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Lack of joint hypermobility increases risk of surgery in adolescent idiopathic scoliosis

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Abstract

Generalized joint hypermobility is a risk factor for developing adolescent idiopathic scoliosis (AIS), however it is not known if joint hypermobility influences risk of progression to surgery. Beighton joint hypermobility scores were assessed in 570 female AIS patients. Multivariate analysis was performed to determine whether Beighton hypermobility scores were predictors of surgical intervention. In this female AIS cohort, 24.7% (141/570) had generalized joint hypermobility (GJH) (Beighton score = 4). Multivariate analysis revealed that GJH did not influence risk of surgery although having no joint hypermobility (Beighton score=0) increased risk [OR 1.89, p=0.003]. Females who had no hypermobility (score=0) had significantly larger curves than individuals who scored at least one point on the Beighton scale [50° (IQR26) vs 42° (IQR24), p=0.001]. Evaluation of specific measures of joint hypermobility revealed that females who could not touch their palms to the floor were 2.1-fold more likely to have had surgery than patients who could perform this task (p=0.001). None of the other features measured on the Beighton score correlated with surgical risk. Lack of joint hypermobility increases the odds of surgery in females with AIS. Specifically, inability to touch the palms to the floor is an indicator of progression to surgery.

Keywords

scoliosis; adolescent; fusion; hypermobility; juvenile

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INTRODUCTION

Adolescent idiopathic scoliosis (AIS) is characterized by a lateral curvature of the spine of $>10^\circ$. Approximately 0.3% of adolescents have scoliosis $>20^\circ$ requiring specialist treatment and more than 1 in 10,000 children have severe spine deformity requiring surgical correction [1]. Several factors influence AIS risk and/or severity, including sex, age of onset, menarcheal status, curve type/characteristics, and skeletal maturity [2–4]. However, factors responsible for curve progression are incompletely understood, and it remains difficult to predict which patients will ultimately require surgery.

Joint hypermobility is a risk factor for developing scoliosis. In females with AIS, generalized joint hypermobility is increased compared to controls (23.2% vs 13.4%) [5]. Joint hypermobility is a common feature of many hereditary disorders of connective tissues, and measures of joint hypermobility are part of the diagnostic criteria for Marfan syndrome [6], Ehlers Danlos syndrome [7], and many other related disorders [8]. Scoliosis, clubfoot, hip dysplasia, and other musculoskeletal complaints are common in these disorders [9,10], therefore orthopedic surgeons encounter these patients frequently in clinical practice.

The increased prevalence of joint hypermobility in AIS suggests a role for extracellular matrix and connective tissues in idiopathic scoliosis pathogenesis, which has been confirmed in genome wide association studies of rare genetic variants [11,12]. Consistent observations that joint hypermobility is more common in females [13,14] also support the possibility that these factors contribute to the gender imbalance of severe scoliosis.

While joint hypermobility is a risk factor for scoliosis, few studies have addressed the relationship between joint hypermobility and scoliosis curve progression. To determine the effect of joint hypermobility and its individual components on AIS curve severity and risk of surgery, we assessed Beighton hypermobility scores in a large cohort of AIS patients.

METHODS

Patients

Patients were recruited prospectively from orthopaedic surgery clinics at St. Louis Children's Hospital and Shriners Hospital for Children, St Louis over a ten-year period (2005–2015). Three trained research coordinators (HZ, SS, TK) carefully pre-screened the scoliosis clinics at both hospitals each week to generate lists of potential study subjects. Then in partnership with scoliosis providers in the clinics, potential study subjects were approached, legibility confirmed, and patients were recruited. Beighton joint hypermobility scores were measured on 821 AIS patients. To minimize confounding of gender and age, which are known to affect Beighton scores, males and patients <12 and >25 years of age were excluded. These exclusions left a total of 570 females (Table 1). Over this period of time not all subjects that met inclusion criteria were recruited due to large number of patients and inability of coordinators to be at every clinic. More than 90% of those who met the inclusion criteria and were approached agree to participate in the study. From hereafter, all data referring to 'patients' will refer to this female age-restricted cohort.

This study was approved by the Institutional Review Board and consent was obtained from all participants and/or their parents. All patients had juvenile or adolescent idiopathic scoliosis with spinal curves measuring $\geq 10^\circ$. Curve measurements are reported for the maximum lateral spinal curve using the Cobb method [15]. Patients with developmental delay, multiple congenital anomalies or known underlying genetic disorders (e.g. Ehlers–Danlos syndrome, Marfan syndrome) were excluded from this study. Of the 570 subjects, 230 had either already undergone spinal fusion at time of enrollment or had surgery at some point during the time frame of the study due to curve progression. Of the remaining 340 non-surgical patients, most had non-progressive curves although 63 patients had curves $>45^\circ$ Cobb angle but were never surgically treated.

