Original Article

Clinical presentation, management and outcomes of sacral metastases: a multicenter, retrospective cohort study

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Background: Sacral metastases are rare and literature regarding their management is sparse. This multicenter, prospective, observational study aimed to determine health related-quality of life (HRQOL) and pain in patients treated for sacral metastases with surgery and/or radiation therapy (RT). The secondary objectives were to describe the adverse event (AE) profile and change in neurologic function in this population.

Methods: Twenty-three patients presenting with symptomatic sacral metastases were identified from the Epidemiology, Process and Outcomes of Spine Oncology (EPOSO) dataset, a prospective multicenter study on spinal metastases. Patients requiring surgery and/or RT between August 2013 and February 2017 were prospectively enrolled. HRQOL, assessed by the Spine Oncology Study Group Outcomes Questionnaire (SOSGOQv2.0), the Short Form-36 version 2 (SF-36v2), and the EuroQol-5Dimension (EQ-5D) was documented at baseline, 6 weeks, 3 and 6 months post-treatment. Pain numeric rating scale (NRS), AEs, lower extremities motor score (ASIA), and bowel and bladder function were also recorded.

Results: Eight patients underwent surgery ± RT and 15 patients underwent RT alone. Mean age was 59.3 (SD 11.7) years and 13 patients were female. At 6 months, 3 (37.5%) surgical patients and 2 (13.3%) RT patients were deceased. There was a trend showing that surgical patients had worse baseline HRQOL and pain. Pain NRS, EQ-5D, SOSGOQv2.0, and the mental component of the SF-36v2 showed improvement, irrespective of treatment (P>0.05). Ten AEs occurred in the surgical cohort, dominated by wound complications (n=3). Bowel and bladder function improved at 6 weeks in both groups.

Conclusions: Surgical treatment and RT are both valid treatment options for symptomatic sacral metastases. Improvement in HRQOL can be expected with an acceptable AE rate.

Keywords: Sacral metastases; surgery; radiation therapy (RT); health related-quality-of-life (HRQOL); adverse events (AEs)

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Introduction

Symptomatic spinal metastases occur in approximately 10–20% of the cancer population with the minority occurring in the sacrum (1,2). Preservation of neurological and physical function as well as addressing mechanical instability is primary objectives in the treatment of spinal metastases. For sacral metastases, a paucity of literature, unfamiliarity to most surgeons, and a historically high rate of adverse events (AEs) have led surgeons to shy away from operating on this population (3).

With the evolution of better surgical implants, less invasive procedures, intraoperative navigation, better blood salvage options and novel methods of radiation therapy (RT), the spinal surgeon is better equipped to effectively treat these patients. The impact of surgery and/or RT for sacral metastases on health related-quality of life (HRQOL) remains largely unknown. The primary objective of this study is to determine HRQOL and pain for patients with sacral metastases treated with surgery and/or RT. Secondary objectives were to describe the AE profile following RT or surgery and to observe how treatment affects neurologic function (lower extremity motor score, bowel and bladder function) in this population.

Methods

Design

Data were obtained from the Epidemiology, Process and Outcomes of Spine Oncology (EPOSO) [ClinicalTrials.gov (NCT01825161)], a prospective multicenter observational study on Spinal Metastases. This study was developed and funded by the AOSpine Knowledge Forum Tumor (AOSKFT) and by an Orthopedic Research and Education Foundation grant. Patients were recruited across 10 participating centers (North America and Europe) selected for their experience in handling patients with metastatic spine tumors. Patient enrollment began in August 2013 and ended in February 2017. Research ethics board approval was obtained at each center. Patients between 18 and 75 years old, treated for sacral metastases (S1 to S5) with surgery and/or radiotherapy were included. Patients were excluded if the primary site of cancer was the central nervous system or spine.

Demographic data, initial Spine Instability Neoplastic Score (SINS), information regarding the oncologic status and treatment data were collected at baseline.

For this study, patients included had at least 12 weeks follow up data completed with data collected at 6 weeks, 3 months and 6 months. A patient was lost to follow-up if he/she did not come for the scheduled study visit. Prior to declared lost to follow-up, three phone calls with at least 2 days in between each call were executed by the study personnel.

Outcomes measures

The baseline status of all patients was assessed using a variety of HRQOL outcome measures including the Spine Oncology Study Group Outcomes Questionnaire (SOSGOQv2.0), the Short Form-36 version 2 (SF-36v2) and the EuroQol-5Dimension (EQ-5D). SOSGOQv2.0 was developed specifically for the metastatic spine population (4). It encompasses 6 domains: physical function, neural function, pain, mental health, social function and post therapy questions. SOSGOQ scores were calculated according to the revised scoring system of the SOSGOQ2.0. A higher score corresponds with a higher level of functioning for the physical function and social function and a lower level of neurological symptoms, pain and symptoms for the mental health domain. The SF-36v2 and EQ-5D are generic measures of patient health status (5,6).

