

Assessment Tools of Physical and Functional Disability in Fibrodysplasia Ossificans Progressiva

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Background and Objectives

FOP is a rare, genetic disease of congenital skeletal malformations and progressive heterotopic ossification (HO) that irreversibly restricts movement and physical function. An on-going, 3-year, global, natural history study (NHS, NCT02322255) of FOP is being conducted to define possible endpoints in interventional studies of therapeutics to treat FOP.

A total of 114 individuals (~14% of the world's known population of FOP patients) from 24 countries were enrolled at seven sites: two in the United States, one each in France, United Kingdom, Italy, Argentina, and Australia. The first subject enrolled on 18 December 2014; the last on 29 December 2016.

One objective of the cross-sectional analysis of baseline data was to determine whether two measures of physical/functional disability, the Cumulative Analogue Joint Involvement Scale for FOP (CAJIS) and the FOP Physical Function Questionnaire (FOP-PFQ), are sensitive to assess disease progression in the context of a clinical study.

Assessments of Physical/Functional Disability

- CAJIS:** an objective measure of joint movement completed by physicians. Developed by the Center for Research in FOP and Related Disorders, range of motion (ROM) across 12 joints (shoulder, elbow, wrist, hip, knee, ankle on both right and left), and three body regions (cervical spine [neck], thoracic/lumbar spine and jaw) are each assessed as: 0=uninvolved; 1=affected; 2=functionally ankylosed. The total score range is 0-30.
- FOP-PFQ:** a disease-specific patient-reported outcome measure. Age-appropriate forms assess functional impairment experienced by subjects; includes questions related to activities of daily living and physical performance. Data are analyzed as a percent of the total possible score, with higher percentages representing greater functional impairment.

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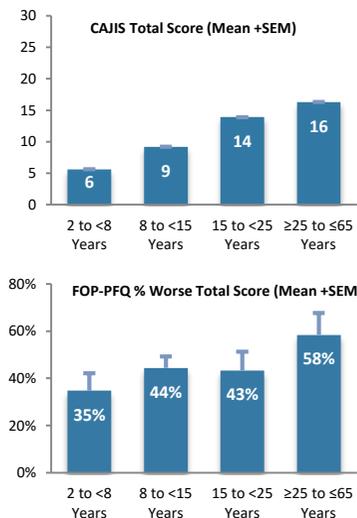
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Demographics and Baseline Disease

		2 to <8 (N=17)	8 to <15 (N=36)	15 to <25 (N=34)	≥25 to ≤65 (N=27)	Total (N=114)
Age (years)	Mean ±SEM	5.9 ±0.3	11.4 ±0.3	18.9 ±0.5	31.7 ±1.3	17.6 ±0.9
	Min, max	4, 7	8, 14	15, 14	25, 56	4, 56
Males	n (%)	9 (52.9)	24 (66.7)	16 (47.1)	13 (48.1)	62 (54.4)
Age at 1 st flare-up	Mean ±SEM	2.9 ±0.5	4.4 ±0.6	5.6 ±0.9	7.2 ±1.0	5.2 ±0.4
	Min, max	1, 6	0, 13	0, 17	0, 20	0, 20
Years since last flare-up	Mean ±SEM	0.7 ±0.2	1.5 ±0.5	1.5 ±0.3	2.3 ±0.7	1.6 ±0.3
	Min, max	0, 2.7	0, 13.5	0, 6.9	0, 15.1	0, 15.1
# flare-ups last 12 months	Mean ±SEM	2.9 ±0.7	6.9 ±2.3	2.2 ±0.4	1.9 ±0.4	3.8 ±0.8
	Min, max	1, 10	1, 40	1, 8	1, 7	1, 40

- There was good representation across the age categories.
- Baseline characteristics were similar to the 500 participants in a retrospective, international survey of FOP (Pignolo et al., 2016).

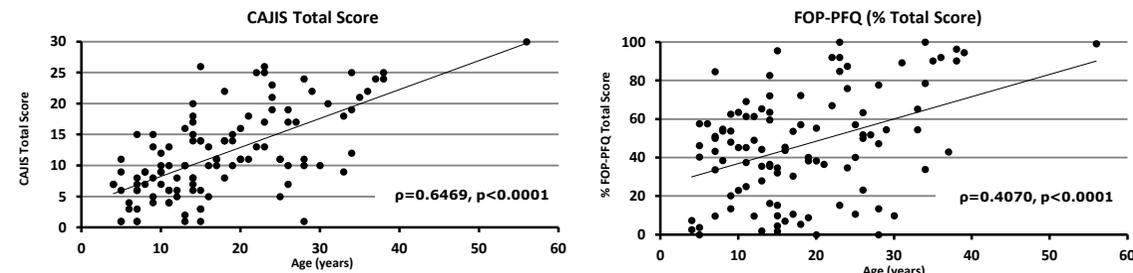
Baseline CAJIS and FOP-PFQ by Age Category



In general, the mean baseline CAJIS and FOP-PFQ scores worsened with age.

Results

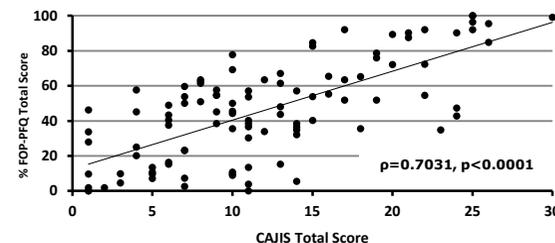
Correlations Between Age and Measures of Physical/Functional Disability



- CAJIS and FOP-PFQ scores worsen over the course of this disease as shown by the positive correlations between age and both assessments.
- The estimated annual mean changes in each of these assessment tools, based on a linear regression model, were small: 0.47 units for the CAJIS and 1.2% for the FOP-PFQ.

The estimated annual mean changes were similar to the observed mean changes (based on 63 subjects in the NHS with available data at baseline and Month 12): 0.70 units for the CAJIS and 3.3% for the FOP-PFQ.

Correlation Between CAJIS and FOP-PFQ



There was a strong correlation between CAJIS and the FOP-PFQ.

As limitations in ROM increase, so does the functional impairment reported by patients with FOP.

Observed Changes in CAJIS and FOP-PFQ at 12 Months

Total CAJIS Score	Mean ±SEM	0.7 ±0.3
	Min, max	-7 to 6
% Worse Total FOP-PFQ	Mean ±SEM	3.3 ±1.5
	Min, max	-39 to 52

Conclusions

- In a cross-sectional analysis of baseline data from 114 subjects with FOP, two measures of physical/functional disability demonstrated disease progression over the lifespan of subjects.
- However, the annual mean changes (estimated and observed) were small.
- While these assessment tools may be useful to assess potential therapeutics for treatment of FOP in the long-term, they are not sensitive to change in a 1- to 2-year timeframe.
- The relationship between the CAJIS and FOP-PFQ and HO as assessed by annual whole body CT scans is currently being assessed.