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CLINICAL INVESTIGATIVE STUDY

Thoracolumbar stenosis and neurologic symptoms: Quantitative MRI in achondroplasia

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Abstract

Background and Purpose: Whole-spine magnetic resonance imaging (MRI) studies, to identify structural abnormalities associated with the development of symptomatic spinal stenosis in achondroplasia.

Methods: Forty-two subjects with achondroplasia were grouped into four age-related categories. Congenital spinal deformities (vertebral body and disc height, interpedicular distance), acquired spinal degenerative changes, thoracic kyphotic (TK) angle, thoracolumbar kyphotic (TLK) angle, spinal canal widths were evaluated by MRI.

Results: Patients in the first three groups were asymptomatic and younger (group 1: 4.4 ± 0.78 years; group 2: 8.18 ± 0.60 years; group 3: 10.95 ± 0.93 years) than the symptomatic group (group 4: 23 ± 1.30 years). Patients showed height of vertebral bodies, whole canal width, and average lumbar interpedicular distance reduced. Discs degeneration was more pronounced in the lumbar region and in symptomatic adult patients. TK and TLK angles showed a positive correlation with age ($p < .05$, $r = .42$; $p < .05$, $r = .41$), whereas thoracic and thoracolumbar canal width had a negative correlation ($p < .05$, $r = -.69$; $p < .05$, $r = -.58$). A negative correlation between lumbar discs degeneration and canal width was found only at L1-L3 level ($p < .05$, $r = -.35$). At L1-L3, the canal width cutoff value of .59 allowed the differentiation between asymptomatic and symptomatic patients (area under the curve of .966, $p < .0001$).

Conclusion: In achondroplasia, the spinal canal narrowing, due to accelerated degenerative changes, is a predisposing factor of symptomatic lumbar spinal stenosis. Lumbar canal MRI is a helpful tool to detect the risk of the development of neurological symptoms; in adult patients, a stenosis higher than 60% of upper lumbar canal could be a critical value for the onset of neurological symptoms.

KEYWORDS
achondroplasia, lumbar canal stenosis, MRI, quantitative analysis

INTRODUCTION

Achondroplasia is a congenital short-limbed dwarfing condition with an estimated prevalence of 1:16,000–25,000 live births, caused by a G380R mutation in the type 3 fibroblast growth factor receptor (FGFR).[1,2]

The disharmonious development of the basicranium and spinal dysplasia in achondroplasia is due to disordered endochondral ossification resulting in a small cranial base, small vertebral bodies, and early fusion of the pedicles to the vertebral bodies.[3] Hence, the narrowing of foramen magnum with obliteration of the subarachnoid space or subtle "nicking" of the posterior cord and thoracolumbar deformity with secondary spinal canal stenosis are recognized problems in patients with achondroplasia.[4–6]

In achondroplasia, the entire length of the spinal canal is reduced, as a result of small vertebral bodies, while the cross-sectional area of the spinal canal is narrowed by the shortened pedicles and the decreased interpedicular distances.[7,8] Moreover, age-related degenerative changes due to disc narrowing and bulging, in-folding and thickening of the ligamentum flavum as well as facet osteoarthritis, further contribute to the reduction of the dimensions of the spinal canal, in particular the lumbar spinal canal.[9,10] Thus, in patients with achondroplasia, spinal deformity is the combined effect of congenital dysplasia and acquired degenerative changes related to ageing[11]; this results in progressive spinal stenosis exacerbated by a dynamic thoracolumbar kyphosis (TLK) and a compensatory lumbar hyperlordosis.[4,12–14]

Although all patients with achondroplasia are predisposed to develop spinal stenosis, only about 20%-47% of patients in adolescence or adulthood become symptomatic due to progressive spine deformity[4,6] and may require surgery.[8]

Magnetic resonance imaging (MRI) provides a useful, noninvasive tool to evaluate spinal deformity, spinal stenosis, spinal cord compression, and intramedullary signal abnormalities.[8,15]

To date, there are few studies on the natural history of thoracolumbar deformity in achondroplasia, which could lead to the development of symptoms in adulthood.[4,16–18] Moreover, to our knowledge, there is a lack of quantitative neuroimaging studies of the whole spine in patients affected by achondroplasia.

We hypothesized that a whole-spine MRI assessment of patients of different ages with achondroplasia could help to better evaluate the progressive spine deformities responsible for the neurological symptoms. The goal of the current study was to identify anatomical factors that predispose patients with achondroplasia to symptomatic lumbar stenosis.

METHODS

Patient population

We interrogated clinical and neuroradiological databases of 42 subjects with confirmed genetic diagnosis of achondroplasia (19 males, 23 females), consecutively enrolled in our Center between January 2011 and December 2018. All patients carried Gly380Arg (G380R) mutation on the FGFR3 gene. Patients were grouped into four age-related categories: between 3 and 6 years (group 1); between 6 and 9 years (group 2); between 9 and 12 years (group 3); and older than 13 years (group 4).

Clinical and neurological symptoms were recorded for all patients along with signs and symptoms of myelopathy and or radiculopathy such as neurogenic claudication, abnormal reflexes, sensory, and motor impairment.

Whole-spinal MRI examinations were reviewed and analyzed. We compared each group of patients with an age-matched group of healthy subjects who had undergone spinal MRI scans for various incidental reasons including trauma, back pain, and whose spine MRIs were unremarkable.