In addition, AEs were followed prospectively using a predefined list of common AEs. Neurologic examination with the ASIA (American Spinal Injury Association) motor score and bowel and bladder function were recorded at baseline and at follow up. Pain was assessed with the numeric rating scale (NRS) (7).

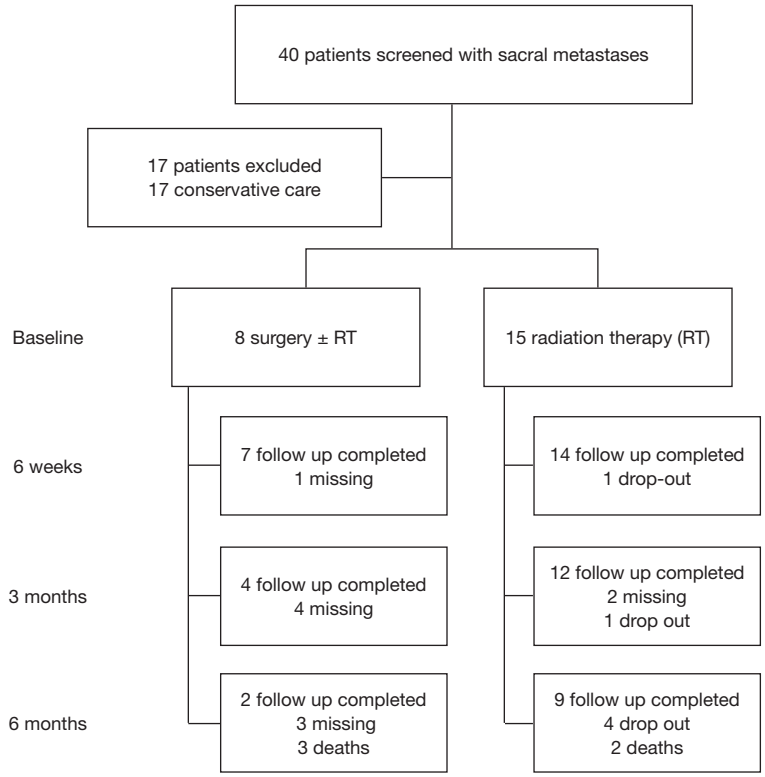

Figure 1 Patient eligibility/screening, treatment, and follow-up.

Statistical analysis

Standard descriptive statistics were used to represent demographic data. Differences in baseline parameters were tested by using Fisher's exact test for categorical variables and *t*-test or Wilcoxon rank sum test for continuous variables. A mixed effect model was used to test for differences in patient reported outcome compared to baseline and between both treatments. P values were adjusted due to multiple testing by Tukey-Kramer. AE data was analyzed per patient and per AE time by using AEs which occurred up to 6 months after treatment. Confidence intervals for AE percentage were calculated using the exact binomial method.

All statistical analyses were performed using SAS (version 9.4, SAS Institute Inc., Cary, NC, USA). Significance was defined as $P<0.05$.

Results

Study population

A total of 40 patients with sacral metastases were screened for inclusion, of which 23 satisfied study inclusion and exclusion criteria (*Figure 1*). Eight patients underwent surgery ± RT and 15 patients underwent RT alone. At 6 months follow up, 3 (37.5%) surgical patients and 2 (13.3%) RT patients were deceased. *Table 1* gives a comparative breakdown of the demographic and tumor characteristics of the population.

Surgery ± RT

All patients underwent a single posterior procedure. *Table 2* summarizes surgical details. Four patients had tumor in S1 extending lower in the sacrum (S2–S5), two had tumor confined to S1 only, and two patients had tumor located from S2–S5. Preoperative embolization was performed in three patients. One patient required a flap for closure. Two patients had postoperative adjuvant therapy and three had surgery after prior history of radiotherapy (more than 2 months before). Adjuvant RT was given at two months postoperatively (one received conventional RT and the other, SBRT). No patients died during the surgical admission.

