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The Correlation of Specific Orthopaedic Features of Polyostotic Fibrous Dysplasia with Functional Outcome Scores in Children

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Background: Polyostotic fibrous dysplasia has a wide clinical spectrum, with substantial variation between patients in terms of orthopaedic manifestations, including the number of fractures, the degree of deformity of the limbs, and the presence of scoliosis. Data from bone scans, skeletal surveys, and records were correlated with the Pediatric Outcomes Data Collection Instrument scales to examine whether any specific facet of orthopaedic involvement could be related to functional abilities.

Methods: All patients who were sixteen years of age or younger and who were part of an ongoing natural history study of polyostotic fibrous dysplasia (including McCune-Albright syndrome) were sent an age-appropriate Pediatric Outcomes Data Collection Instrument outcomes tool. The medical records and radiographs of the patients who returned forms were reviewed. Radiographic measurements of scoliosis, the femoral neck-shaft angle, and limb deformities were then performed. The extent of skeletal involvement with polyostotic fibrous dysplasia (disease burden) was assessed on bone scans with use of a validated tool. A chart review was performed to determine the fracture rate, the use of bisphosphonates, and the endocrine status. These measurements were correlated with the Pediatric Outcomes Data Collection Instrument scores.

Results: The outcomes tool was sent to twenty-seven patients and the completed instrument was returned by twenty patients, for a response rate of 74%. The parent-child form was filled out for twelve patients and the parent-adolescent form was filled out for eight patients. The mean standardized Pediatric Outcomes Data Collection Instrument scores for all twenty patients were lowest for sports (62; range, 14 to 100) and happiness (72; range, 25 to 100). Adolescents and parents disagreed with regard to sports (with adolescent scores being higher than parental scores) and pain (with parental scores being higher than adolescent scores). However, the overall global scores correlated well between the parents and the adolescents ($r = 0.78$, $p = 0.03$) . The femoral neck-shaft angle correlated strongly with the Pediatric Outcomes Data Collection Instrument score for sports ($r = 0.46$, $p = 0.03$) but not for transfers. The bone scan scores for the lower extremity disease burden correlated with both the transfer scale ($r = 0.76$, $p = 0.03$) and the sports scale ($r = 0.77$, $p = 0.02$). Deformity of the limbs, the presence of scoliosis, the prevalence of endocrine dysfunction, and the number of fractures did not correlate with the Pediatric Outcomes Data Collection Instrument scores.

Conclusions: In patients with polyostotic fibrous dysplasia, the loss of the normal femoral neck-shaft angle and the disease burden in the lower extremities appear to have the greatest effect on functional activity as measured with the Pediatric Outcomes Data Collection Instrument tool.

Polyostotic fibrous dysplasia occurs in association with point mutations during embryogenesis in the $G_s\alpha$ transcript of *GNAS,* resulting in increased production of intracellular cAMP[1]. The mutation in osteogenic cells and their precursors results in an inhibition of differentiation and an accumulation of osteogenic precursors and fibrous tissue in place of marrow[1,2]. In fibrous dysplastic lesions of bone, the bone trabeculae are poorly mineralized, causing a softening of the

TABLE I Characteristics of Patients

	Children (N = 12)	Adolescents (N = 8)	Nonresponders (N = 7)
Mean age *(yr)*	6.4	12.9	10.7
Male:female ratio*	7:5	5:3	3:4
Average no. of fractures per patient	1.6	4.0	1.2
Bisphosphonate use*	4	2	2
Mean bone score scale *(points)*	22	30	19
Precocious puberty*	6	6	4
Hyperthyroidism*	2	4	1
Growth hormone use*	1	1	1
Phosphate wasting*	1	4	1

*The data are expressed as the number of patients.

bone[3,4]. The bone is thus susceptible to failure, resulting in a deformity or fracture[5]. The presence of either café au lait lesions in the skin or endocrinopathy in conjunction with polyostotic fibrous dysplasia defines the McCune-Albright syndrome.

Because of the somatic mosaic nature of the disease[6], polyostotic fibrous dysplasia represents a wide disease spectrum. Some patients have only a few lesions or have lesions of the cranium or ribs that do not cause much loss of skeletal function. Other patients have substantial involvement of the musculoskeletal system with deformities of the hip (coxa vara, shepherd's crook deformity), scoliosis, or angular deformities of the limbs[7].