Image acquisition

All spine MRIs were performed on a 1.5 Tesla Signa unit (General Electric Healthcare; Milwaukee, WI, USA) with a standard head coil. The MRI included 3-mm-thick T1- and T2-weighted images of the entire spine on the sagittal and coronal planes in the neutral position. All analyses were supplemented by axial planes when deemed appropriate.

Quantitative and semiquantitative analyses of spinal changes were performed. All measurements were performed twice by the same neuroradiologist with 10 years of experience, in two different sittings. Measurements were subsequently verified by a second reader, with 9 years of experience, to ensure consistency among measurements. The study was approved by the institutional review board.

Quantitative and semiquantitative analysis

Spinal MRI measurements

Spinal MRIs were evaluated in order to measure vertebral bodies height, vertebral discs height, and interpedicular distance from the T1 level until L5 level.

The height of each dorsal and lumbar vertebral body/disc was assessed on sagittal T2 images.

Interpedicular distance was measured on coronal T2 images as the width between the pedicles of two contiguous vertebrae. The average vertebral bodies and vertebral discs height and the average interpeduncular distance respectively from T1 to T12 and from L1 to L5 were calculated. The length of the thoracic and lumbar segments (discs + vertebrae) was also calculated (Figures 1 and 2).

Acquired spinal degenerative changes were inferred from thoracolumbar discs degeneration. Thoracolumbar discs degeneration was graded, at multiple levels from T1 to L5, using the 5-grade Pfirrmann grading system[8,19] (Figure 2).

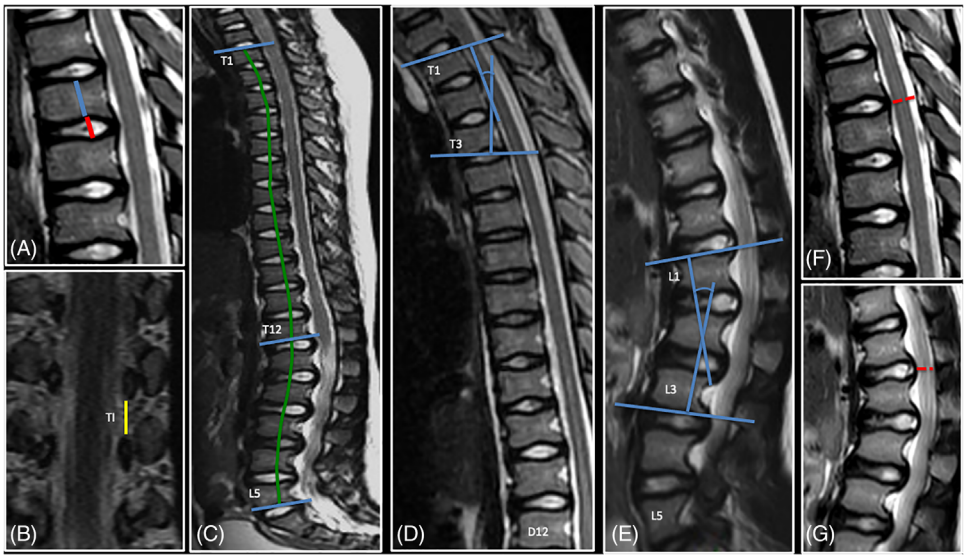

FIGURE 1 Spinal measurements recorded in patients affected by achondroplasia. Sagittal view T2-images (A, C-G) and coronal view T2 image (B). Vertebral body height measured as the distance from the superior endplate of the vertebra to the inferior one (blue line in panel A); vertebral disc height measured in the middle of the disc (red line in panel a); interpedicular distance measured as the width between the pedicles of two contiguous vertebrae (yellow line in panel B). Average length of the thoracic and lumbar segments was calculated as the sum of discs and vertebrae in their corresponding thoracic and lumbar segments (C). The degree of thoracic kyphosis and lumbar kyphosis was assessed at thoracic (T1-T3; cobb angle in panel D) and lumbar levels (L1-L3; cobb angle in panel E). They included one vertebra above and below the vertebra to the highest level of thoracic and thoracolumbar curvature measuring the angle between the superior endplate of the vertebra above and the inferior endplate of the vertebra below. The degree of thoracolumbar stenosis was performed by measuring the anteroposterior diameters of the spinal canal at the midpoint of intervertebral level (red dotted line in panels F and G). D, dorsal; T, thoracic; L, lumbar.

The degree of thoracic kyphosis (TK) and thoracolumbar kyphosis (TLK) was quantified on the sagittal plane.[20] In particular, regional patterns of kyphosis were assessed at thoracic (T1-T3 or T2-T4) and thoracolumbar levels (T12-L2 or L1-L3 levels). They included one vertebra above and below the vertebra with the highest level of thoracic and thoracolumbar curvature by measuring the angle between the superior endplate of the vertebra above and the inferior endplate of the vertebra below (Figure 1).

A quantitative evaluation of the degree of thoracolumbar stenosis was performed on sagittal T2 images by measuring the anteroposterior diameters of the spinal canal at the midpoint of each intervertebral level, from T1 to L5. The average anteroposterior diameter of the spinal canal from T1 to T12 and from L1 to L5 was also calculated (Figure 1).

Statistical analysis

Descriptive statistics were expressed as mean ± standard deviation, as median and interquartile range (IQR) for continuous variables and as numbers and percentage for categorial variables. For continuous variables, Shapiro-Wilk test was used to test the normality of data distribution. Mann-Whitney *U*-test was performed to compare the quantitative data (vertebral bodies height, vertebral discs height, interpedicular distance, canal width, thoracic and lumbar segments length) and the semiquantitative data (disc degeneration) of each group to their respective control group in the thoracic and lumbar segments.