Table 1 Cohorts characteristic

Characteristic	Treatment group for sacral metastases			P value
	Surgery (+/– radiotherapy), N=8	Radiotherapy, N=15	Total, N=23	
Female (%)	2 (25.0)	11 (73.3)	13 (56.5)	0.039‡
Age, mean (SD)	53.4 (15.6)	62.4 (8.0)	59.3 (11.7)	0.160¶
Site of the primary cancer, n (%)	8	15	23	0.071‡
Breast	1 (12.5)	6 (40.0)	7 (30.4)	
Lungs	0 (0.0)	3 (20.0)	3 (13.0)	
Prostate	1 (12.5)	4 (26.7)	5 (21.7)	
Kidney	2 (25.0)	0 (0.0)	2 (8.7)	
Myeloma	1 (12.5)	0 (0.0)	1 (4.3)	
Other	3 (37.5)	2 (13.3)	5 (21.7)	
Location of sacral metastases, n (%)*	8	15	23	
S1	6 (75.0)	7 (46.7)	13 (56.5)	
S2–S5	6 (75.0)	12 (80.0)	18 (78.3)	
Time since initial diagnosis of metastatic tumor of spine (months) (SD)	10.9 (12.4)	4.9 (12.4)	7 (12.5)	0.042§
Major treatment at baseline given for, n (%)	8	15	23	0.526‡
Exclusive sacral mets treated	8 (100.0)	12 (80.0)	20 (87.0)	
Further levels treated	0 (0.0)	3 (20.0)	3 (13.0)	
Pain type*, n (%)	8	15	23	
None	0 (0.0)	4 (26.7)	4 (17.4)	
Axial pain	7 (87.5)	10 (66.7)	17 (73.9)	
Radicular pain	7 (87.5)	7 (46.7)	14 (60.9)	
Total SINS score, mean (SD)	8.1 (2.1)	5.9 (3.6)**	6.7 (3.3)	0.134
Use of steroid, n (%)	1 (12.5)	1 (6.7)	2 (8.7)	1.000‡

*, multiple choices possible; **, n=14; ¶, *t*-test; ‡, Fisher's exact test; §, Wilcoxon rank sum test.

RT

In the RT group, 7 (46.7%) received stereotactic body radiotherapy (SBRT) and 8 (53.3%) conventional radiotherapy. For SBRT, the mean dose was 27.4 (SD 3.2) Gy with a mean number of fraction of 3.3 (range: 2–5). For patients who underwent conventional RT, the mean dose was 17.5 (SD 10.9) Gy with a mean number of fraction of 5 (range: 1–12). No heavy particle radiation was used.

HRQOL

SOSGOQv2.0

The postoperative SOSGOQv2.0 scores were better than the preoperative score at any time points for the surgical cohort. The baseline score for the RT group was higher than the surgical cohort and improved at 6 weeks and 6 months. The results of each domain at every follow up time are presented in *Table 3*.

Table 2 Surgical details

Variable	Surgical cohort (n=8)
Surgical duration, mean (SD), min	248 (151.6)
Estimated intra-operative blood loss, mean [range], mL	700 [100–7,500]
Length of stay, mean (IQR), day	11.5 (8–20.5)
Decompression performed, n (%)	Yes: 6 (75%), no: 2 (25%)
Posterior instrumentation, n (%)	Yes: 4 (50%), no: 4 (50%)
Levels instrumented, n (%)	
L3–S1	2 (50%)
L4–S1	1 (25%)
L5–S1	1 (25%)
Posterolateral vertebrectomy, n (%)	4 (50%)

Table 3 Descriptive SOSGOQv2.0 domains per sacral treatment

Treatment	SOSGOQv2.0 domains	Baseline, mean (SD)	6 weeks, mean (SD)	3 months, mean (SD)	6 months, mean (SD)
Surgery (+/– radiotherapy)	n	8	7	5	3
	Pain	31.9 (28.5)	57.1 (17.3)	44.0 (14.7)	48.3 (44.8)
	Physical function	58.0 (29.4)	47.0 (31.7)	51.6 (28.4)	44.7(41.0)
	Mental health	50.3 (19.0)	59.1 (24.8)	70.2 (22.5)	71.3 (28.9)
	Social function	60.5 (24.0)	66.6 (22.4)	65.2 (23.0)	58.3 (33.5)
	Neurological function	71.9 (18.9)	70.3 (26.1)	76.8 (20.7)	50.3 (38.8)
Radiotherapy	n	14	12	12	8
	Pain	51.4 (29.4)	61.3 (18.7)	57.2 (23.5)	78.1 (11.6)
	Physical function	70.3 (30.4)	69.9 (27.6)	65.1 (28.7)	80.4(15.0)
	Mental health	61.7 (28.2)	68.9 (29.4)	64.9 (24.8)	80.0(18.8)
	Social function	79.2 (24.9)	75.7 (17.6)	69.4 (23.2)	95.9 (6.3)
	Neurological function	83.7 (19.5)	82.7 (14.0)	76.2 (20.1)	87.6(14.0)
All patients	n	22	19	17	11
	Pain	44.3 (30.0)	59.7 (17.8)	53.1 (21.6)	70.0 (26.3)
	Physical function	65.8 (30.0)	61.5 (30.5)	61.1 (28.4)	70.6(28.0)
	Mental health	57.5 (25.4)	65.3 (27.5)	66.6 (23.5)	77.6 (20.7)
	Social function	72.4 (25.7)	72.3 (19.4)	68.2 (22.5)	85.6 (23.7)
	Neurological function	79.4 (19.7)	78.1 (19.6)	76.4 (19.6)	77.5 (27.1)

