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Associations between height and health-related quality of life (HRQoL) and functional independence in children with achondroplasia

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Background and Objectives

- Achondroplasia, the most common skeletal dysplasia, is characterized by severe short stature with a height deficit of approximately -6 SDS compared to average stature and is associated with a reduced quality of life[1,2]
- Several studies have assessed the impact of short stature on health-related quality of life (HRQoL)[3]
- Our objective was to evaluate the impact of height deficit on HRQoL and functional independence in children with achondroplasia

Methods

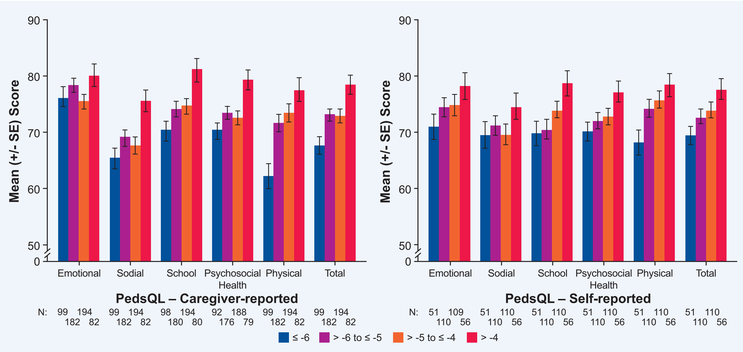
- Height Z-score, HRQoL, and functional independence data were obtained from children with achondroplasia who enrolled in the vosoritide Phase 3 trial (study 111-301; EudraCT number, 2015-003836-11).[4] Subjects completed at least six months of a baseline observational growth study (study 111-901; ClinicalTrials.gov number, NCT01603095) prior to enrolling in the Phase 3 trial and the subsequent open label extension study (study 111-302; ClinicalTrials.gov number, NCT03424018)
- Height Z-scores were assessed every 3 months
  - Height Z-scores were derived using age-sex specific reference data (means and standard deviations) in reference to Centers for Disease Control and Prevention (CDC) normative data on average stature children
- The Pediatric Quality of Life Inventory (PedsQL)[5], the Quality of Life in Short Stature Youth (QoLISSY)[6], and the Functional Independence Measures in Children (WeeFIM)[7] questionnaires were completed by the children and/or their caregivers every 6 months
  - For both PedsQL and QoLISSY, self-reporting started at age 8 years
  - The WeeFIM considers the child's functional performance from the perspective of caregivers, and is therefore only completed by caregivers
- All visit matched pairs of height Z-score and HRQoL data pooled from studies 901, 301 and 302 were analyzed using a mixed effect model to assess the relationship of a 1 SDS change in height deficit on domain scores of the PedsQL, QoLISSY, and WeeFIM, without reference to treatment assignment or timepoint
  - All pairs of assessments (height Z-scores and HRQoL scores) were categorized according to the height Z-score classifications: ≤ −6, > −6 to ≤ −5, > −5 to ≤ −4, > −4 SDS below the average stature. Mean HRQoL scores were calculated for each category

Results

Participant characteristics

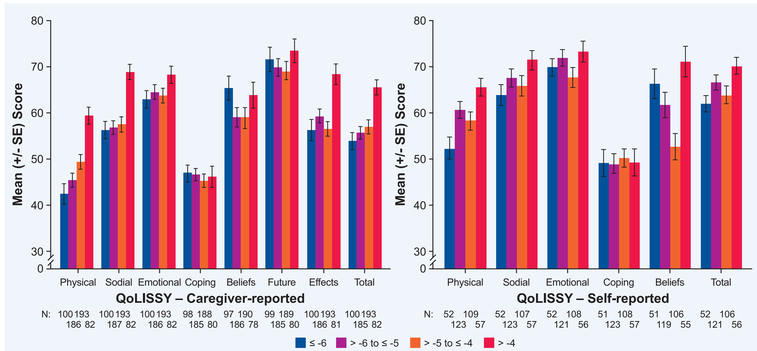
- 121 children (64 boys, 57 girls) were included in this exploratory analysis
- Age at the time of individual assessments ranged from 4–15 years