Pearson correlation was used to assess the relationship between canal width and the patients' ages, between canal width and discs degeneration, between canal width and kyphosis, between discs degeneration and kyphosis, and between discs degeneration and the patients' ages, at thoracic and lumbar levels. The canal width value of each patient was normalized to a control group by dividing the canal width value of each patient by the canal width mean value of the corresponding control cohort.

The analysis of receiver operating characteristic (ROC) curves and area under the curves (AUC) were used to determine optimal cut-off values of lumbar canal width, which allowed the differentiation of asymptomatic from symptomatic groups.

Statistical analyses were conducted using Statistical Package for the Social Sciences (SPSS) for Windows version 25.0 (SPSS Inc., Chicago, IL, USA). The level of significance was set at $p < .05$, and significance levels were adjusted, according to the Bonferroni correction, for multiple comparisons.

RESULTS

Demographics of enrolled patients are summarized in Table 1 according to age classes.

All patients allocated in the first three groups were asymptomatic and younger than the patients in group 4 where all patients were symptomatic. They showed severe persistent low back pain with

TABLE 1 Clinical features in enrolled patients affected by achondroplasia

	Group 1	Group 2	Group 3	Group 4
	n = 18 (%)	*n* = 8 (%)	*n* = 8 (%)	*n* = 8 (%)
Male	8 (44%)	5 (62%)	4 (50%)	2 (25%)
Mean age ± SD (years)	4.4 ± 0.78	8.18 ± 0.60	10.95 ± 0.93	23 ± 1.30
Neurological symptoms	None	None	None	8 (100%)
Impairment of evoked potentials	None	None	None	6 (75%)
Spine surgery	None	None	None	8 (100%)
Signs/symptoms after surgery	None	None	None	1 (25%)

Abbreviations: *n*, number; SD, standard deviation.

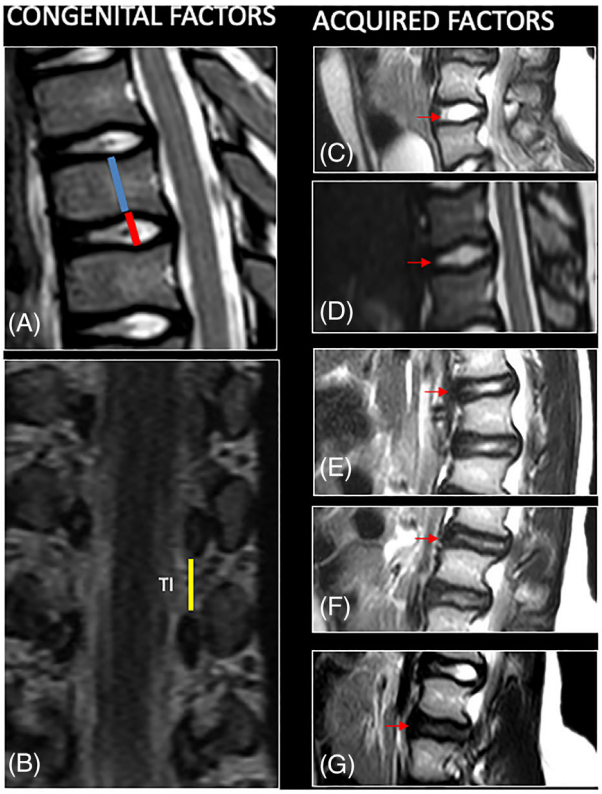

FIGURE 2 Congenital and acquired degenerative changes in a representative patient with achondroplasia. Sagittal view T2-images (A, C-G) and coronal view T2 image (B). Congenital factors (A and B): vertebral body height (blue line in panel A); vertebral disc height (red line in panel A); interpedicular distance (yellow line in panel B). Acquired factors: discs degeneration was graded using the 5-grade Pfirrmann grading system (C-G). Grade1, homogeneous disc with bright high signal intensity, normal disc height (arrow in panel C). Grade 2, inhomogeneous disc with white signal intensity, and normal height (arrow in panel D). Grade 3, inhomogeneous disc with intermediate gray signal intensity, unclear distinction between nucleus and annulus, and slightly decreased disc height (arrow in panel E). Grade 4, inhomogeneous disc with dark low signal intensity, no possible distinction between nucleus and annulus, and moderately decreased disc height (arrow in panel F). Grade 5, inhomogeneous disc with black low signal intensity, no possible distinction between nucleus and annulus, and complete disc narrowing (arrow in panel G). T, Thoracic.

neurogenic claudication, paraparesis, abnormal reflexes to neurological examination, and impairment of motor and/or somatosensory evoked potentials. No patient showed signs or symptoms of dorsal nerve root compression or spinal cord compression (Table 1). All symptomatic patients underwent spinal neurosurgery ($n = 6$ lumbar decompression; $n = 2$ thoracolumbar decompression) and 1 patient had permanent motor impairment.

In the thoracic segment, compared to healthy subjects, all groups of patients showed increased TK angle and vertebral discs height as well as reduced vertebral bodies height and canal width. All groups have a mild degree of dorsal disc degeneration but the thoracic segment length did not differ in comparison with the controls.