Beighton joint hypermobility scoring

Joint hypermobility was assessed once by one of the three trained research coordinators during an evaluation with an orthopedic surgeon using the Beighton scoring system [13]. The Beighton score assesses the ability to touch palms to the floor with straight knees (1 point) and hyperextension of knees (2 points), elbows (2 points), thumb (2 points), and little finger (2 points), for a total possible score of nine points (Figure 1). Generalized joint hypermobility was diagnosed for scores of 4 or higher on the 9 point Beighton score [16].

Statistical Analysis

All analyses were performed in SAS 9.4 software. Patients were divided into two groups for analysis based on whether or not they had surgical treatment. Correlations and partial correlations were calculated using the Spearman's Rank correlation. Comparisons between Cobb angle and Beighton score between the two groups were calculated using Wilcoxon Rank Sum tests, due to skewed data. Two sample t-tests were used for comparisons between ages among groups. Linear and logistic regressions were also used.

RESULTS

This patient cohort consisted of 570 AIS cases with a range of spinal curvatures from 15 to 105 degrees (Figure 2A). As expected, surgically treated patients were older and had greater median Cobb angle (Table 1). Scores of at least one on the Beighton scale occurred in 71.6% (408/570) of all patients in this cohort (Figure 2B). Generalized joint hypermobility (GJH), defined as a Beighton score of four or higher [17], was present in 25% (141/570) of patients though the data was skewed with significantly more individuals having lower scores. Mean Beighton score was significantly smaller in surgical compared to non-surgical patients ($p=0.0001$) (Table 1). A weak negative correlation was noted between Beighton score and age ($r_{sp} = -0.1641$, $p=0.0001$), reflecting the loss of flexibility with age. There was also a weak negative correlation between Beighton score and Cobb angle ($r_{sp} = -0.1454$, $p=0.0005$) that remained significant even when controlling for age ($r_{s(partial)} = -0.103$, $p=0.014$) (Figure 2C). Scoring no points on the Beighton scale was associated with a significantly larger spinal curve [50° (IQR26) vs 42° (IQR24), $p=0.001$]. Patients with GJH (score ≥ 4) had smaller curves compared to those with lower scores, though the difference was less significant [38° (IQR26) vs. 46° (IQR28), $p=0.03$]. Patients with surgical curves (defined as curve of $\geq 45^\circ$) had significantly less flexibility than their counterparts with smaller curves,

though the difference was less than a full point on the Beighton scale (mean Beighton 2.4 ± 2.0 vs 2.0 ± 2.0) ($p=0.002$). To control for the effects of age on both hypermobility and maximal spinal curve, multivariate analysis including age as a variable was performed to determine whether joint hypermobility was predictive of increased risk of surgical intervention. As expected, age was a strong predictor of surgical intervention ($p<0.0001$) (Table 2). In multivariate analysis, presence of GJH was not predictive of surgical intervention ($p=0.90$), though scoring 1 point on Beighton was associated with 1.89-fold decreased risk of surgery ($p=0.003$).

To determine if individual components of the Beighton score were predictors of surgery, odds ratios were calculated for each (Table 3). Patients who could not touch their palms to the floor with their knees straight were 2.1 times more likely to have surgery, when controlling for age (OR= 2.1, 95% CI: 1.34, 3.22, $p=0.001$). This was supported by a logistic regression utilizing backward variable selection, in which the only predictors remaining in the model were the ability to palm the floor ($p= 0.0005$) and age ($p<0.0001$), which together explained 71% of the variance. None of the other individual components of the Beighton score were predictors of surgical intervention.

Because of the concern that surgery could affect the ability of a patient to touch their palms on the floor, we repeated the analysis after excluding 133 patients for whom the measurement was obtained post-operatively. Measurements had been taken at least 6 months after surgery when activity was no longer restricted. Multivariate analysis using this cohort of 437 AIS patients revealed that scoring 0 on the Beighton test resulted in a 1.9-fold increase in the risk for surgery (OR 1.95, C.I. 1.15, 3.30, $p=0.01$) compared to individuals who scored 1. More specifically, being unable to touch palms to floor resulted in a 2.5-fold increase in risk of surgery, when controlled for age (OR 2.5, C.I. 1.37, 4.6, $p=0.003$). These data are consistent with the data obtained on the entire cohort, and suggest that spinal surgery did not significantly alter the joint hypermobility measurements.

