Patient-reported Outcomes in Arthrogryposis

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Background: Little is known about patient-reported health status in children and adolescents with arthrogryposis. Utilizing the Patient-Reported Outcome Measurement Information System (PROMIS) and Pediatric Outcomes Data Collection Instrument (PODCI) questionnaires, we investigated functional and psychosocial measures in arthrogryposis.

Methods: A total of 118 patients with arthrogryposis were identified from a prospective longitudinal cohort (the Congenital Upper Limb Difference Registry) from 2014 to 2018. Demographics and patient-reported outcome measures were evaluated, including the PROMIS [upper extremity (UE) function, pain, depression, anxiety, and peer relations] and PODCI questionnaires (UE function, pain, happiness, and global function).

Results: A total of 29 arthrogrypotic patients had complete PROMIS and PODCI data. This cohort was divided into distal arthrogryposis and amyoplasia groups, with 15 and 14 patients in each group, respectively. There were 8 males in the distal arthrogryposis group with a median age of 9 years and 7 males in the amyoplasia group with a median age of 8 years. For both cohorts, the median UE function PROMIS scores were significantly below population norms, 31 for distal arthrogryposis and 22 for amyoplasia. PODCI UE function was statistically lower for amyoplasia compared with the distal arthrogryposis cohort. PROMIS pain, depression, anxiety, and peer relations were in the normal range for both amyopasia and distal arthrogryposis. Median PODCI pain and happiness ranged from 85 to 88 for all patients with no statistical difference between groups.

Conclusions: Arthrogryposis patients have lower UE function scores compared with population normals, but they have emotional states that are consistent with populations norms. Amyoplasia patients were functionally worse than distal arthrogryposis patients.

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Patient-reported outcomes aid in our understanding of patient health status in many domains including function and psychosocial states. The Pediatric Outcomes Data Collection Instrument (PODCI) has been used as the traditional tool in pediatric orthopaedics to assess outcomes.[1] More recently, the National Institute of Health developed the Patient-Reported Outcome Measurement Information System (PROMIS),[2,3] which can be tailored for pediatrics and provides another instrument to assess a wide variety of outcomes, such as function, pain, and mental well-being.[4–10] Recently investigators have begun to look at subjective outcomes in the pediatric orthopaedic population, in both the traumatic[11] and congenital populations.[12,13] At this time, subjective outcomes measures have not been applied directly to the upper limb in the arthrogryposis population.

Arthrogryposis is a condition that ranges in severity and spans a wide spectrum of involvement,[14] from amyoplasia to distal involvement only and, less commonly to neurogenic causes. Arthrogrypotic patients typically have multiple joint contractures and underdeveloped muscles and joints. Classically, amyoplasia affects the upper and lower extremities, with limited shoulder motion together with postures of elbow extension, wrist flexion, thumbs in palm, and fingers with limited motion. In contrast, distal arthrogryposis primarily involves the distal aspects of the limbs, including finger (typically camptodactyly) and thumb contractures and club feet. The effects of these conditions on perceived upper extremity (UE) function, pain, and psychological well-being have yet to be reported. In this study we investigated UE functional and psychosocial measures in patients with arthrogryposis, comparing amyoplasia and distal only involvement, utilizing the PROMIS and PODCI questionnaires.

METHODS

After IRB approval, all patients with the diagnosis of arthrogryposis were identified from the Congenital Upper Limb Differences (CoULD) registry, a multicenter (7 institutions) prospective longitudinal cohort study of patients with congenital hand and UE differences. For inclusion into the registry, patients are only eligible before any surgical intervention. Patients with arthrogryposis