In the lumbar segment, compared to healthy subjects, all groups of patients showed increased lumbar kyphotic angle and reduced vertebral bodies height, canal width, and lumbar interpedicular distance. All patients had lumbar discs degeneration, but in symptomatic and older patients (group 4) it was more severe even if disc height was comparable to the healthy subjects. Thus, in asymptomatic groups, lumbar segment length did not differ compared to the controls, while in the symptomatic group the lumbar segment length was reduced.

Anteroposterior diameter of the spinal canal showed progressively lower values when age increased, and lower values were observed at lumbar level and, in particular, at L1-L3 (Table 2) (Figures 3 and 4).

The TK angle, the TLK angle, the thoracic and lumbar canal width correlated with age; higher values of kyphosis, and lower values of canal width were observed in older groups. However, only in the lumbar region, the discs degeneration showed a positive correlation with age. Moreover, at L1-L3 level, we found a positive correlation between lumbar discs degeneration and kyphotic angle, whereas a negative correlation between lumbar discs degeneration and canal width and between canal width and kyphotic angle was found (Table 3).

In order to assess optimal cutoff values to discriminate symptomatic from asymptomatic patients, an ROC curve analysis, for normalized lumbar canal width, was performed at L1-L3 and L1-L5 levels. ROC curve analysis showed cutoff value of .59 with the best combination of sensitivity (89.2%) and specificity (100%) and AUC of .966, $p < .0001$ at L1-L3 level and cutoff value of .6509 with the best combination of sensitivity (78.4%) and specificity (100%) and AUC of .939, $p < .0001$ at L1-L5 level.

TABLE 2 Spinal MRI measures in patients affected by achondroplasia at different ages and in control groups

	Group 1 ($n = 18$)	Control group ($n = 36$)	
	Median [IQR]	Median [IQR]	*p*-value
Age (years)	4.5 [IQR 4-5]	5 [IQR 4-5]	.67
Congenital factors			
Thoracic vertebral bodies height (mm)	9.35 [IQR 8.85-9.92]	10.65 [IQR 10.06-11.11]	<.001*
Thoracic interpediculate distances (mm)	19.35 [IQR 18.12-20]	19.66 [IQR 18.54-20.87]	.19
Lumbar vertebral bodies height (mm)	13.96 [IQR 13.46-14.34]	15.33 [IQR 14.62-15.6]	<.001*
Lumbar interpediculate distances (mm)	24.3 [IQR 23.2-26.6]	27.4 [IQR 25.6-27.9]	.002*
Acquired factors			
Thoracic vertebral discs height (mm)	4.59 [IQR 4.27-5]	3.6 [IQR 3.24-3.84]	<.001*
Thoracic disc degeneration (T1-T6)	1 [IQR 1-1.3]	1 [IQR 1-1]	.02*
Thoracic disc degeneration (T7-T12)	1.58 [IQR 1.16-1.83]	1 [IQR 1-1]	<.001*
Lumbar vertebral discs height (mm)	6.33 [IQR 5.4-6.84]	5.02 [IQR 4.4-5.78]	<.001*
Lumbar disc degeneration (L1-L5)	2 [IQR 1.8-2.2]	1.5 [IQR 1.4-1.6]	<.001*
Combined factors			
Thoracic-length (vertebrae + discs, mm)	170.45 [IQR 156.4-175.5]	168.3 [IQR 165–180.7]	.27
Thoracic regional kyphotic angle (T1-T4 level)	3.69 [IQR 3–5.96]	1.8 [IQR 0–3.6]	<.001*
Thoracic canal width (mm)	10.27 [IQR 9.91-10.5]	13.08 [IQR 12.37-13.62]	<.001*
Lumbar length (vertebrae + discs, mm)	99.65 [IQR 96.9-105.4]	100.7 [IQR 97.2-105.6]	.75
Lumbar regional kyphotic angle (T12-L3 level)	10.41 [IQR 5.41-14.35]	0 [IQR 0–3.1]	<.001*
Lumbar canal width (L1-L5) (mm)	10.55 [IQR 9.4-11]	14.5 [IQR 13.9-15.1]	<.001*
Lumbar canal width (L1-L3) (mm)	10.25 [IQR 9.33-11.1]	14.66 [IQR 13.83-15.66]	<.001*
	Group 2 ($n = 22$)	**Control group ($n = 11$)**	
	Median [IQR]	**Median [IQR]**	***p*-value**
Age (years)	8 [IQR 8-9]	8.5 [IQR 8-9]	.21
Congenital factors			
Thoracic vertebral bodies height (mm)	10.84 [IQR 10.40-11.55]	12.30 [IQR 11.58-12.90]	<.001*
Thoracic interpediculate distances (mm)	21.20 [IQR 20.5-21.33]	22.08 [IQR 21.16-22.54]	.08
Lumbar vertebral bodies height (mm)	15.34 [IQR 14.98-16.5]	16.74 [IQR 16.4-16.98]	.002*
Lumbar interpediculate distances (mm)	26 [IQR 23.6-28]	33.4 [IQR 31.7-34.1]	<.001*
Acquired factors			
Thoracic vertebral discs height (mm)	4.60 [IQR 4.40-4.96]	3.18 [IQR 2.91-3.58]	<.001*
Thoracic disc degeneration (T1-T6)	1 [IQR 1-1.5]	1 [IQR 1-1]	.03*
Thoracic disc degeneration (T7-T12)	1.5 [IQR 1.16-2]	1.16 [IQR 1-1.16]	<.001*
Lumbar vertebral discs height (mm)	7.26 [IQR 6.72-7.38]	5.92 [IQR 4.98-6.58]	<.001*
Lumbar disc degeneration (L1-L5)	2.4 [IQR 2-2.6]	2 [IQR 2-2]	.003*
Combined factors			
Thoracic-length (vertebrae + discs) mm	190 [IQR 177.8-193.5]	188.55 [IQR 173.9-197.9]	.89
Thoracic regional kyphotic angle (T1-T4 level)	4.2 [IQR 2-8]	0 [IQR 0-2]	<.001*
Thoracic canal width (mm)	10.25 [IQR 9.91-10.75]	12.81 [IQR 12.5-13.71]	<.001*
Lumbar length (vertebrae + discs, mm)	114 [IQR 110.4-115.6]	112.8 [IQR 106.3-117]	.80
Lumbar regional kyphotic angle (T12-L3 level)	16.3 [IQR 12.5-23.56]	0 [IQR 0-2.6]	<.001*
Lumbar canal width (L1-L5) (mm)	8.48 [IQR 7.72-8.58]	11.78 [IQR 11.28-12.4]	<.001*
Lumbar canal width (L1-L3) (mm)	7.9 [IQR 7.33-9.03]	12.06 [IQR 12-12.96]	<.001*