Orthopaedic treatment of polyostotic fibrous dysplasia has not been standardized. Clear guidelines may be lacking because of the rarity of this condition, so the decision to correct a deformity surgically or to prevent further fractures of bone is decided on a case-by-case basis by individual surgeons. It is possible that a determination of which specific aspects of the disease are associated with functional morbidity will aid in the development of treatment guidelines. By obtaining functional outcome data on patients with polyostotic fibrous dysplasia and by correlating function with disease burden and deformity with use of a variety of different tools (including bone scans, radiographic measurements, and patient history), we hypothesized that the Pediatric Outcomes Data Collection Instrument (PODCI) tool would be able to allow identification of the particular facets of the disease spectrum that have the most impact on function.

Materials and Methods

Patients

An ongoing, institutional-review-board-approved natural history study of patients with polyostotic fibrous dysplasia included a subpopulation of twenty-seven patients who were sixteen years of age or younger. As part of the natural history study, patients were managed with a standardized protocol and were evaluated with yearly technetium-99 bone scans, a skeletal survey, and a battery of laboratory tests to assess endocrine function. For this specific study, patients were sent the PODCI, which was downloaded from the American Academy of Orthopaedic Surgeons web site (www.aaos.org). The tool, developed by the American Academy of Orthopaedic Surgeons and the Pediatric Orthopaedic Society of North America, is broken down into individual scales. The upper extremity scale measures the ability to perform activities of daily living and upper extremity function in school; the transfer scale is designed to measure routine motion and mobility; the sports scale is designed to measure higher functional abilities making participation in sports possible; the pain scale is designed to evaluate pain that has occurred during the previous week; the happiness scale is designed to rate self-satisfaction and the ability to fit in and be like other children; and the global scale is an average of all of the previously mentioned scales. The PODCI tool was selected as the most effective instrument for the assessment of neuromuscular function in children and adolescents[8,9]. Children who were ten years of age or younger were sent the parent-child version, and adolescents were sent both the adolescent form and the parent-adolescent form. Twenty-eight outcomes instruments were returned by twenty subjects. Twenty-seven patients had been sent questionnaires, for a response rate of 74%. The parent-child form was filled out for twelve subjects with an average age of 6.4 years; seven subjects were male, and five were female. The parent-adolescent form and/or the adolescent form was filled out for eight subjects with an average age of 12.9 years; five of these subjects were male, and three were female (Table I).

Radiographic Measurements

As part of the natural history study, patients underwent annual radiographic skeletal surveys, which were available for review. Radiographs of the femur, tibia, humerus, radius, ulna, and spine were categorized as demonstrating (1) normal findings, (2) the presence of lesions without deformity, or (3) the presence of lesions with deformity. When there was deformity, it was measured, as was the direction of deformity (primarily varus or valgus). The femoral neck-shaft angle was measured, and the Cobb angle was utilized to quantify the degree of scoliosis or kyphosis. In addition, all of the deformities in the

bones of the limbs were correlated with the PODCI scores.

Skeletal Disease Burden

On the basis of the bone scans that were available for every subject, skeletal disease burden was determined as described by Collins et al.[10]. This score, obtained by grading the amount of disease in eleven discrete skeletal locations in a nonlinear gradient, has been shown to have excellent interobserver and intraobserver agreement[10]. In addition to the total skeletal burden scores, the amount of involved bone in each anatomical segment was analyzed and correlated with individual PODCI scores.

Other Analyses

Patient histories were reviewed to determine the number of fractures that the patient had sustained as well as the patient's medication history, including the use of bisphosphonates[11]. As polyostotic fibrous dysplasia is known to be associated with endocrine abnormalities, patients underwent standardized laboratory testing for endocrinopathies, including precocious puberty, hyperparathyroidism, hyperthyroidism, acromegaly, and Cushing syndrome, according to the study protocol. Patients also were tested for phosphaturia to rule out renal phosphate wasting, which is prevalent in patients with fibrous dysplasia and McCune-Albright syndrome and has been recently shown to be correlated to increased serum levels of fibroblast growth factor-23[12].

Statistical Analyses

Statistical analyses were performed with the use of SAS software (version 8.2; SAS Institute, Cary, North Carolina). Means were compared with use of one-way analysis of variance. Data from the radiographic measurements were evaluated in two separate analyses: one analysis evaluated lesions that were not causing deformity, and the second analysis evaluated lesions that were causing deformity and assessed the actual amount of deformity at the site of each lesion. Because patients had one outcome score but two limbs, data from right and left limbs either were averaged together (as was the case for bone scan scores) or were examined on the basis of a minimum or maximum value (as was the case for neck-shaft angles and angular deformities in the long bones).