Table 4 Mixed effect models derived estimates of the differences in mean scores of efficacy endpoints (Pain NRS, EQ-5D, SF-36v2 and SOSGOQv2.0) by time measurement and treatment group

Variable	n	Surgery (+/– radiotherapy)		Radiotherapy		P value[§]
		Mean (95% CI)	Adj. P value[†]	Mean (95% CI)	Adj. P value[†]	
Pain NRS						
Baseline	23	6.4 (4.1–8.7)		4.7 (3.0–6.3)		0.223
6 weeks	19	4.4 (2.3–6.5)	0.689	3.3 (1.7–4.9)	0.776	0.409
3 months	18	5.8 (3.5–8.2)	1.000	4.8 (3.3–6.3)	1.000	0.436
6 months	12	4.3 (1.7–6.9)	0.871	2.3 (0.9–3.7)	0.309	0.158
EQ-5D (3L)						
Baseline	21	0.50 (0.28–0.72)		0.65 (0.49–0.80)		0.255
6 weeks	19	0.56 (0.42–0.70)	0.996	0.77 (0.67–0.87)	0.653	0.019
3 months	16	0.71 (0.56–0.87)	0.560	0.71 (0.60–0.81)	0.993	0.927
6 months	11	0.53 (0.30–0.77)	1.000	0.78 (0.62–0.94)	0.876	0.088
SF-36v2 PCS						
Baseline	22	30.5 (21.1–39.8)		37.2 (30.2–44.3)		0.241
6 weeks	19	32.0 (23.5–40.5)	0.995	35.4 (29.0–41.8)	0.940	0.514
3 months	16	26.4 (18.4–34.3)	0.878	35.0 (29.1–40.8)	0.962	0.086
6 months	11	25.0 (10.8–39.1)	0.983	40.4 (31.0–49.8)	0.991	0.071
SF-36v2 MCS						
Baseline	22	39.6 (32.0–47.3)		49.5 (43.8–55.3)		0.044
6 weeks	19	40.3 (32.4–48.2)	1.000	52.9 (46.9–58.9)	0.513	0.015
3 months	16	47.1 (38.7–55.5)	0.685	50.5 (45.0–56.1)	1.000	0.477
6 months	11	53.1 (44.2–62.0)	0.110	50.6 (44.9–56.2)	1.000	0.603
SOSGOQV2.0						
Baseline	22	50.4 (35.8–64.9)		65.8 (54.8–76.8)		0.094
6 weeks	19	57.3 (44.4–70.2)	0.767	69.0 (59.2–78.8)	0.970	0.146
3 months	16	56.9 (40.7–73.0)	0.967	63.4 (51.9–74.9)	0.999	0.498
6 months	11	56.1 (36.0–76.3)	0.985	76.2 (62.6–89.8)	0.274	0.097

[†], adjusted P value by Tukey-Kramer for comparison of change to baseline value per treatment group; [§], P value for comparison of mean value of both treatment groups.

SF-36v2

As expected, the baseline values for the SF-36v2 PCS for both cohorts were lower than the general population. The PCS value for the surgical cohort improved slightly initially and then decreased at longer follow-up. Conversely, the RT group scores decreased at early follow-up and improved thereafter (*Table 4*). The differences from baseline at different time points and between the 2 cohorts did not reach statistical significance either for the SF-36v2 PCS.

Worse SF-36v2 MCS score were observed at baseline for the surgical group (P=0.044). Both groups achieved values close to the normative population at 3 and 6 months with higher improvement in the surgical group (*Table 4*).

EQ-5D

For the entire cohort, the observed mean pre-treatment

EQ-5D score was 0.60 (SD 0.28). It improved post treatment gradually to 0.73 (SD 0.24) at 6 months. The surgical cohort started with worse preoperative scores compared to the RT group (P=0.255) (*Table 4*).