(Continues)

TABLE 2 (Continued)

	Group 3 ($n = 8$) Median [IQR]	Control group ($n = 16$) Median [IQR]	*p*-value
Age (years)	10 [IQR 10-13]	11 [IQR 11-12]	.07
Congenital factors			
Thoracic vertebral bodies height (mm)	12.41 [IQR 11.95-12.81]	14.12 [IQR 13.33-14.66]	<.001*
Thoracic interpediculate distances (mm)	24.66 [IQR 21.75-25.16]	25.37 [IQR 23.71-26.54]	.06
Lumbar vertebral bodies height (mm)	14.64 [IQR 13.4-16.1]	16.26 [IQR 15.64-17.1]	.006*
Lumbar interpediculate distances (mm)	32.6 [IQR 28.8-35.1]	34.7 [IQR 34.2-34.8]	.03*
Acquired factors			
Thoracic vertebral discs height (mm)	5.03 [IQR 4.93-5.19]	3.12 [IQR 2.91-3.38]	<.001*
Thoracic disc degeneration (T1-T6)	1.25 [IQR 1-1.66]	1 [IQR 1-1]	.02*
Thoracic disc degeneration (T7-T12)	1.83 [IQR 1.66-2.16]	1.16 [IQR 1.16-1.5]	<.001*
Lumbar vertebral discs height (mm)	6.46 [IQR 6.32-8.44]	5.16 [IQR 4.88-5.54]	.17
Lumbar disc degeneration (L1-L5)	2.6 [IQR 2.4-3]	2 [IQR 1.8-2]	<.001*
Combined factors			
Thoracic-length (vertebrae + discs) mm	210.3 [IQR 205.1-216.1]	206 [IQR 200.6-210.9]	.78
Thoracic regional kyphotic angle (T1-T4 level)	6.8 [IQR 1.8-12]	0 [IQR 0-2]	.003*
Thoracic canal width (mm)	10.12 [IQR 9.91-10.29]	12.21 [IQR 11.91-13.12]	<.001*
Lumbar length (vertebrae + discs, mm)	109.95 [IQR 100–115.9]	108.05 [IQR 102.6-112.2]	.88
Lumbar regional kyphotic angle (T12-L3 level)	20.7 [IQR 20.4-21.4]	0 [IQR 0-2]	<.001*
Lumbar canal width (L1-L5) (mm)	8.55 [IQR 7.6-9.16]	11.58 [IQR 11.06 –12.46]	<.001*
Lumbar canal width (L1-L3) (mm)	7.65 [IQR 7.33-8.5]	12.3 [IQR 12.16-13.13]	<.001*
	Group 4 ($n = 8$) Median [IQR]	**Control group ($n = 16$) Median [IQR]**	***p*-value**
Age (years)	22.5 [IQR 22-25]	22.5 [IQR 22-24]	.97
Congenital factors			
Thoracic vertebral bodies height (mm)	16.87 [IQR 16.62-17.14]	17.53 [IQR 17.16-20.01]	<.001*
Thoracic interpediculate distances (mm)	25.14 [IQR 24.21-31.66]	26.91 [IQR 26.08-529.91]	.41
Lumbar vertebral bodies height (mm)	22.99 [IQR 22.32-25.58]	25.42 [IQR 23.94-28.2]	.02*
Lumbar interpediculate distances (mm)	34.2 [IQR 34-35]	38.8 [IQR 38.2-42.2]	.002*
Acquired factors			
Thoracic vertebral discs height (mm)	4.12 [IQR 4.01-4.42]	3.43 [IQR 3.35-3.99]	.002*
Thoracic disc degeneration (T1-T6)	1.25 [IQR 1.16-1.33]	1 [IQR 1-1]	.002*
Thoracic disc degeneration (T7-T12)	1.83 [IQR 1.5-2]	1 [IQR 1-1]	<.001*
Lumbar vertebral discs height (mm)	7.21 [IQR 7.06-7.8]	7.24 [IQR 7.06-8.66]	.23
Lumbar disc degeneration (L1-L5)	2.8 [IQR 2.8-3]	2 [IQR 2-2]	<.001*
Combined factors			
Thoracic-length (vertebrae + discs) mm	248.4 [IQR 247.6-258.5]	250.7 [IQR 242.1-288]	.65
Thoracic regional kyphotic angle (T1-T4 level)	9.65 [IQR 8.7-12]	2.5 [IQR 0-4]	<.001*
Thoracic canal width (mm)	8.50 [IQR 7.82-9.45]	13.65 [IQR 11.93-14.27]	<.001*
Lumbar length (vertebrae + discs, mm)	152.1 [IQR 146.9-162.5]	163 [IQR 162.4-176.3]	.002*
Lumbar regional kyphotic angle (T12-L3 level)	18.2 [IQR 16-29.68]	1 [IQR 0 - 6]	<.001*
Lumbar canal width (L1-L5) (mm)	8.25 [IQR 7.64-9.42]	14.75 [IQR 13.86-16.6]	<.001*
Lumbar canal width (L1-L3) (mm)	7.45 [IQR 7–8.53]	15.23 [IQR 13.1-16.7]	<.001*