Results

Outcomes Scales

The mean PODCI scores for the entire study population were lowest for sports (62; range, 14 to 100) and happiness (72; range, 25 to 100) (Fig. 1). Bisphosphonate use was noted as a possible factor that might affect the pain scale. Six patients had a history of pamidronate use (primarily for bone pain) or alendronate use (as part of a research study); however, there was no correlation between the pain scale and bisphosphonate use. The PODCI scales for the entire population were correlated with happiness. Significant correlations were found between happiness and transfers ($r = 0.60$, $p < 0.005$), pain ($r = 0.60$, $p < 0.05$), and sports ($r = 0.55$, $p < 0.05$).

Parental Reporting Compared with Self-Reporting on the Adolescent Forms

The differences in reporting between parents and children showed discrepancies in the sports and pain scales, with adolescent scores being higher than parental scores on the sports scale and with parental scores being higher than adolescent

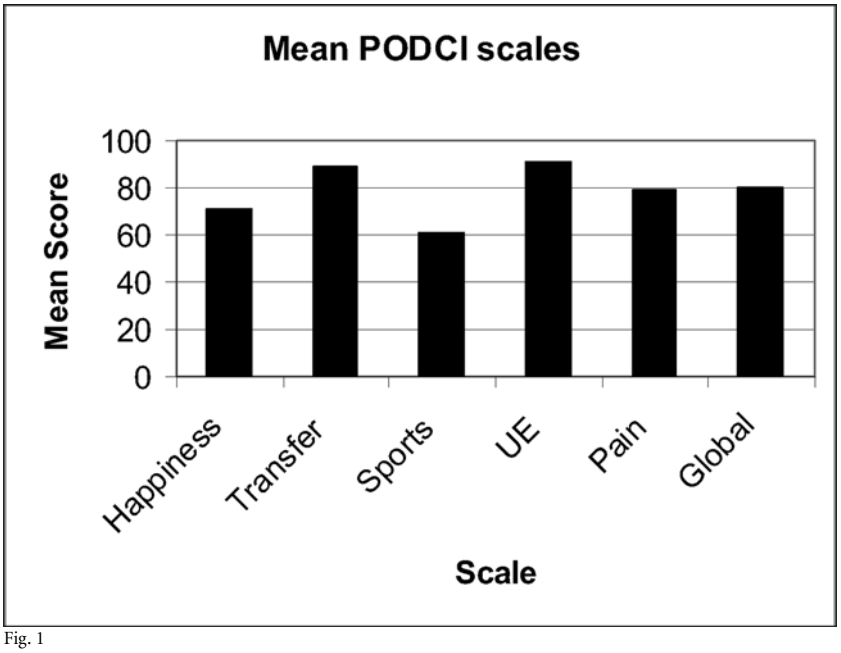

Fig. 1

Graph illustrating the mean scores on the PODCI standardized scales. The lowest scores are for sports and happiness. UE = upper extremity.

scores on the pain scale (Fig. 2). The global scales given by the parents and adolescents were comparable ($r = 0.78$, $p = 0.03$).

Child Forms Compared with Adolescent Forms

With the numbers available, there were no significant differences between the mean scores for the twelve patients whose parents filled out the child form and those for the eight patients whose parents filled out the adolescent form.

Endocrinopathy

With the numbers available, precocious puberty, hyperthyroidism, Cushing syndrome, phosphate wasting, and acromegaly did not correlate with any of the PODCI scales.

Skeletal Disease Burden Data

With use of a previously described method[10], bone scan scores were utilized to estimate the amount of disease burden by determining the ratio of normal to diseased bone. When bone scans were examined according to distinct anatomic locations, the lower extremity scores correlated with both the transfer scale ($r = 0.76$, $p = 0.03$) and the sports scale ($r = 0.77$, $p = 0.02$). However, the cumulative bone scan scores had no significant relationship with any of the PODCI scales.

Scoliosis

Ten of the twenty patients had scoliosis, with the majority having very small curves (average Cobb angle, 17°; range, 14° to 38°). Only one patient had excessive kyphosis, but it was to a mild degree, with a Cobb sagittal angle of 48°. No patient had been managed with bracing or surgery for the treatment of scoliosis. With the numbers available, the presence of scoliosis did not correlate with any of the PODCI scales.

Fractures

No subject was currently undergoing treatment for an acute fracture. Fifty-one fractures occurred among the twenty patients who returned the survey, with more cumulative fractures reported in the adolescents than the children. Children who were less than ten years of age had a mean of 1.6 fractures per patient, whereas adolescents had a mean of 4.0 fractures per patient (Table I). With the numbers available, the number of fractures did not correlate with any of the PODCI scales.