DISCUSSION

While joint hypermobility is more frequent in patients with adolescent idiopathic scoliosis (AIS) [5,18], the current study suggests, paradoxically, that having at least some hypermobility is protective against scoliosis progression. Overall, we found that lack of any joint hypermobility, which occurred in 28% of patients who could not complete any of the tasks and scored zero on the Beighton measurements, predicted a nearly 2-fold increased risk of progression to surgery that was associated with, on average, an 8° greater Cobb angle. While Czaprowski found no association of generalized joint hypermobility (GJH) with scoliosis severity, we reported significantly smaller curves in AIS patients with GJH perhaps because of our much larger sample size [5]. Interestingly, we noted that patients at the extreme end of the hypermobility spectrum (Beighton scores >7) that make up an even smaller subgroup, appeared to have greater Cobb angles and higher rates of surgery, suggesting that degree of hypermobility and the specific underlying mechanism responsible for scoliosis/hypermobility, may also independently influence scoliosis progression.

The mechanism by which having some joint hypermobility protects against scoliosis progression may be spinal flexibility because the ability to palm the floor was the only individual task of the Beighton score that predicted reduced progression to surgery. The other components of the Beighton score measure only joint hypermobility of the extremities. The ability to palm the floor reflects flexibility of multiple joints, including hips, lumbar spine, and shoulders as well as the trunk and extremity length [19,20]. As a measure of spinal flexibility, it suggests that patients with this ability may have intrinsic protection from scoliosis progression or have spinal curves that respond better to bracing. To support the latter, previous studies have shown that curve flexibility, as measured by the degree of correction while in brace, negatively correlates with progression to surgery [21–23]. Future studies to determine whether the ability to palm the floor corresponds with the degree of correction in brace are needed to support the hypothesis that the protective effect of joint hypermobility/spinal flexibility is due to the positive response to bracing that it confers.

Our study has some limitations. We did not have the ability to recruit every patient that met the inclusion criteria over the ten-year period which raises concerns of selection bias for patients with severe curves in our cohort. To exclude the possibility that our results were confounded by the impact of spinal fusion surgery on the ability to palm the floor, we found nearly identical results by restricting our analysis to patients in whom the measurements were made pre-operatively. However, the major limitation of the study is that we cannot account for the possibility that spinal curves themselves could reduce the overall length of spine or mechanical impair spinal flexibility, which both may affect the ability to palm the floor. While previous studies have shown the spine is more flexible in mild scoliosis [24], spines with larger curve angle and apical vertebral rotation show less flexibility, at least on supine bending films[25]. It remains unknown whether the reduced flexibility of severe curves is itself present prior to curve progression or is a secondary consequence of mechanical changes due to the scoliosis. An ideal prospective study design would assess Beighton scores at the beginning of treatment, when curves are small or prior to curve progression, in order to eliminate this potential confounder. As Beighton scores are measured on all patients recruited for our genetic studies, we will eventually have data and long-term follow up from a sufficiently large cohort of patients for whom measurements were made early in their course to be able to answer this question.

As a screening tool, Beighton joint hypermobility scores take less than 60 seconds to administer, have no direct cost, are noninvasive and quantitative, and highly reliable. Because inability to touch palms flat to the floor was the only component predictive of progression to surgery, our data suggests that it may be sufficient to test for this task alone. In addition to their utility in predicting scoliosis progression, higher Beighton scores indicate patients at risk for Ehlers-Danlos syndrome [7], generalized joint hypermobility [16], and many other related disorders [8]. Thus, implementation of this screening tool may improve identification of patients with hereditary disorders of connective tissue that would benefit from genetics referral for definitive diagnosis.

Clinical measures of joint hypermobility will eventually be supported by genetic tests that provide diagnostic specificity. While pathogenic variants in genes responsible for hereditary disorders of connective tissue will occasionally be identified patients thought to have

idiopathic scoliosis, our genetic data suggest that AIS patients with variants in these genes only rarely have the full syndrome [26], though these do contribute to isolated skeletal abnormalities. Furthermore, we have previously demonstrated that patients with AIS harbor more rare variants in connective tissue genes compared to controls, particularly in collagen and fibrillin genes that are responsible for Ehlers-Danlos syndrome and Marfan Syndrome [11,12]. Accumulation of rare variants in more than one extracellular matrix gene is also associated with higher Beighton joint hypermobility scores [11], therefore our prior genetic data supports a common etiology for both joint hypermobility and AIS.