Abbreviations: IQR, interquartile range; L, lumbar; MRI, magnetic resonance imaging; *n*, number; T, thoracic.
*Significant *p*-values.

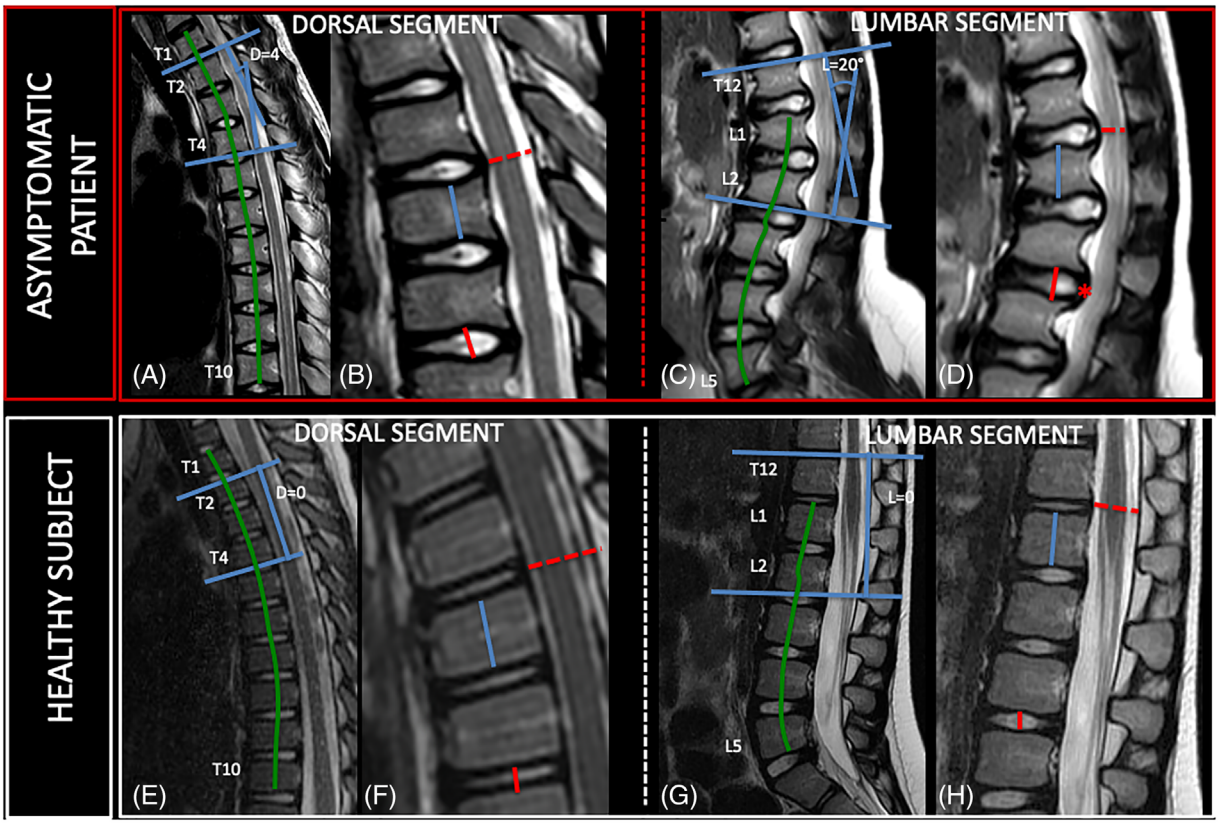

FIGURE 3 Anatomical factors linked to spinal deformity in a representative asymptomatic patient with achondroplasia compared to a healthy control subject. Sagittal view T2 images in a 12-year-old asymptomatic patient (A-D) and in a 12-year-old healthy control subject (E-H). Thoracic segment (A, B, E, F): in asymptomatic achondroplasic patient, please note increased dorsal kyphotic angle (cobb angle 4° in A) increased vertebral disc height (red line in panel B), reduced vertebral body height (blue line in panel B), and reduced canal width (dotted red line in panel B). Thoracic segment length did not differ from control (green lines in panels A and E). Lumbar segment (C, D, G, H): in asymptomatic achondroplasic patient, please note increased lumbar kyphotic angle (cobb angle 20° in panel C), reduced vertebral body height (blue line in panel D), and reduced canal width (dotted red line in panel D). Lumbar discs were degenerated with bulging posteriorly (red asterisk in panel D) but, compared to control, discs were increased in height (red line in panel D) and no difference in lumbar segment length was detect than control subject (green lines in panels C and G). D, Dorsal; T, Thoracic; L, Lumbar.