Pain

Pain at baseline was different between groups. Pain in the surgical cohort was experienced by 7 of the 8 patients and clearly showed a predominance of mechanical pain: 57.1% of the axial pain was mechanical alone, 28.6% was both mechanical and biological. In the RT group, in the 10/15 patients who experienced pain, axial and radicular pain was predominantly biological (70% and 71.4%).

The overall NRS pain improved from the pre-treatment level in the whole population. A worse pain score was observed at baseline in the surgical group but did not reach statistical significance. Both groups improved at 6 weeks and at 6 months although this was not statistically significant (P>0.05) (*Table 4*). In the surgical group, six patients experienced axial mechanical pain pre-operatively with a median NRS pain score of 7.5 (IQR: 5–8). The median pain improved progressively at 6 weeks, 3 and 6 months. In the RT group, 3 patients had mechanical axial pain which showed improvement over time (*Figure 2*).

Neurologic function

None of the 23 patients had complete loss of bowel and bladder function. Pre-treatment, 2 patients in the surgical group and 1 patient in the RT group experienced partial bowel and bladder loss. Two of these patients recovered normal function at 6 weeks and 1 patient in the surgical group was lost to follow up (*Table 5*). Using the SOSGOQv2.0 specific question regarding bladder and bowel function, the impact on HRQOL of the deficits appeared to be mild and stable in both cohorts.

At baseline, the mean lower extremity motor score was 48.4 (range: 29–50) for the overall cohort and was similar at 3-month follow-up (48.7). Interestingly, neurologic deficit tended to be stable over time in the RT cohort. In the surgical cohort, one patient showed neurologic improvement at 6 weeks and the other patient was lost to follow up (*Table 6*). At baseline, the neurologic function domain of the SOSGOQv2.0 was worse in the surgical group compared to the RT group: mean 71.9 (18.9) *vs.* 83.7 (19.5). The scores in both groups tended to remain nearly stable over time. The lower extremity motor function domain of the SOSGOG however remained stable at 12 weeks in the RT group and slightly improved in the surgical cohort.

AEs

A total of 10 AEs occurred in 3 patients of the surgical cohort. Wound infection (n=3) was the most common postoperative AEs. Two patients experienced thromboembolic events and 1 patient presented with a systemic infection. Only one intra-operative AE was reported (massive blood loss) (*Table 7*).

AEs related to chemotherapy and/or RT occurred 10 times in four (66.7%) patients in the surgical cohort and 24 times in 7 (46.7%) patients in the RT cohort (*Table 8*). An L5–S1 neuritis was observed in one patient following surgery combined with RT. Pain flare was reported in 2 cases following RT.

Discussion

This is the first study to assess HRQOL outcomes, a key outcome measure, in patients with symptomatic sacral metastases. Moreover, this paper represents the largest retrospective study of a prospective cohort of sacral metastases treated with either surgery and/or RT. This analysis demonstrated that these patients improved their pain and their quality of life with treatment. Using a generic (EQ-5D) tool, HRQOL increased maximally at 3 months in the surgical cohort and then declined, likely secondary to progression of systemic disease. On the other hand, early and sustained modest improvement in HRQOL was found when using a disease specific tool (SOSGOQv2.0). Improvement in HRQOL was less dramatic in the radiation cohort but is likely due to a ceiling effect as their baseline HRQOL was substantially better.

Interestingly, looking at surgery in other metastatic spinal locations, the improvement in the EQ-5D compares favourably (8). de Ruiter *et al.* reported an improvement of 0.15 at 3 months following surgical intervention for tumors predominantly located in the thoracic and lumbar spine, compared to a 0.22 improvement at 3 months in our study (9). Although the minimum clinically important difference (MCID) thresholds for EQ-5D has not been determined in the metastatic spine population, and a definition of MCID thresholds is inconsistent throughout the literature, it has been fixed at 0.1 by Wilson in patients with chronic pain (10). As pain palliation is the main surgical indication in this population, we believe that the improvement in EQ-