Overall, this observational study suggests that lack of joint hypermobility is a risk factor for idiopathic scoliosis progression to surgery. Generalized joint hypermobility with increased flexibility at multiple joints is not required, as most protection was conferred by the ability to touch the palms to the floor which decreases the risk of surgery by two-fold. This simple measure of flexibility is a useful and easy-to-implement clinical predictor of curve progression for female AIS patients. Longitudinal data is needed to determine whether the ability to touch the palms to the floor changes during treatment, is protective in males, or predicts response to bracing. Our findings are an important step toward the development of personalized treatment strategies for AIS patients based on better assessment of individual risk of curve progression.

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Figure 1. Components of the Beighton joint hypermobility score. The Beighton score assesses hyperextension of (A) little finger (2 points), (B) thumb (2 points), (C) elbow (2 points), and (D) knees (2 points), and (E) the ability to touch palms to the floor with straight knees (1 point) for a total possible score of nine points.

Figure 2.

Relationship of Beighton score and Cobb angle in female AIS study cohort. **(A)** Number of AIS patients by Cobb angle in surgical and non-surgical groups. Surgically treated AIS patients had greater mean Cobb angle compared to non-surgically treated group (62° vs 33°) ($p < 0.0001$) **(B)** Number of AIS patients by Beighton score in surgical and non-surgical groups. Median Beighton score was significantly smaller in surgical compared to non-surgical patients (2.2 vs 2.4) ($p = 0.0001$). **(C)** Relationship between Beighton score and Cobb angle. Beighton score and Cobb angle were negatively correlated ($r_{sp} = -0.1454$, $p = 0.0005$) even when controlling for age ($r_{s(partial)} = -0.103$, $p = 0.014$)

Table 1

Demographics of female adolescent idiopathic scoliosis patients

		Total (N=570)	Non-Surgical Females (N=340)	Surgical Females (N=230)	<i>p</i>
Cobb Angle	<i>Mean (SD)</i>	44.65° (19.0)	33.05° (11.36)	61.8° (14.5)	
	Median (IQR)	45° (26)	32.0° (15.5)	59° (12)	<0.0001
Beighton	<i>Mean (SD)</i>	2.17 (2.0)	2.39 (1.96)	1.85 (2.02)	
	Median (IQR)	2 (3)	2 (3)	2 (3)	0.0001
Age	<i>Mean (SD)</i>	16.48 (2.77)	15.7 (2.3)	17.64 (3.0)	
	Median (IQR)	16.01 (3.9)	15.2 (3.35)	17.4 (4.11)	<0.0001

SD=standard deviation, IQR=interquartile range

Table 2

Effect of generalized joint hypermobility or some joint hypermobility on risk of surgical intervention for adolescent idiopathic scoliosis

Characteristic	N	Univariate Analysis		Multivariate Analysis	
		P-Value	OR (95%CI)	P-Value	OR (95%CI)
Beighton score of 0	162	0.0001	2.07 (1.43, 3.00)	0.0031	1.89 (1.24, 2.87)
Lack of GJH (< 4 points)	429	0.0510	1.41 (0.83, 2.42)	0.9019	0.97 (0.62, 1.54)
Age	570	<0.0001	1.32 (1.23, 1.41)	<0.0001	1.31 (1.22, 1.40)

GJH=generalized joint hypermobility; OR=odds ratio

Effect of individual measures of joint hypermobility on risk of surgical intervention for adolescent idiopathic scoliosis

Table 3

Characteristic	N	Univariate Analysis		Multivariate Analysis	
		P-Value	OR (95%CI)	P-Value	OR (95%CI)
Inability to:					
Palm the Floor	424	0.0003	2.15 (1.43, 3.25)	0.0011	2.08 (1.34, 3.22)
Hyperextend Knees	502	0.1539	1.48 (0.86, 2.53)	0.7226	1.11 (0.62, 2.02)
Hyperextend Elbows	425	0.0401	1.51 (1.02, 2.25)	0.1013	1.44 (0.93, 2.22)
Thumbs Touch Wrist	387	0.0724	1.40 (0.97, 2.01)	0.2866	1.25 (0.83, 1.89)
Little finger past 90°	457	0.4415	1.18 (0.77, 1.81)	0.3516	0.80 (0.50, 1.28)
Age	570	<0.0001	1.32 (1.23, 1.41)	<0.0001	1.32 (1.23, 1.42)

OR=odds ratio