were divided into amyoplasia versus distal arthrogryposis, based upon surgeon applied classification. Distal arthrogryposis is defined as contracture or ≥ 2 body parts,[14] at the wrist level or distal. Patients with neurogenic causes of arthrogryposis were not included in this study secondary to confounding effects of the neurologic condition on psychological development. The timeframe of inclusion was 2014 to 2018. Only patients with completed PODCI and PROMIS questionnaires were included (minimum of 5 y of age). Minimum age for the PODCI is 2 years, but PROMIS only applies to 5 years of age and older. Parent (as proxy) reported PODCI and PROMIS questionnaires were utilized and administered at the same time point. PODCI scores range from 0 to 100 with 0 being the worse and 100 being the best/normal. UE function, pain, happiness, and global function domains for PODCI were utilized. PROMIS scores range from 0 to 100 with 50 being normal, a SD of 10, and a higher the score denoting a greater amount of the domain being measured is present. Domains for PROMIS included were UE function, pain interference, depression, anxiety, and peer relations. Patient demographics were also included.

Patient and condition characteristics were summarized for analyzable subjects by frequency and percent or median and interquartile range, as appropriate. Comparisons in demographic characteristics and patient-reported outcome measures were conducted using Fisher exact test, Student *t* test, or Wilcoxon rank sum test, as appropriate. All tests were 2 sided and *P* values <0.05 were considered significant.

RESULTS

From the CoULD registry, 118 arthrogrypotic patients were identified with arthrogryposis, and 29 (18%) with complete PROMIS and PODCI data were included in this analysis. A total of 84 patients were too young for inclusion and 5 patients had incomplete forms. There were 15 amyoplasia patients including 7 males and an overall median age of 8 years (range, 6 to 10 y). There were 14 distal arthrogryposis patients including 8 males and median age of 9 years (range, 8 to 12 y). There were no differences across arthrogryposis subgroups with respect to patient age ($P = 0.44$) or sex ($P = 0.57$) (Table 1).

For both cohorts, the median UE function PROMIS scores were well below population norms; patients with distal arthrogryposis had higher UE scores compared with amyoplasia (median, 31 vs. 22; $P = 0.004$). Both cohorts had normal peer relationship scores, but amyoplsia had statistically lower scores (median, 46 vs. 56; $P = 0.04$) (Table 1 and Fig. 1). There was no difference detected across subgroups for PROMIS pain ($P = 0.88$), depression ($P = 0.20$), or anxiety ($P = 0.84$).

The PODCI outcome domain scores demonstrated that those with distal arthrogryposis also had higher UE scores compared with amyoplasia (median, 75 vs. 42; $P < 0.001$) and higher global function scores (median, 87 vs. 54; $P = 0.007$) (Table 1 and Fig. 2). There was no difference detected across subgroups for PODCI pain ($P = 0.82$) or happiness ($P = 0.40$).

DISCUSSION

Arthrogryposis limits function of the upper extremities, specifically grasp and fine motor function secondary to congenital contractures and underdevelopment of muscle. Although objective measurements of task performance can delineate these limitations, the perceived functional limitations by families and patients and the overall psychological well-being of pediatric patients with arthrogryposis have not been previously reported with objective measures. Psychosocial aspects have been investigated in an adult arthrogryposis population, through assessment of 2 studies conducted in Norway.[15] Steen el al[15] identified through focus groups that the use of wheelchairs, influenced a patient's social interactions, but universally patients desired more research on how they could improve their wellness and social acceptance. Another study identified 52 arthrogrypotic patients, 27 adults patients included, with a range of severity of involvement.[16] From this cohort, Sodergard et al[16] reported that as a group, arthrogrypotic patients "cope well

TABLE 1. Demographics and Median PROMIS and PODCI Scores

Characteristics	Median (IQR)			*P*
	All Subjects (N = 29)	Distal Arthrogryposis (n = 14)	Amyoplasia (n = 15)	
Age (y)	9 (6-11)	9 (8-12)	8 (6-10)	0.44
Sex (% male individuals)	15 (52)	8 (57)	7 (47)	0.57
PROMIS domains				
Pain	50 (38-55)	46 (38-53)	50 (38-55)	0.88
Upper extremity	28 (18-32)	31 (28-36)	22 (17-26)	**0.004**
Depression	50 (44-55)	53 (47-56)	47 (39-52)	0.20
Anxiety	50 (47-55)	51 (41-55)	49 (47-54)	0.84
Peer relationships	50 (44-62)	46 (43-54)	56 (48-62)	**0.04**
PODCI domains				
Pain	87 (82-100)	88 (73-100)	87 (82-100)	0.82
Upper extremity	67 (39-75)	75 (72-88)	42 (24-60)	**< 0.001**
Happiness	85 (70-95)	88 (80-99)	85 (70-95)	0.40
Global function	75 (44-88)	87 (81-93)	54 (40-70)	**0.007**

