Scoliosis in Costello Syndrome:
Insights into Orthopedic Manifestations and Complications Using Natural Language Processing

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INTRODUCTION: Costello syndrome is a rare RASopathy (a group of rare genetic disorders caused by mutations in genes that affect the RAS/MAPK pathway, which controls cell growth, maturation, and movement) with multisystem clinical manifestations. While cardiopulmonary and neurologic complications are well recognized, musculoskeletal features—particularly scoliosis and its treatment-related risks—remain poorly described. Given the syndrome's estimated prevalence of fewer than 1 in 300,000 live births, systematic data on scoliosis are exceptionally scarce. This study uses natural language processing (NLP)-driven data extraction to characterize the orthopedic presentations, scoliosis progression, and treatment outcomes of patients with Costello syndrome.

METHODS: Following IRBA approval, a custom validated NLP pipeline (Accuracy 99%, Sensitivity 99%, Specificity 99%) was applied to all operative notes at a large tertiary pediatric hospital from 2010–2020 to identify scoliosis cases. This pipeline is directly connected to our institutional data warehouse and applies several different search and classifications directly on existing structured (e.g., demographics) and unstructured (e.g., clinical notes) data. Costello syndrome was flagged using targeted keyword searches across longitudinal records. Patients with confirmed Costello syndrome and scoliosis diagnosis were then identified and included. Demographics, radiographic parameters, comorbidities, and detailed musculoskeletal findings were extracted from both structured and unstructured sources. Scoliosis treatments and complications were recorded and classified using the modified Clavien-Dindo-Sink system.

RESULTS: Thirteen patients with Costello syndrome and scoliosis were identified. Median age at presentation was 8 years (range 3–14), with 69% male. Median baseline Cobb angle was 16° (10–51°), progressing to 23° (11–38°) at last follow-up despite interventions. Neurologic comorbidities were nearly universal (85%), followed by cardiac (54%) and urologic (38%) complications. All patients exhibited developmental delay and short stature (<5th percentile). Musculoskeletal abnormalities were diverse and pervasive. Ligamentous laxity was present in 92%. Spine and chest manifestations included kyphosis (38%), lordosis (31%), and pectus excavatum (46%). Extremity involvement was frequent: shoulder contractures (54%), abnormal gait in 73% of ambulatory patients, tight Achilles tendon (62%), pes planus (46%), and hip flexion contracture (23%).
Treatment approaches varied: bracing (54%), growth-friendly surgery (15%), and spinal fusion (23%). Complications occurred across all modalities. Three braced patients developed Grade I skin irritation; one growth-friendly patient experienced Grade IIIb hardware prominence; and two fusion patients suffered significant complications—one with a Grade II wound complication, and one with Grade IIIb hardware failure and wound breakdown requiring reoperation.

DISCUSSION: This series highlights scoliosis in Costello syndrome as part of a broader, multisystem musculoskeletal phenotype. Scoliosis progression occurred despite conservative treatment, while surgical management carried substantial complication risk. The combination of ligamentous laxity, growth impairment, and comorbid systemic disease may contribute to both curve progression and surgical vulnerability.

SIGNIFICANCE: Leveraging NLP-based identification across a decade of clinical records enabled one of the largest systematic cohorts of scoliosis in Costello syndrome to date. These findings provide a comprehensive view of the orthopedic burden in this rare disease, emphasizing the challenges of both disease progression and treatment complications. Early recognition, proactive multidisciplinary monitoring, and individualized treatment planning are essential for optimizing care in this high-risk population.

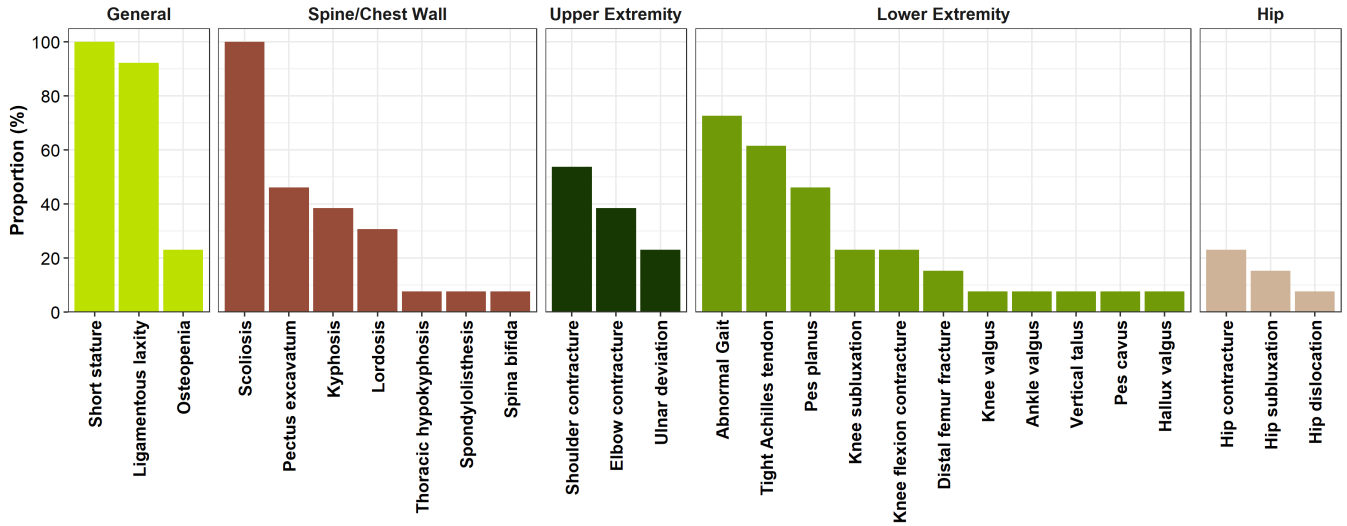

Figure 1: Orthopedic findings in patients with Costello syndrome