The lumbar interpediculate distance is widened in adults with the Marfan syndrome

Data from 32 cases

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ABSTRACT – 32 patients with Marfan syndrome, diagnosed with DePaepe's criteria, volunteered for this study. All patients underwent standard anteroposterior radiographs of the lumbar spine. Interpediculate distances (IPD) at each level were compared to those of previously established norms. Criteria were developed to determine the presence of Marfan using "cut-off values" for the IPDs at each lumbar level. The IPDs were significantly larger in the Marfan patients at all lumbar levels. Cut-off values were calculated setting the specificity at 95% at each lumbar level. The cut-off value at L4 yielded the greatest sensitivity. We conclude that the IPDs are widened in patients with Marfan syndrome. The IPD at L4 is a good criterion for Marfan with specificity of 95% and sensitivity of 75%. One must consider using this as a skeletal criterion or a screening tool for Marfan.

The normal interpediculate distance (IPD) in adults on plain radiographs has been established (Schwarz 1956, Hinck et al. 1966) and these measurements have been correlated in studies employing CT scans and anatomic evaluation (Eisenstein 1977, Ullrich et al. 1980, Malmivaara et al. 1986). Despite the fact that the Marfan spine has been well described in numerous well-performed cross-sectional studies (Sponseller et al. 1995, 1997, Hobbs et al. 1997), the IPD in the lumbar spine has not been studied in detail. Nelson (1958) reported 4 Marfan patients, 2 with widened IPD values and 2 with normal IPD values. Arroyo and Garcia (1989) described a patient with Marfan syndrom who had dural ectasia and anterior sacral meningocele with widened IPD values. Thus, while it has been thought that the IPD values are widened in patients with Marfan syndrome, no study has compared such patients with normal controls. Furthermore, knowledge of the normal values of the IPD at different levels in the lumbar spine of these patients is not known.

This knowledge may be of importance since it may help in diagnosing Marfan syndrome. The IPD may be a useful criterion for Marfan syndrome in the initial evaluation of the patient, in much the same way as protrusio acetabuli is used as a skeletal criterion for making this clinical diagnosis (DePaepe et al. 1996). That is why this study was done.

Patients and methods

32 volunteers with Marfan syndrome, diagnosed with the criteria established by DePaepe et al. (1996), were identified in the human genetics clinic at Johns Hopkins Hospital, the National Marfan Foundation, or the Marfan internet newsgroup. Exclusion criteria included history of previous back surgery, spinal tumor, or lumbar scoliosis more than 20 degrees. Patients with the latter finding were excluded because significant lumbar scoliosis made the IPD measurements inaccurate due to the altered projection of the rotated vertebrae.

222 patients with a diagnosis of Marfan syndrome were found in the patient records in the genetics clinic. 83 of them were between the ages of 30 and 50 years. 51 had no history of previous back surgery, spinal tumor, spinal stenosis, or lumbar scoliosis exceeding 20 degrees. 16 of them were available for study.

Information notices were sent to the National Marfan Foundation chapters and the Marfan internet newsgroup requesting volunteers who met the above exclusion criteria. 47 volunteers replied to our inquiry, of whom 27 met the criteria. 16 of them could participate in our study.

Of the 32 patients, 18 were female. In each case, the diagnosis of Marfan syndrome was confirmed by the geneticist or by the present authors with strict attention to the DePaepe criteria (DePaepe et al. 1996).

After informed consent was obtained, all volunteers underwent standard anteroposterior (AP) and lateral radiographs of the lumbosacral spine from L1-S5 at a standard distance of 101 mm. The radiographs were examined and IPD values were measured as the shortest distance between the medial surfaces of the pedicles.

An unpaired t-test was used to compare the findings with those of established norms, as determined by Hinck and Clark (1966). The statistical calculations were possible in particular because the aforementioned study gave not only means but also sample sizes (N) and standard deviations.

5 patients in our study had lumbosacral transition vertebrae. 4 had spondylolisthesis on the lateral radiograph. 2 of these were of the isthmic type and 2 degenerative. The mean slip was 26%.

Results

The mean interpediculate distances at each level were as follows: 29.5 mm at L1; 30.3 mm at L2; 32.1 mm at L3; 34.8 mm at L4; and 39.6 mm at L5 (Table). Our results show that the lumbar IPD values in Marfan patients were significantly greater than those of the normal population at all levels of the lumbar spine.