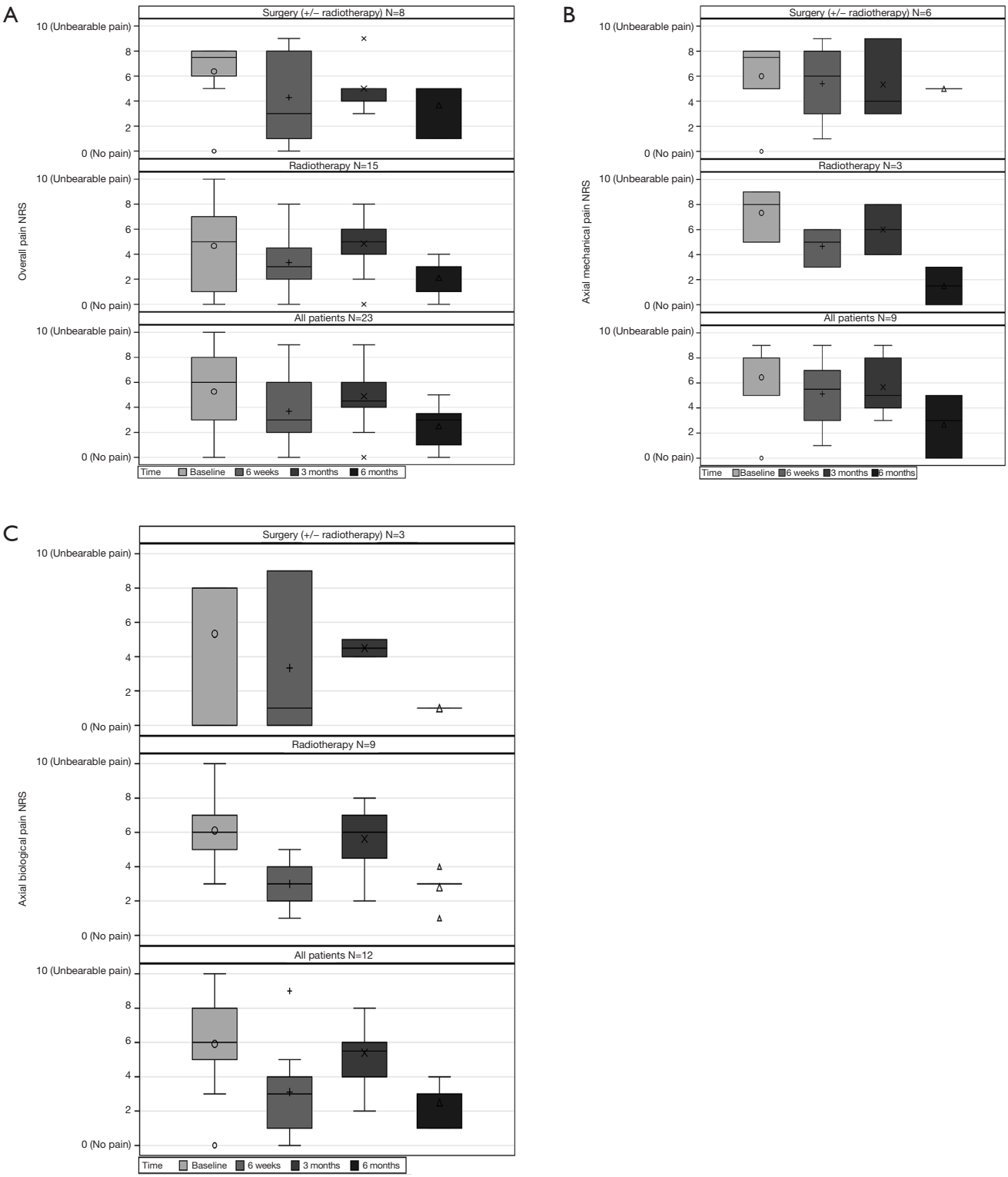

Figure 2 Box plots of descriptive data showing numeric rating scale (NRS) for (A) overall pain, (B) mechanical pain, and (C) biological pain for each treatment over 6 months. The symbol in each box represents the mean while any symbol outside the whiskers represents an outlier (more than 1.5 interquartile from the median value).

Table 5 Bowel and bladder function per sacral treatment

Treatment	Bowel and bladder function	Baseline (%)	6 weeks (%)	3 months (%)	6 months (%)
Surgery (+/– radiotherapy)	n	8	7	4	2
	Normal function	6 (75.0)	7 (100.0)	3 (75.0)	2 (100.0)
	Partial loss	2 (25.0)	0 (0)	1 (25.0)	0 (0)
	Complete	0 (0)	0 (0)	0 (0)	0 (0)
Radiotherapy	n	15	14	12	9
	Normal function	14 (93.3)	14 (100.0)	11 (91.7)	9 (100.0)
	Partial loss	1 (6.7)	0 (0)	1 (8.3)	0 (0)
	Complete	0 (0)	0 (0)	0 (0)	0 (0)
All patients	n	23	21	16	11
	Normal function	20 (87.0)	21 (100.0)	14 (87.5)	11 (100.0)
	Partial loss	3 (13.0)	0 (0)	2 (12.5)	0 (0)
	Complete	0 (0)	0 (0)	0 (0)	0 (0)

5D is clinically significant although our results should be interpreted with caution due to low numbers.

