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Collagen X Biomarker (CXM) is Predictive of Growth Cessation in Idiopathic Scoliosis

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LOE-Diagonstic-Level IV

Purpose: Assessment of the cessation of growth for patients being treated with bracing for pediatric spinal deformity is critical. Risser score (RS) was the gold standard but subsequent studies have shown that it can result in the mistreatment of 1 in 4 braced patients with AIS. Sanders stage (SS) was then thought to be an improvement but Grothaus et al demonstrated that over 20% of ss7 patients had curve progression at cessation of bracing. It is unknown if progression is due to remaining growth or if it's due to other causes such as relaxation of the curve. Type X collagen (COLX) is produced in the growing physis during enchondral ossification. CXM is a breakdown product from COLX that can be measured in serum. CXM, thus, is a direct measure of enchondral ossification and longitudinal bone growth. In this study we sought to evaluate if SS7 patients still had measureable growth and if their biomarker level was predictive of cessation of growth

Methods: IRB approved Prospective Comparative Study. Q6mo anthropometrics and spine PA biplanar slot scanner images including the hand were assessed for major curve magnitude, RS, triradiate cartilage status (TRC), Greulich and Pyle bone age (BA), and SS. Serial Dried Blood Spots (DBS) to obtain CXM levels were collected 3 consecutive days Q1-2months based on SS.

Results: During the 2.5 year period of the study 47 patients with idiopathic scoliosis, Cobb ≥20 were enrolled. Only SS7 patients were included in this subanalysis, 10 patients became SS7 during that period. CXM levels were assayed in quadruplicate for a total of 604 samples. CXM results were highly reproducible with an intraassay coefficient of variation of 3%, and interassay of 12%. Only one patient with a CXM level <5ng/ml had remaining growth. But they consistently provided poor samples that may have lowered their CXM level

Conclusions: CXM is the first identifiable biomarker specific to longitudinal bone growth. We previously established that it is a patient-specific, real time measure of growth velocity with high correlation to the established anthropometric and radiographic measures of growth. In this study we found that all SS7 patients with a CXM >5ng/ml had remaining growth and only one of the patients <5ng/ml had remaining growth. Longer term follow-up is required to determine what characteristics are predictive of curve progression after growth cessation.

Significance: CXM levels are predictive of growth cessation. No patients with a CXM <5ng/ml experienced significant remaining growth.

Growth Velocity vs CXM in SS 7 patients

Subject	Sex	Height Velocity (cm/yr)	Closest CXM (ng/ml) to visit	# of samples	Major Cobb closest to visit	Mean CXM (ng/ml) between visits	Change in Cobb between visits
1003	F	1.6	9.56	6	24	9.5	
		0.6	6.65	5	22	7.24	-2
		0.5	5.92	7	23	6.47	1
		0	4.59	4	24	3.49	1
1014	F	4	6.85	5	37	6.66	
		0	4.43	12	44	5.74	7
		0	3.38	1 fusion		3.38	-1
1015	M	4.88	15.68	5	20	18.67	
		3.4	10.34	6	18	11.84	-2
1021*	F	3.2	4.92	6	33	6.98	-5
		3	3.41	7	43	3.47	10
1022	F	4.8	13.18	6	24	10.06	-1
		2.06	9.22	7	31	10.07	6
		1	8.12	6	29	7.89	-2
1024	M	7.04	16.31	10	35	24.55	-2
1027	F	3.4	9.35	6	20	10.97	1
		0.6	6.51	5	21	7.61	1
1036	F	2.01	6.11	8	37	9.06	8
1039	F	2	9.74	10	28	10.53	-8
		2.92	6.53	5	30	7.79	2
1044	F	2	7.16	6	23	8.93	2

* pt 1021 consistently provided poor quality samples that may have lowered her CXM levels or decreased their reliability