DISCUSSION

In children affected by achondroplasia, TLK is commonly observed.[12,21] It has been hypothesized that degenerative changes and congenital factors together with muscle hypotonia, causing abnormal biomechanical forces on the anterior column of the spine vertebrae, may be responsible for TLK occurrence.[8,22,23]

Lumbosacral spinal stenosis, with compression of the spinal cord or nerve roots, is the most common complication, occurring in adolescence and adult age.[15,24]

However, to date, anatomical factors associated with the progression of spine abnormalities and the subsequent development of symptomatic canal stenosis, observed in some patients, remain not fully understood.

The first goal of this study was to analyze congenital and degenerative anatomical features in patients of different age groups that are affected by achondroplasia in order to identify factors contributing to spine abnormalities and predisposing some patients to the onset of neurological symptoms.

In agreement with previous reports, our data showed that in patients with achondroplasia the entire spine was dysplastic and anatomical changes were already present in childhood.[4,8] In fact, all groups showed hypoplastic dorsal and lumbar vertebrae, reduced lumbar interpedicular distances, and a variable degree of thoracic and lumbar discs degeneration. However, only lumbar discs degeneration worsened with age causing, in older patients, disc narrowing and disc bulging laterally and posteriorly.

A difference emerged between asymptomatic and symptomatic groups with regard to lumbar discs height. In asymptomatic patients, the lumbar discs, although degenerated, remained hyperplastic, while in symptomatic and older patients lumbar intervertebral disc height was comparable to controls. These data confirm that discs degeneration worsened with age and, in particular, in symptomatic patients. It resulted in a shortened length of the lumbar spinal segment in symptomatic patients. Previous data reported that the entire length of the spinal canal was reduced in patients affected by achondroplasia,[7,8] but our data showed that the spinal segment was reduced only in symptomatic patients as only they had a shortened length of the lumbar