The main objective of this study was not to compare different treatment modalities for sacral metastases, but to describe this population and provide a better understanding of treatment outcomes. Nevertheless, interesting findings emerged. Surgical patients consistently had worse baseline pain and HRQOL. The nature of the pain was also different: surgical patients had a predominance of mechanical pain resulting from instability whereas radiation patients suffered from biological pain resulting from tumor invasion. Mechanical pain is related to instability and typically is exacerbated with movement and relieved with recumbency. Biological or tumoral pain is a pain that is constant and not modified by movement. Pain improved significantly in both groups. This could be explained by the instantaneous stability conferred by surgical stabilisation, which was the driving surgical indication observed in our cohort. Although it would be expected that patients with mechanical pain improved with surgery, it was interesting that patients with mechanical pain who underwent RT alone also showed improvement. This limits the generalization that mechanical pain equals surgery, but the samples size is too small to make any conclusions. As neurological compression in sacral metastases may be secondary to tumors extending into the foramen and ventrally to the sacrum, surgery may not provide an appropriate decompression and may thus be futile to restore neurologic function. Nonetheless, surgical decompression remains a valid treatment when progressive neurological deficits are seen secondary to focal spinal canal involvement.

A systematic review on the management of metastatic sacral tumors published in 2012 revealed two prospective case-series that addressed these tumors: Gerszten *et al.* (11) reported on local control rate for 103 sacral tumors treated with radiosurgery and Akasu *et al.* (3) described survival and local control for abdominal sacral resection for rectal cancer (12). The other studies included were retrospective or case reports (13-23). More recently, Feiz-Erfan *et al.* (24) retrospectively reported that patients with sacral metastases showed significant and sustained pain improvement following surgery. Similarly to Feiz-Erfan *et al.* (24), we showed that surgical treatment is associated with marginal improvement in motor score and preservation of sphincter function. Du *et al.* (25) were the first to report HRQOL for this population using the QLQ-C30, a cancer specific outcome tool. In their retrospective study of 154 patients, QLQ-C30 improvement at 3 months post-operatively was observed. However, no information regarding loss to follow up and missing data were reported, limiting generalizability. Finally, our surgical related AE rate of 37.5% compares favourably to other contemporary case-series on sacral metastases (24,25).

This study adds to the literature by showing that select patients should be considered for surgery, especially when there is a stability issue or localized neurologic compromise

Table 6 Neurologic function per sacral treatment

Treatment	Bowel and bladder function	Baseline (%)	6 weeks (%)	3 months (%)	6 months (%)
Surgery (+/– radiotherapy)	ASIA impairment scale	8	7	4	2
	A	0 (0)	0 (0)	0 (0)	0 (0)
	B	0 (0)	0 (0)	0 (0)	0 (0)
	C	0 (0)	0 (0)	0 (0)	0 (0)
	D	4 (50.0)	2 (28.6)	1 (25.0)	0 (0)
	E	4 (50.0)	5 (71.4)	3 (75.0)	2 (100.0)
	AIS lower extremity motor scale	7	6	4	2
	Mean (SD)	48.6 (2.1)	48.8 (2.4)	48 (4.0)	50 (0)
Radiotherapy	ASIA impairment scale	15	14	12	9
	A	0 (0)	0 (0)	0 (0)	0 (0)
	B	0 (0)	0 (0)	0 (0)	0 (0)
	C	0 (0)	0 (0)	0 (0)	0 (0)
	D	1 (6.7)	1 (7.1)	1 (8.3)	1 (11.1)
	E	14 (93.3)	13 (92.9)	11 (91.7)	8 (88.9)
	AIS lower extremity motor scale	15	13	10	9
	Mean (SD)	48.3 (5.4)	48.3 (6.1)	49 (3.2)	48.8 (3.7)
All patients	ASIA impairment scale	23	21	16	11
	A	0 (0)	0 (0)	0 (0)	0 (0)
	B	0 (0)	0 (0)	0 (0)	0 (0)
	C	0 (0)	0 (0)	0 (0)	0 (0)
	D	5 (21.7)	3 (14.3)	2 (12.5)	1 (9.1)
	E	18 (78.3)	18 (87.5)	14 (87.5)	10 (90.9)
	AIS lower extremity motor scale	22	19	14	11
	Mean (SD)	48.2 (4.6)	48.5 (5.1)	48.7 (3.3)	49 (3.3)