PedsQL and height Z-score



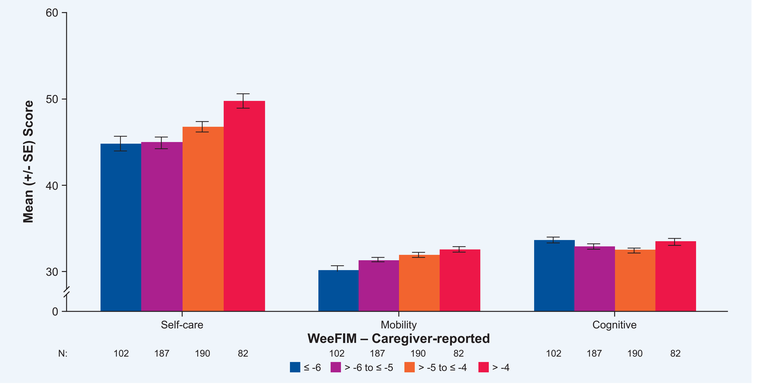
Reported Domain/ Total Score	Number of Observations	Estimate of coefficient for height Z-score		
		Parameter Estimate (Standard error)	95% Confidence Interval	P-value
Caregiver Reported:				
Emotional	557	1.52 (1.05)	-0.56, 3.59	0.1510
Social	557	2.73 (1.18)	0.42, 5.05	0.0209
School	552	3.56 (1.13)	1.35, 5.77	0.0017
Psychosocial Health Summary	535	2.74 (0.95)	0.88, 4.61	0.0040
Physical	557	4.36 (1.27)	1.87, 6.85	0.0006
Total Score	**557**	**3.26 (0.97)**	**1.35, 5.17**	**0.0008**
Self-Reported:				
Emotional	326	1.54 (1.35)	-1.13, 4.21	0.2560
Social	327	-0.21 (1.38)	-2.93, 2.51	0.8781
School	327	2.78 (1.23)	0.35, 5.20	0.0252
Psychosocial Health Summary	327	1.40 (1.04)	-0.66, 3.45	0.1819
Physical	327	2.10 (1.19)	-0.25, 4.45	0.0803
Total Score	**327**	**1.63 (0.99)**	**-0.33, 3.58**	**0.1025**

QoLISSY and height Z-score



Reported Domain/ Total Score	Number of Observations	Estimate of coefficient for height Z-score		
		Parameter Estimate (Standard error)	95% Confidence Interval	P-value
Caregiver Reported:				
Physical	561	4.83 (1.27)	2.34, 7.31	0.0002
Social	562	3.21 (1.24)	0.77, 5.64	0.0099
Emotional	561	0.71 (1.27)	-1.77, 3.20	0.5730
Coping	551	-0.71 (1.18)	-3.02, 1.61	0.5477
Beliefs	551	0.55 (1.75)	-2.90, 4.00	0.7534
Future	553	-0.44 (1.59)	-3.57, 2.69	0.7829
Effects	560	2.15 (1.35)	-0.50, 4.79	0.1115
Total Score	**560**	**2.88 (1.14)**	**0.64, 5.13**	**0.0119**
Self-Reported:				
Physical	341	3.83 (1.39)	1.10, 6.56	0.0061
Social	339	2.43 (1.48)	-0.49, 5.36	0.1021
Emotional	337	1.25 (1.45)	-1.61, 4.11	0.3889
Coping	339	-0.87 (1.55)	-3.92, 2.17	0.5736
Beliefs	330	1.46 (2.09)	-2.66, 5.57	0.4861
Total Score	**334**	**2.72 (1.27)**	**0.22, 5.21**	**0.0328**

WeeFIM and height Z-score



Caregiver Reported Domain/ Total Score	Number of Observations	Estimate of coefficient for height Z-score		
		Parameter Estimate (Standard error)	95% Confidence Interval	P-value
Caregiver Reported:				
Self-Care	561	1.36 (0.53)	0.32, 2.40	0.0103
Mobility	561	0.71 (0.23)	0.27, 1.15	0.0018
Cognitive	561	-0.10 (0.26)	-0.61, 0.41	0.7017
Total Score	**561**	**1.96 (0.80)**	**0.39, 3.52**	**0.0144**

- For all instruments, mean scores were generally lower in subjects with greater height deficit (≤ -6 SDS) compared to taller subjects with height Z-score greater than -4 SDS
- Clear linear relationships between height Z-scores and several domain scores were observed, most notably in the PedsQL Physical domain, the height-specific QoLISSY Physical domain, and the WeeFIM Self-care and Mobility domains
- These data corroborate other findings that suggest height Z-score is a predictor of physical functioning and overall HRQoL[8]

Conclusions

- These data suggest that height deficit in achondroplasia impacts HRQoL and function
- Therapies that have the potential to reduce height deficit in achondroplasia may improve HRQoL and functional independence

References

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