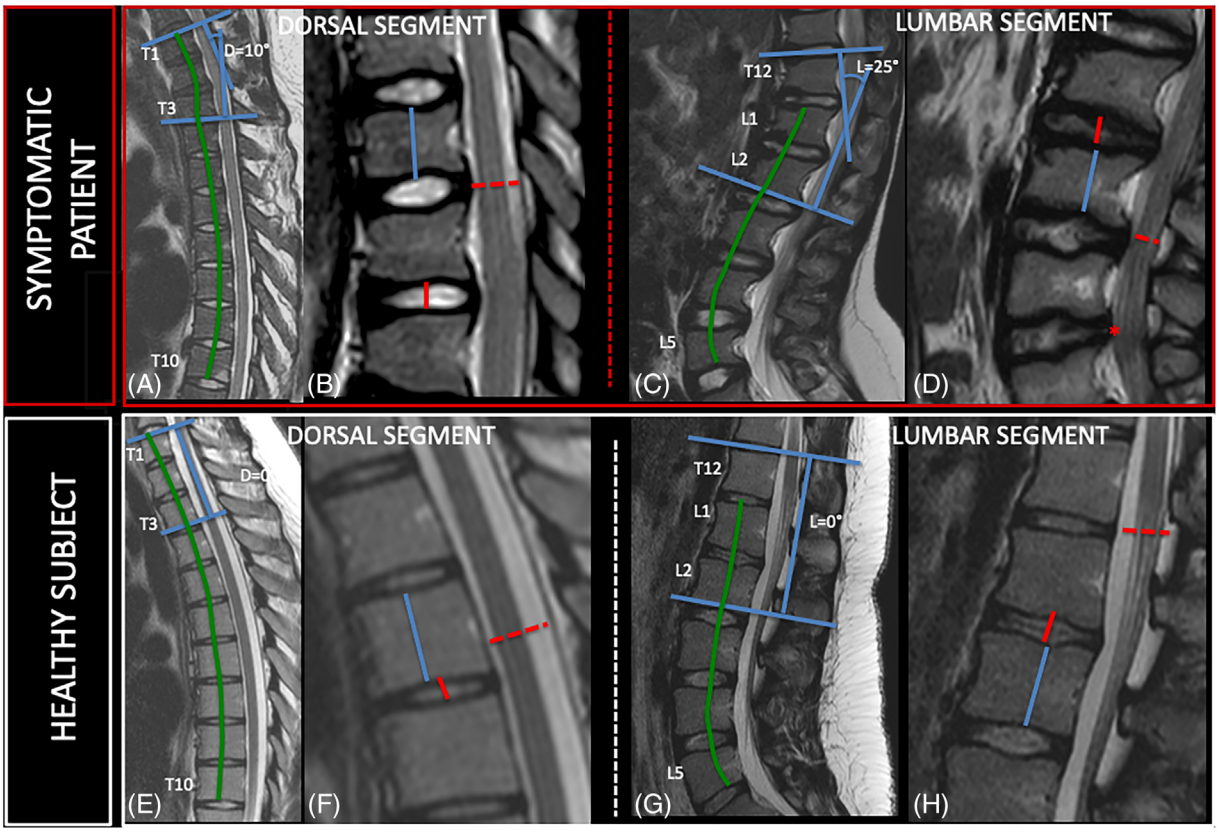

FIGURE 4 Anatomical factors linked to spinal deformity in a representative symptomatic patient with achondroplasia compared to a healthy control subject. Sagittal view T2 images in a 22-year-old symptomatic patient (A-D) before surgical decompression and in a 22-year-old healthy control subject (E-H). Thoracic segment (A, B, E, F): in symptomatic achondroplasic patient, please note increased dorsal kyphotic angle (cobb angle 10° in panel A), increased vertebral disc height (red line in panel B), reduced vertebral body height (blue line in panel B), and canal width (dotted red line in panel B). Thoracic segment length did not differ from control (green line in panels A and E). Lumbar segment (C, D, G, H): in symptomatic achondroplasic patient, please note increased lumbar kyphotic angle (cobb angle 25° in panel C), vertebral wedging with reduced body height (blue line in panel D), and decreased canal width (red line dotted in panel D) with multiple-level spinal canal stenosis. Lumbar discs were degenerated with bulging posteriorly (red asterisk in panel D), disc height was comparable to control (red line in panel D); lumbar segment length was shortened (green lines in panels C and G). T, Thoracic; L, Lumbar.

spinal segment. These data suggest that acquired lumbar degeneration may concur to develop neurological deficits in the dynamic process of growth in already congenitally involved spine.[25]

The second goal was to clarify how the association of congenital and acquired spinal features may exacerbate TLK and spinal stenosis in age-related groups, predisposing older patients to the onset of neurological symptoms.

We detected an age-related increase of dorsal and lumbar regional kyphotic angles and reduced thoracic and lumbar canal width; in particular, higher values of kyphosis and lower values of canal width were detected in the lumbar region in older groups. This finding is in agreement with previous studies because the thoracolumbar junction, being a transition region from the relative rigidity of the thoracic cage to the upper lumbar spine, creates a major stress riser on the anterior column of the lumbar spine. This causes, at lumbar level, a higher degree of lumbar kyphosis and a reduced canal width.[23] Moreover, because discs degeneration was more severe in lumbar segment and progressed in older groups, in the symptomatic group, TLK angle was more increased and lumbar canal width was smaller, particularly at L1-L3 level.

These data confirm that degenerative changes occur mainly in the lumbar segment, at L1-L3 tract, and they concur with congenital factors in increasing TLK and the severity of canal stenosis, which is a predisposition to the onset of neurological symptoms.[8,11,23]

The last goal was to determine the cutoff value of lumbar canal width associated with the onset of neurological symptoms. Our data showed that patients with a narrower lumbar canal width were more likely to develop symptoms of spinal stenosis than other patients and, according to previous studies, we found that L1-L3 were the levels more altered.[8] Moreover, we found that at L1/L3 level, the cutoff value of .59 allowed the differentiation between asymptomatic and symptomatic patients with the best combination of sensitivity and specificity.

Thus, a reduction of normal lumbar canal width by more than 60% could be a critical point of spinal stenosis capable of predicting the development of neurological symptoms in adulthood.

In conclusion, TLK and canal stenosis worsen with ageing and they are the effect of both congenital and acquired findings. The evaluation of lumbar canal stenosis, measured at the level of the

TABLE 3 Correlations among demographic and spinal measures in patients affected by achondroplasia

Thoracic segment		
Thoracic canal width ratio (T1-T12)	Age (years)	$p < .001^*$; $r = -.69$
Thoracic kyphotic angle	Age (years)	$p = .004^*$; $r = .42$
Thoracic disc degeneration	Age (years)	$p = .17$; $r = .21$
Thoracic disc degeneration	Thoracic canal width ratio (T1-T12)	$p = .75$; $r = -.04$
Thoracic disc degeneration (T1-T4)	Thoracic kyphotic angle	$p = .67$; $r = .06$
Thoracic canal width ratio (T1-T4)	Thoracic kyphotic angle (T1-T4 level)	$p = .61$; $r = -.07$
Lumbar segment		
Lumbar canal width ratio (L1-L5)	Age (years)	$p < .001^*$; $r = -.58$
Lumbar disc degeneration (L1-L5)	Age (years)	$p < .001^*$; $r = .68$
Lumbar disc degeneration (L1-L5)	Lumbar canal width ratio (L1-L5)	$p = .08$; $r = -.26$
Lumbar canal width ratio (L1-L3)	Age (years)	$p < .001^*$; $r = -.65$
Thoracic-lumbar kyphotic angle	Age (years)	$p = .006^*$: $r = .41$
Lumbar disc degeneration (L1-L3)	Age (years)	$p < .001^*$; $r = .58$
Lumbar disc degeneration (L1-L3)	Lumbar canal width ratio (L1-L3)	$p = .018^*$; $r = -.35$
Lumbar disc degeneration (L1-L3)	Thoracic-lumbar kyphotic angle	$p = .016^*$; $r = .35$
Lumbar canal width ratio (L1-L3)	Thoracic-lumbar kyphotic angle	$p = .005^*$; $r = -.41$

Abbreviations: L, lumbar; T, thoracic.
*Significant *p*-values.

intervertebral disc, where degenerative changes mainly occur, demonstrated that stenosis in symptomatic patients was more severe than in asymptomatic patients, confirming that the stenosis was mainly degenerative.

Age-related narrowing of the spinal canal, due to accelerated degenerative changes, seems to be an important factor for the development of neurological symptoms in patients with lumbar canal stenosis affected by achondroplasia. The quantitative MRI assessment of lumbar canal width in patients with achondroplasia is a simple and a helpful tool to detect children at risk of developing neurological symptoms; a stenosis higher than 60% of the upper lumbar canal could be a critical value for the onset of neurological symptoms in adulthood.

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