Femoral Neck-Shaft Angle

The mean femoral neck-shaft angle (and standard deviation) was 120° ± 24° (range, 62° to 150°). The first statistical analysis evaluated the actual femoral neck-shaft angles, with the right and left neck-shaft measurements for each subject being compared with the outcome scales. The second statistical analysis evaluated the minimum and maximum femoral neck-shaft angles for each subject to better correlate the two femoral neck-shaft values with one set of functional outcome scores. A

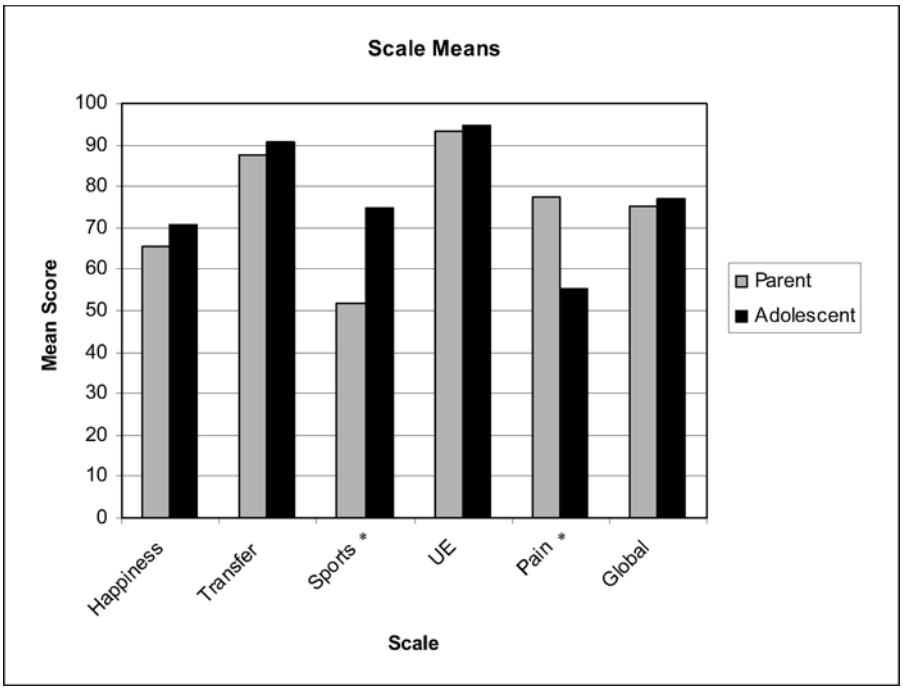

Fig. 2

Graph illustrating the comparison of the normative scales for adolescents who self-reported with use of the adolescent form with those for adolescents whose parents completed the parent-adolescent form. The adolescents reported higher sports scores than did the parents, whereas the parents reported higher pain scores than did the adolescents. The global scores were comparable. UE = upper extremity. *$p \leq 0.05$.

TABLE II Description of Skeletal Lesions by Location

Bone Quality	Number of Limbs	Amount of Deformity *(deg)*
Humerus		
Normal	15	
Disease	20	
Deformity	5	
Valgus	1	13
Varus	4	10, 18, 20, 55
Forearm		
Normal	13	
Disease	18	
Deformity	9	
Valgus	8	6, 10, 10, 11, 12, 12, 18, 20
Varus	1	12
Femur		
Normal	6	
Disease	24	
Deformity	10	
Valgus	2	8, 12
Varus	8	5, 10, 11, 17, 20, 20, 23, 40
Tibia		
Normal	17	
Disease	17	
Deformity	6	
Valgus	4	7, 8, 9, 12
Varus	2	10, 10

significant negative correlation was demonstrated in both analyses, with a decrease in the neck-shaft angle correlating with the sports scale ($r = 0.46$, $p = 0.03$) but not with the transfer scale or any of the other PODCI scales.

Presence of Extremity Disease and Deformity

The skeletal survey radiographs of long bones were categorized as demonstrating (1) normal findings (no lesions of fibrous dysplasia in the bone), (2) bone lesions but no deformity, or (3) both bone lesions and angular deformity. Both right and left sides were examined. With regard to the upper extremity, twenty-eight limbs were normal, thirty-eight limbs had bone lesions but no deformity, and fourteen limbs had bone lesions and deformity (Table II). With regard to the lower extremity, twenty-three long bones were normal, forty-one had lesions without deformity, and sixteen had an angular deformity in the shaft (the femoral neck shaft was excluded in this analysis because neck-shaft angles were evaluated separately). With the numbers available, no correlations were found between the PODCI scales and the presence or absence of bone lesions or between the PODCI scales and the amount of angular deformity.