Bold values indicate significant $P < 0.05$.
IQR indicates interquartile range; PODCI, Pediatric Outcomes Data Collection Instrument; PROMIS, Patient-Reported Outcome Measurement Information System.

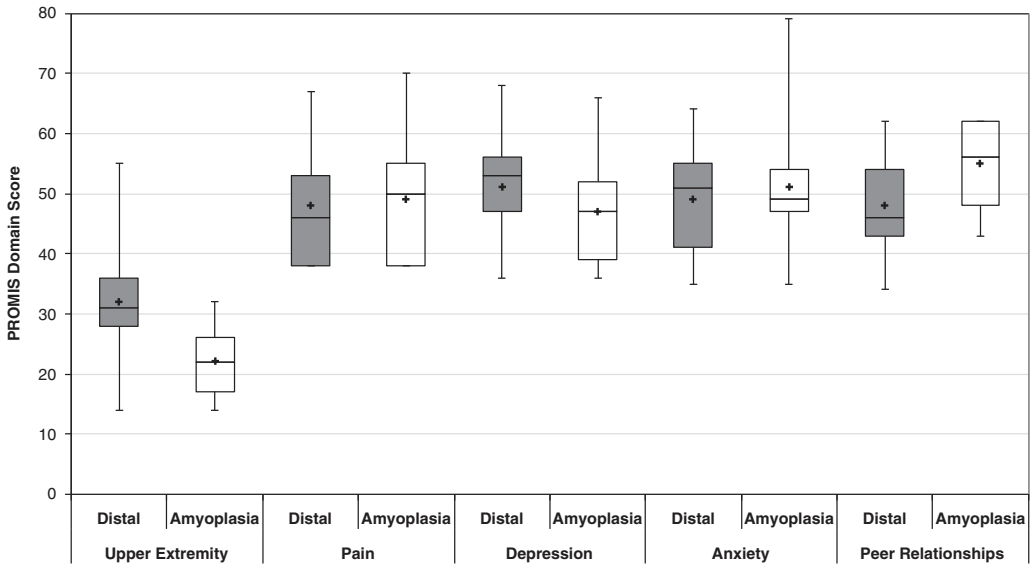

FIGURE 1. Distribution of PROMIS domain scores by arthrogryposis subgroup. The boxes represent the lower quartile, median, and upper quartile, whereas the I-bars span the minimum and maximum. + sign indicates the mean of the data; PROMIS, Patient-Reported Outcome Measurement Information System.

socially, participating in social activities corresponding to their needs," though no quantitative assessment of psychosocial well-being was utilized.

This study reveals that there are perceived limitations by the entire cohort of arthrogrypotic patients/care-givers with lower UE functional scores compared with the population norms. Functional limitations in patients with congenital UE anomalies have been previously reported in the CoULD registry cohort, which included 15 patients with arthrogryposis.[12] This prior report also showed that patients with hand-only anomalies had statistically higher PODCI scores for UE function compared with those with entire UE involvement and lower PROMIS UE function when anomalies were bilateral (vs., unilateral). This finding mirrors the results of our current study, in which amyoplasia patients, with full UE involvement, reported more limitations compared with distal arthrogryposis patients.

The trend for lower than normal UE function was also seen in a prior study evaluating PODCI outcomes in amyoplasia.[17] Amor and colleagues reported an UE function score of 60 (SD ± 24) in amyoplasia patients. Interestingly, this score was higher than our score from amyoplasia patients of 43. The difference may be attributed to a smaller number of amyoplasia patients in our cohort, or perhaps the exclusion of younger children because of the limitations of PROMIS. As might be expected, the distal arthrogrypotic cohort had lower than normal scores, but higher scores (better function) compared with the amyoplasia patients.

