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Predictive Value and Interrater Reliability of Radiographic Factors in Neurofibromatosis Patients With Dystrophic Scoliosis

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Abstract

Background: Scoliosis in patients with neurofibromatosis type I (NF1) can manifest as dystrophic or nondystrophic curves. Dystrophic scoliosis is rapidly progressive, rendering treatment challenging. Radiographic characteristics have been reported to predict dystrophic scoliosis, but their reliability and predictive value have not been well described. The purpose of this study is to assess the interobserver reliability for eight radiographic characteristics of dystrophic scoliosis and to evaluate the sensitivity and specificity of these characteristics relative to the gold standard of a definitive clinical diagnosis.

Methods: Spine radiographs of 122 NF1 patients from multiple institutions were graded by five spine surgeons as dystrophic or nondystrophic, based on eight radiographic characteristics of dystrophic modulation: rib penciling, vertebral rotation, scalloping, wedging, spindling of transverse processes, short sharp angular curve, widened interpedicular distance, and atypical location. The curves were classified by each submitting institution as dystrophic or nondystrophic based on clinical outcome. Interobserver reliability analysis was performed using Fleiss kappa.

Results: For the 122 cases, the interrater agreement among the five readers for the diagnosis of dystrophic scoliosis was good at 0.61. The agreement for individual radiographic characteristic ranged from 0.62 for wedging to 0.14 (poor) for scalloping. Surgeons underestimated the number of dystrophic curves, rating from 45% to 67% of the curve patterns as dystrophic, compared to the gold standard, which revealed 68% of the curves to be dystrophic. On multivariate analysis, rib penciling, vertebral rotation, vertebral wedging, and atypical location were significantly associated with true dystrophic status (odds ratios of 2.4, 3.0, 2.4, and 3.0, respectively).

Conclusion: Overall dystrophic diagnosis can be assessed by radiographic characteristics. Better understanding of the predictive value of specific radiographic features may assist in early diagnosis of patients with dystrophic NF and assist surgeons in identifying dystrophic curve patterns and instituting prompt, appropriate treatment.

Level of Evidence: Level III.

Keywords: Nondystrophic; Modulation; Neurofibroma; Rib penciling

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Introduction

Neurofibromatosis Type 1 (NF1) is an autosomal dominant genetic disorder occurring in approximately 1:4000 individuals worldwide across all ethnicities [1]. The *NF1* gene mutation leads to loss of the neurofibromin protein that downregulates p21-Ras, an oncogene. For unknown reasons, scoliosis, kyphosis, and spinal deformity are among the most common skeletal problems in patients with NF1 with a prevalence of 8% to 60% [2,3]. A distinctive osseous lesion such as dystrophic scoliosis is included in the clinical criteria for diagnosis of NF1 [4]. There are two types of scoliosis associated with NF1—nondystrophic and dystrophic curve patterns [5]. Nondystrophic scoliosis behaves and evolves similarly to that of idiopathic scoliosis and may be amenable to bracing and observation. Dystrophic changes do not always appear at initial presentation and may progress over time. Dystrophic scoliosis is associated with rapid progression and poor prognosis and has specific radiographic findings (Table 1) [5]. Therefore, the development and validation of a radiographic scheme to distinguish dystrophic and nondystrophic disease would be beneficial, allowing for early detection and appropriate treatment interventions. Careful validation of these predictive factors may facilitate early detection and timely treatment interventions to improve outcomes, as dystrophic curve patterns frequently require surgical management [6].

Predictive rating systems must have high interrater reliability to be generalizable. There is limited data regarding the interrater reliability of the specific radiographic features of a dystrophic curve pattern. We hypothesized that the early radiographic findings of NF1 dystrophic scoliosis as described by Durrani et al. would have a high interrater reliability and be predictive of future progressive dystrophic disease [5]. We further sought to determine which specific radiographic factors seen on presenting radiographs are most predictive of a dystrophic curve.

Table 1
Nine radiographic characteristics of dystrophic deformity in neurofibromatosis type 1*.

Characteristics	% incidence
Rib penciling	62
Vertebral rotation	51
Posterior vertebral scalloping†	31
Vertebral wedging	36
Spindling of transverse processes	31
Anterior vertebral scalloping†	31
Widened interpedicular distance	29
Enlarged intervertebral foramina†	25
Lateral vertebral scalloping†	13

* From Durrani AA, Crawford AH, Choudry SN, et al. *Spine* 2000.
† For this study, anterior/posterior/lateral scalloping and enlarged intervertebral foramina were considered as one parameter.

Methods

A digitized multicenter database of 122 presenting radiographs for established patients with scoliosis, NF1, and known clinical outcome (dystrophic vs. nondystrophic curve pattern) was assembled. Sites submitted PA and lateral radiographs taken at presentation to orthopedics for the database. Cases included patients with operative and nonoperative management, and sites were asked to submit cases across the spectrum of their practice with a variety of disease severity. Sites also submitted the 'gold standard' diagnosis, as these patients had been followed over time at the individual sites until either surgical intervention or skeletal maturity. The sites thus provided the 'gold standard' diagnosis for each case based on behavior of the curve over time. Further data such as age at presentation, genetic confirmation of diagnosis, indications for surgical treatment, or outcomes were not collected. Five experts who specialize in NF1 spinal deformities evaluated a series of spinal radiographs to assess interrater reliability