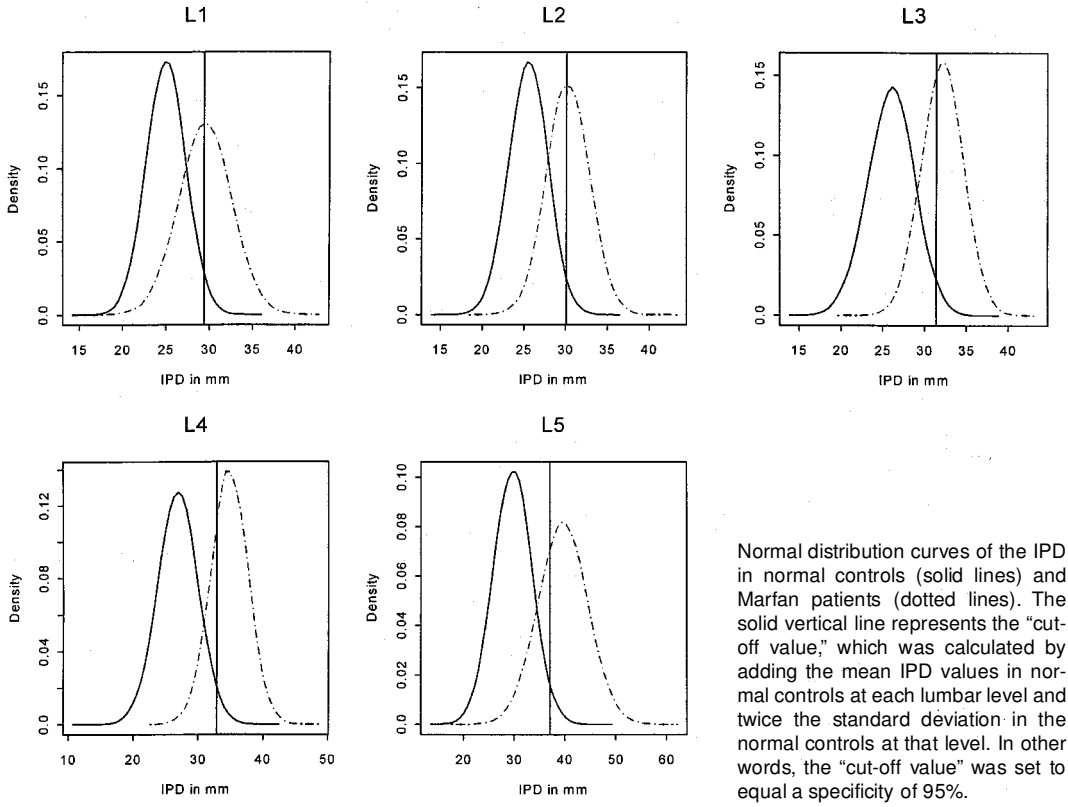
To determine appropriate criteria for diagnosing Marfan based on IPD values, we took the mean IPD values for the normal controls at each lumbar level and added twice the standard deviation for normal controls at that level; this was called the "cut-off value." An IPD value greater than this "cut-off value" suggests that the patient has Marfan; values lower than the cut-off value suggest that the patient is normal. In this way, the specificity of using the cut-off value as a screening tool was set at 95%. We assumed that the IPD values at each level the normal controls had a normal distribution.

The sensitivity of the cut-off value at each lumbar level was then calculated using our data (Table and Figure). We again assumed that the IPD values for the Marfan patients at each lumbar level had a normal distribution. The sensitivity of the IPD cut-off was greatest at L4 (75%).

Comparison of lumbar IPDs at each level in Marfan patients (in the present study) and normal controls (from Hinck et al. 1966). Note that the IPD values are significantly greater at all levels. "Cut-off values" show IPDs differing from the means of both the normal and Marfan spines by $p < 0.0001$. A lumbar spine with IPDs greater than these "cut-off values" is highly indicative of Marfan syndrome

Level	IPD (mm) Normal adults [a]			IPD (mm) Marfan adults			P-value	"Cut-off value" (mm)	Specificity [b] (%)	Sensitivity [b] (%)
	n	mean	SD	n	mean	SD				
L1	59	25.0	2.2	32	29.5	3.0	< 0.001	29.4	95	51
L2	57	25.5	2.3	32	30.3	2.5	< 0.001	30.1	95	53
L3	53	26.0	2.7	32	32.1	2.4	< 0.001	31.4	95	61
L4	52	26.9	3.0	32	34.8	2.8	< 0.001	32.9	95	75
L5	50	29.7	3.7	32	39.6	4.7	< 0.001	37.1	95	70

[a] Data from Hinck et al. 1996.
[b] Sensitivity and specificity refer to use of the "cut-off value" as a screening tool to determine if a patient has Marfan; an IPD value larger than the "cut-off value" is considered positive for Marfan.



