–2.40)	0.45
Hematoma	2 (2%)	0 (0%)	N/A	0.21
Enteric Fistula	1 (1%)	2 (2%)	0.57 (0.05–6.50)	1.0
Seroma	1 (1%)	1 (1%)	1.17 (0.07–18.98)	1.0
Optic Nerve Ischemia	0 (0%)	1 (1%)	N/A	1.0

Factors (Hazard Ratios and 95% CI) Associated with Wound Complications and Sacral Stress Fractures Following Surgical Excision of a Sacral Chordoma

Table 5:

Patient and Tumor Factors	Wound Complication	P Value	Stress Fracture	P Value
Males	1.02 (0.61–1.74)	0.93	1.39 (0.59–3.64)	0.45
Age 55 Years	1.07 (0.63–1.77)	0.79	0.53 (0.19–1.28)	0.16
Tumor Dimension 9 cm	2.44 (1.43–4.22)	<0.001	3.15 (1.29–8.40)	0.01
Tumor Volume 500 cm ³	1.62 (0.90–2.84)	0.10	2.48 (0.96–6.40)	0.06
High Sacral Resection	1.74 (1.02–3.06)	0.04	1.28 (0.55–3.12)	0.55
Radiotherapy Factors				
Any Radiotherapy	2.76 (1.64–4.82)	<0.001	4.73 (1.88–14.38)	<0.001
Only Preoperative Radiotherapy	2.10 (1.15–3.64)	0.01	0.27 (0.01–1.29)	0.11
Only Postoperative Radiotherapy	0.72 (0.22–1.77)	0.52	-	-
Pre- and Postoperative Radiotherapy	2.28 (1.32–3.83)	0.003	14.42 (5.82–41.04)	<0.001
Total Dose 50 Gy	2.76 (1.64–4.82)	<0.001	4.73 (1.88–14.38)	<0.001
Total Dose 70 Gy	2.01 (1.15–3.40)	0.01	12.11 (5.00–33.78)	<0.001
Proton Therapy	2.37 (1.39–3.96)	<0.001	5.67 (2.44–13.61)	<0.001