in a radio-resistant tumor. Many tools are available to overcome the inherent difficulties associated with these cases. Multidisciplinary management is paramount. Pre-operative embolization is useful in avoiding transfusions and significant blood loss (26,27). The cell saver is a promising adjunct. Recent evidence supports the use of cell saver in surgery for spinal metastases. The absence of viable tumor cells in the salvaged blood has been demonstrated (28-31). Kumar *et al.* have shown that tumor cells that passed through the cell saver device, with or without the leucocyte depletion filter, are morphologically altered and have lost the ability to form new metastatic deposits (32). A recent systematic review on the safety and efficacy of lysine analogues in cancer patients did not show an increased risk of venous thromboembolism while being effective in reducing blood loss (33). Percutaneous sacroplasty is increasingly popular with a low rate of complication (34). Alternatively, neuropathic and neoplastic pain can effectively be controlled with neuromodulation options. Finally, good local control can be achieved with SBRT (35). This was observed in our study with only one patient showing progression at 6 months.

Limitations of this study are derived from the type of population studied and the relative rarity of sacral metastases. To overcome the rarity, this study was designed to be multicenter. Still, due to the small sample size,

Table 7 Summary of operative adverse events on patient level

Event occurred*	Surgery (+/– radiotherapy), N=8	
	n	% (95% CI†)
Any intraoperative event	1	12.5 (0.3–52.7)
Massive blood loss	1	12.5 (0.3–52.7)
Any postoperative event	3	37.5 (8.5–75.5)
Dysphasia/dysphonia	1	12.5 (0.3–52.7)
Pain	1	12.5 (0.3–52.7)
Systemic infection	1	12.5 (0.3–52.7)
Thromboembolic event	2	25.0 (3.2–65.1)
Wound dehiscence	1	12.5 (0.3–52.7)
Superficial wound infection	1	12.5 (0.3–52.7)
Deep wound infection	2	25.0 (3.2–65.1)

*, adverse events were collected at 4 time points (baseline, 6 weeks, 12 weeks, and 26 weeks). All adverse events of the same term will be aggregate per patient. The same patient can contribute to more than one category; †, confidence intervals for percentages were calculated using the exact binomial method.

the ability to perform a detailed multivariate analysis was impossible. Furthermore, due to the nature of the population studied, follow up data were difficult to capture, even though a systematic approach was used. Finally, this study was performed in experienced centers, limiting generalization. However, this study is a representative sample of an underreported population. It may stimulate interest within the spinal community and lead to larger studies in the future.

Conclusions

Modern management of sacral metastases encompasses surgery and/or RT. Both alternatives appear to be reasonable therapeutic options. Based on patient symptomatology, more aggressive treatment, including surgery, may be beneficial. This cohort study described improvements in HRQOL and pain following both treatments. Furthermore, an acceptable AE rate and stabilisation of the neurologic deficits can be anticipated with either surgery and/or RT.

Table 8 Summary of radiation and chemotherapy adverse events

Event occurred*	Surgery (+/– radiotherapy), N=6		Radiotherapy, N=15	
	n	% (95% CI†)	n	% (95% CI†)
Any event	4	66.7 (22.3–95.7)	7	46.7 (21.3–73.4)
Skin	0	0.0 (0.0–45.9)	1	6.7 (0.2–31.9)
Mucous membrane	2	33.3 (4.3–77.7)	0	0.0 (0.0–21.8)
Salivary gland	1	16.7 (0.4–64.1)	0	0.0 (0.0–21.8)
Pharynx & esophagus	1	16.7 (0.4–64.1)	0	0.0 (0.0–21.8)
Larynx	1	16.7 (0.4–64.1)	0	0.0 (0.0–21.8)
Upper GI	1	16.7 (0.4–64.1)	4	26.7 (7.8–55.1)
Lower GI (including pelvis)	1	16.7 (0.4–64.1)	4	26.7 (7.8–55.1)
Hemoglobin	0	0.0 (0.0–45.9)	1	6.7 (0.2–31.9)
Other	1	16.7 (0.4–64.1)	6	40.0 (16.3–67.7)

*, adverse events were collected at 4 time points (baseline, 6 weeks, 12 weeks, and 26 weeks). All adverse events of the same term will be aggregate per patient. The same patient can contribute to more than one category. Note: n=2 patients of the surgery +/– radiotherapy group were never under the risk of any radiation or chemotherapy; †, confidence intervals for percentages were calculated using the exact binomial method.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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