Normal distribution curves of the IPD in normal controls (solid lines) and Marfan patients (dotted lines). The solid vertical line represents the "cut-off value," which was calculated by adding the mean IPD values in normal controls at each lumbar level and twice the standard deviation in the normal controls at that level. In other words, the "cut-off value" was set to equal a specificity of 95%.

Discussion

The normal interpedicular distances of the spine on plain radiographs were studied by Hinck et al. (1966). Although Schwarz (1956) and Elsberg and Dyke (1934) had established normal values, they provided no information on sample size and standard deviations and therefore their norms could not be used for statistical comparison. Hinck et al. (1966) not only gave norms which were consistent with those of the previous authors but also included information on sample size and standard deviation, making this study the most useful and widely cited for comparison with various populations. The fact that all of these studies showed similar IPD values at each level indicates that the IPD can be reliably and reproducibly measured.

The interpediculate distance is useful for diagnosing various diseases. A narrowed IPD has been found to be characteristic of numerous disorders, including achondroplasia (Schorr 1977), diastrophic dwarfism (Bethem et al. 1980), acrodysostosis (Butler et al. 1988, Hamanishi et al. 1993), and cloacal exstrophy (Weaver et al. 1997). It has also been seen in patients with trauma (Quesada et al. 1975), tumors (Elsberg and Dyke 1934, Nelson 1958, Natarajan et al. 1975), diastematomyelia (Nelson 1958), and neurofibromatosis (Mitchell et al. 1967). Several authors have shown that the IPD can be readily measured on plain radiographs with little interobserver variability (Simril and Thurston 1955, Schwarz 1956, Hinck and Clark 1966, Roberson et al. 1973, McCall 1993). Therefore, the finding of an abnormal IPD in a disease is a useful, noninvasive, and inexpensive way of establishing a criterion for a disease.

Our results show that the IPD is significantly wider subjects at all levels of the lumbar spine with Marfan than in the normal population. Furthermore, we have created "cut-off values" for screening persons suspected of having Marfan; patients with IPDs greater than the cut-off values may have Marfan. These values were set at a specificity of 95%; calculation of sensitivities at each

lumbar level showed that the IPD at L4 yielded the highest sensitivity (75%). Thus, the cut-off value we used for IPD (33 mm) at L4 can serve as a useful criterion or screening tool for diagnosing Marfan.

Our finding of widened IPDs in the Marfan lumbar spine can be explained by several factors. The growth of the vertebrae may be abnormal in persons with Marfan. Sponseller et al. (1995, 1997) showed that in children with Marfan, spine exhibits irregular patterns of scoliosis and kyphosis. Likewise Tallroth et al. (1995) observed that the lumbar spine in Marfan has a high prevalence of developmental anomalies such as biconcave vertebrae, transition vertebrae, and lengthened transverse process distance. 5 of our patients had transition vertebrae. Thus, the widened IPD values may simply reflect abnormal growth and formation of the vertebral elements secondary to the connective tissue disorder itself. On the other hand, Pyeritz et al. (1988) found that dural ectasia, a process in which the dural sac balloons in its most caudal portion, is present in the lumbosacral spine in two thirds of Marfan patients. Arroyo and Garcia (1989) describe a case of dural ectasia in a Marfan patient with documented widened IPDs in the lumbar spine. The widened IPDs in our patients may be secondary to dural ectasia.

We also noted a high prevalence of spondylolisthesis (5/32) in our study. This may be due to dural ectasia causing bony erosions and destabilizing the lumbosacral spine causing slippage of the bony elements. It may also be due to the weakened connective tissue structures that support the columns of the lumbosacral spine. thus causing instability and translation. Sponseller et al. (1995) had 5 patients with spondylolisthesis in his series of 82 skeletally-mature patients with Marfan syndrome. The fact that we used DePaepe's criteria, but Sponseller et al. did not, may explain the higher prevalence of spondylolisthesis in our study. Conversely, the increased prevalence in our series may be due to the higher mean age of our population, since Sponseller included all patients who were skeletally mature, the youngest being 16. 2 of the 4 cases of spondylolisthesis in our series were of the degenerative type, indicating that the higher age in our series may have been a factor.

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