Discussion

In this group of young patients with fibrous dysplasia, the femoral neck-shaft angle was correlated with the PODCI scale for sports. Thus, decreases in the femoral neck-shaft angle may play a role in inhibiting children with polyostotic fibrous dysplasia from the higher levels of function required to participate in sports but do not hinder them from the lower functional skills required for transfer activities. This finding supports the need for a future multicenter clinical trial focusing on correction of the deformity in the proximal part of the femur, with preoperative and postoperative PODCI scores being used to assess improvement in outcomes, particularly on the sports scale.

The amount of bone involvement in the lower, but not the upper, extremities also correlated with functional ability. Unlike the neck-shaft angle, which can be improved through operative intervention, the amount of disease that is present in the lower extremities cannot be decreased currently; however, intramedullary rod fixation is used to stabilize the long bones and to limit the number of fractures. Improvement in quality-of-life parameters was reported for a small cohort of five children undergoing both intramedullary rodding and bisphosphonate treatment[13]. However, additional clinical studies will be necessary in order to determine the indications for prophylactic intramedullary rod fixation in patients with polyostotic fibrous dysplasia.

Some of our findings were unexpected. A child with a large number of fractures might have been predicted to report limitations in the sports, transfer, global, and happiness scales, but we did not find this to be the case. Perhaps the transient nature of fractures and fracture treatment, leading to the eventual return to baseline activity, was responsible for the lack of any correlation between the number of fractures and scores. As no patient was undergoing active treatment for a fracture at the time of the survey, the memory of increased disability resulting from past fractures may have been short-lived. The fact that fractures per se do not appear to be associated with a change in function could be reassuring to parents of children with polyostotic fibrous dysplasia.

The prevalence of scoliosis in the population was lower than that in our previous report on scoliosis in adults with polyostotic fibrous dysplasia[14]. Some of the children may be expected to have development of scoliosis during adolescence and were still too juvenile to rule out the development of a future curvature. Scoliosis did not appear to independently impact the functional outcomes scales; however, most patients or their parents were not aware of the presence of a scoliotic curve and no treatment for scoliosis had been used. In a study by Lerman et al.[15], patients with adolescent idiopathic scoliosis had lower-than-normal scales for sports, pain, and happiness, with the magnitude of the Cobb angle correlating with a decrease in the numerical value of the scales.

Deformities in the lower and upper extremities did not appear to correlate with a decrease in function in the present study; however, the number of patients with a deformity was small and the degree of deformity in our patients was relatively mild.

The present study involved the use of an outcomes tool in a new manner, in a group of patients with multiple orthopaedic issues, to determine the specific orthopaedic problems that had

the greatest effect on patient function. However, our data may be biased by the fact that all of the patients were evaluated with the outcomes tool as part of an ongoing research study and all filled out the form at our request and not as part of a routine medical visit—the setting for which the PODCI tool was designed. By taking on the role of a research subject, parents or adolescents may have been more susceptible to answering the outcomes tool with a bias toward producing expected responses. This phenomenon, in which responses are targeted in an attempt to please the researcher, known as the Hawthorne effect[16], may have been present in this study. This could potentially account for the strongly *positive* correlation between the pain and happiness scales in this patient population. While the ability to play sports and to perform transfers may be expected to lead to happiness, increased pain would not be expected to correlate with an increase in the happiness scale at first glance. An alternative explanation may be that participation in sports leads to an increase in bone pain. If this latter explanation is true, then physicians need to treat bone pain more aggressively in children who have polyostotic fibrous dysplasia.

Polyostotic fibrous dysplasia can produce a myriad of orthopaedic disorders, with loss of the normal femoral neck-shaft angle being the most commonly seen deformity[13]. Surgery to stabilize the bone and to correct the deformity can be complex. The usual plate-and-screw implants achieve less rigid fixation in diseased bone than in normal bone, and bone graft materials are often resorbed over time[17]. The present study suggests that proximal valgus femoral osteotomy may help to improve function; however, the complications of attempting this procedure may outweigh the benefits of correcting the mechanical deformity. A multicenter study involving the use of preoperative and postoperative outcomes tools will be necessary to determine whether there is a lasting benefit from proximal valgus femoral osteotomy in this complex group of young patients. ■

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