



Defining preoperative imaging findings of sacral chordomas associated with decreased overall survival and local recurrence

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Sacral chordomas represent the most common primary malignant tumor found in the sacrum (1). Arising from the remnants of the notochord (2), these slow-growing tumors often present with vague symptoms, usually low back pain, in patients in the 5th and 6th decade of life (2,3). The clinical repercussions of the indolent nature of sacral chordomas are two-fold. Firstly, these tumors frequently demonstrate extra-compartmental invasion into the adjacent spine and pelvic structures at the time of diagnosis (2). Secondly, sacral chordomas are often refractory to isolated radiation and chemotherapy (4). Therefore, the gold standard treatment modality for management is complete surgical resection. Although the morbidity of wide *en bloc* surgical resection is quite high, it has been shown to yield a lower incidence of local recurrence (LR) and increase the disease-free survival rates when compared to intralesional excision (5).

In their recent paper entitled: “Predictive value of preoperative magnetic resonance imaging findings for survival and local recurrence in patients undergoing *en bloc* resection of sacral chordomas,” Zuckerman and colleagues described a retrospective case series of 41 patients who underwent *en bloc* resection of sacral chordomas. Exclusion criteria included those with less than a 1-year follow-up, mobile spine chordomas, metastatic disease at diagnosis, and non-chordoma metastasis. The objectives of their study were the following: (I) describe preoperative magnetic resonance imaging (MRI) characteristics; (II) report the patterns of both local and distant recurrence; and (III)

investigate the MRI predictors of overall survival (OS) and LR by univariate and multivariate analysis (6). All MRIs were reviewed by a fellowship-trained musculoskeletal radiologist as well as the attending neurosurgeon.

Based on prior literature, three categories were assessed for every MRI reviewed. The first was morphology, which included the volume of the lesion, the shape of the lesion (lobulated *vs.* round), and the presence or absence of a soft tissue tail. The second was distal extension to the surrounding soft tissue or spine. The third was the effect on the adjacent venous plexus (normal *vs.* congested *vs.* invaded). It was logical to correlate these three features representing aggressiveness such as lobulated growth pattern, presence of a soft tissue tail, and involvement of neurovascular structures with local recurrence even after attempted *en bloc* excision. The findings in this study demonstrated that the majority of these tumors were lobulated (93%), around half contained a soft-tissue tail (54%), and most did not extend above the sacroiliac (SI) joint (85%). Regarding prognostic factors of LR, the authors noted transverse length, craniocaudal length, soft tissue tail length, extension above L5/S1, SI joint invasion, and piriformis extension demonstrated statistical significance on univariate analysis. Involvement of the lumbosacral venous plexus was not associated with LR on univariate analysis. None of the factors were noted to be statistically significant on multivariate analysis. For prognostic indicators of decreased OS, subcutaneous fat

extension was noted to be statistically significant on both univariate and multivariate analysis (6).

There have been numerous prior studies describing prognostic factors of sacral chordomas. Known prognostic indicators associated with decreased OS include age (7,8), metastasis at the time of diagnosis (8), invasion of the surrounding muscle (9), inadequate surgical margins (10,11), lack of radiation therapy (12), increased tumor size (12), prior intralesional surgical intervention at another facility (2,10), and pre-operative motor deficit (7). Prognostic factors associated with LR include: tumor level in the sacrum (8), inadequate surgical margins (8), invasion of the surrounding muscle (13), involvement of the SI joint (13), prior intralesional surgical intervention at another facility (4), and Enneking inappropriate resection (14). Immunohistochemical markers associated with shorter continuous disease-free survival time include low expression of PHLPP1 (15), overexpression of Raf-1 (16), high expression of SPHK1 (17), negative expression of PTEN (18), positive expression of mTOR (18), positive expression of MMP-9 (19), and positive expression of survivin (20).

Many of these prior investigations have focused on post-operative factors associated with decreased OS and LR. We believe one of the key elements separating this manuscript from prior investigations is the focus on imaging characteristics to provide pre-operative indicators of prognosis for sacral chordomas. As noted in the discussion, a prior study by Kayani and colleagues investigated pre-operative MRI findings associated with LR, systemic metastasis, and decreased OS. On univariate analysis, the group found that tumor size greater than 8 cm conferred increased risk of systemic metastases and decreased survival. Additionally, the group noted SI joint invasion and muscular invasion conferred decreased OS (21).

We believe a key strength of this manuscript is the decision to perform a multivariate analysis to account for the confounding post-operative prognostic factors previously shown to be associated with LR and decreased OS (6). The variables were determined by a large, multi-institutional study which demonstrated associations between age and pre-operative motor deficit for decreased OS and previous spinal tumor operation and Enneking inappropriate resection for LR (7). The multivariate analysis emphasizes the importance of subcutaneous fat extension and its association with decreased OS. Furthermore, the significance demonstrated on multivariate analysis provides strong evidence to alter surgical technique when this

finding is noted on pre-operative MRI. We support authors' suggestion that when subcutaneous fat extension is noted on pre-operative MRI, more caution should be taken and a wider skin incision should be made to ensure an appropriate wide resection with a tumor-free margin (6).

The inability to demonstrate statistically significant prognostic indicators for LR on multivariate analysis, despite multiple variables demonstrating significance on univariate analysis, highlights one of the major limitations of this article: a small patient cohort. Sacral chordomas represent a rare tumor with an overall incidence rate of 0.03 per 100,000 (22). Collecting the required number of cases to provide the adequate power to demonstrate significance is understandably challenging. In addition to LR, the small patient cohort may have hindered the ability to demonstrate a statistically significant association between extension into subcutaneous fat and distant metastasis. As noted by the authors, extension into subcutaneous fat requires invasion through the lumbosacral fascia and may be a surrogate marker for a more aggressive pathology. Although the authors postulated this may be associated with a higher incidence of distal metastasis, the small patient cohort may have hindered the demonstration of this association.

Overall, we applaud the efforts of Zuckerman and colleagues for providing pre-operative prognostic indicators of decreased OS and LR for sacral chordomas. The major challenges in reviewing the prognostic investigations of sacral chordomas include small patient cohorts, various prognostic factors studied, and several methods of statistical analysis. Limitations stemming from the diversity of methods and conclusions in the prior literature may preclude the ability to apply the significant findings to clinical practice. Therefore, we believe further research and possibly a multi-center prospective studies with rigorous clinical and imaging data sets may provide a unifying list of pre-operative and post-operative indicators of prognosis for spinal chordomas.

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None.

Footnote

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

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