

Does pain signal malignancy? Investigating the reliability of pain symptoms in predicting chondrosarcoma

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Significance & Hypothesis: Pain commonly serves as a surrogate marker of aggressiveness in chondrosarcoma and often influences diagnostic urgency and surgical decision-making. Whether this symptom consistently reflects tumor biology across anatomic sites remains uncertain. To address this, we investigated the relationship between anatomic location and pre-operative pain presentation in chondrosarcoma. We hypothesized that pre-operative pain in chondrosarcoma varies by anatomic location, independent of tumor size and histologic grade.

Innovation: This study identifies specific “symptom-silent” anatomic sites where malignant tumors frequently present without pain. This has immediate clinical implications, highlighting a critical gap in current practice and supporting a shift toward greater reliance on imaging and objective diagnostic criteria rather than symptom-driven triage in these locations.

Approach: We performed a retrospective cohort study of patients undergoing surgical treatment for conventional or dedifferentiated chondrosarcoma between 1999-2024. Pre-operative pain presentation was evaluated across anatomic locations (long bone, pelvis, flat bone, skull, laryngeal cartilage, and vertebra). Multivariable logistic regression was used to assess the independent association between anatomic location and pre-operative pain after adjusting for histology (grades 1–3 and dedifferentiated chondrosarcoma) and tumor size (maximum dimension, cm).

Results: 193 patients with chondrosarcoma were eligible for inclusion. Pre-operative pain prevalence varied markedly by anatomic location, with high rates in long-bone (93.9%, n=82) and pelvic tumors (90.7%, n=43), but substantially lower rates in flat-bone (50.0%, n=40), skull (44.4%, n=9), and laryngeal cartilage lesions (8.3%, n=12). Tumors presenting with pre-operative pain were larger than those without pain (median 8.9 cm [IQR 5.2–12.1] vs 6.9 cm [IQR 3.7–9.0]). However, after controlling for tumor histology and tumor size, only anatomic location was independently associated with presence of pain on presentation (likelihood ratio test $\chi^2=55.44$, $p < 0.001$). Compared with long-bone tumors, flat-bone (OR 0.06, 95% CI 0.02–0.21) and laryngeal cartilage (OR 0.08, 95% CI 0.009–0.81) chondrosarcomas demonstrated dramatically lower odds of pre-operative pain. Tumor histology and tumor size were not independently associated with pain after adjustment for anatomic location (all $p > 0.25$).

Discussion & Impact: The association between pain and chondrosarcoma is strongly determined by anatomic location and does not reliably reflect tumor aggressiveness or burden in several clinically important sites. Flat bone and laryngeal cartilage chondrosarcomas frequently present without pain despite malignant potential, exposing a critical limitation of symptom-based risk stratification. These findings emphasize the need for greater reliance on imaging and objective features when evaluating chondrosarcoma in symptom-silent locations.

Table 1. Pre-operative Pain Prevalence by Anatomic Location of Chondrosarcoma

Anatomic Location	Pain Present, n (%)	Pain Absent, n (%)	Total (n)
Long bone	77 (93.9)	5 (6.1)	82
Pelvis	39 (90.7)	4 (9.3)	43
Flat bone	20 (50.0)	20 (50.0)	40
Laryngeal Cartilage	1 (8.3)	11 (91.7)	12
Skull	4 (44.4)	5 (55.6)	9
Vertebra	6 (85.7)	1 (14.3)	7

Table 2. Adjusted Association Between Anatomic Location (Long Bone as Reference) and Pre-operative Pain in Chondrosarcoma

Anatomic Location	Adjusted OR for pain	95% CI	p-value
Pelvis	12.0	3.39–42.7	<0.001
Flat bone	0.06	0.02–0.21	<0.001
Laryngeal Cartilage	0.08	0.008–0.75	0.027
Skull	0.53	0.10–2.81	0.46
Vertebra	4.62	0.47–45.2	0.19

Wald tests within a multivariable logistic regression model were used to calculate p-Values.
Significance was defined as $p < 0.05$.