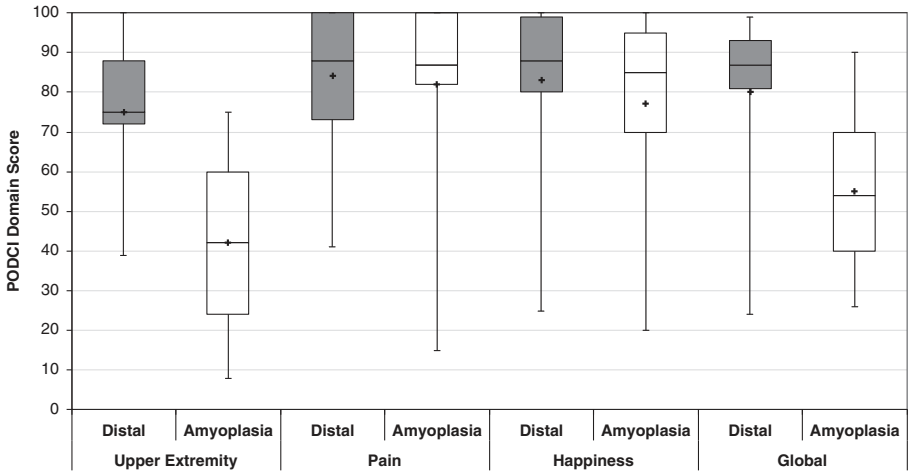

FIGURE 2. Distribution of PODCI domain scores by arthrogryposis subgroup. The boxes represent the lower quartile, median and upper quartile, whereas the I-bars span the minimum and maximum. + sign indicates the mean of the data; PODCI, Pediatric Outcomes Data Collection Instrument.

We found subjective function, as assessed by PROMIS, to be nearly 3 SDs lower than normal for amyoplasia and 2 SDs lower than normal for distal arthrogryposis. Separating arthrogryposis into 2 cohorts allows one to identify those patients with more functional limitations and highlights the difference between these patients who are often classified within the same unifying diagnosis.

Perhaps more important than the functional scores, this study found that arthrogrypotic patients have emotional states consistent with population healthy norms. Amor et al[17] identified that amyoplasia patients had PODCI scores for happiness of 80 (SD ± 18), which was similar though slightly lower to the current findings, in which median happiness scores were 85 for amyoplasia and 88 for the distal cohort. These findings are also in line with previous studies looking at congenital anomalies in general.[12] Through analysis of the entire CoULD registry, patients with a range of congenital UE anomalies, Bae et al[12] identified that this population reported good peer relations and positive psychosocial well-being for both patients with hand plate only anomalies and those with entire limb involvement.

Finally, although this study did not seek to compare or correlate PODCI and PROMIS scores for arthrogryposis, the scores show similar results as demonstrated in (Figs. 1, 2). With more critical inspection, the PROMIS scores seem more precise through the boxplots and may potentially provide a more sensitive assessment than the PODCI scores. However, given the small numbers in this study, statistical analysis was not performed. Analysis of a larger cohort is needed to ascertain whether PROMIS is a more precise instrument to quantify health states. Indeed, while the aim of this study was not to displace the traditionally used PODCI with the PROMIS, our findings do provide support for the use of the PROMIS in this unique population. Waljee et al[13] evaluated differing patient-reported outcomes in a pediatric congenital population. Through evaluation of 33 congenital patients, it was identified that the PROMIS correlated well with the PODCI.

A few limitations are inherent to the current study bear mention. More patients were identified in the registry than were able to be included for two primary reasons. First, as with any database cohort, there were missing data. Over time, with continued data cleaning efforts, this will improve. In addition, we are limited in analysis by the data points that are collected by the registry. Other factors such as lower extremity function, spine involvement, and economic advantages/disadvantages would also impact patient-reported outcomes and potentially affect our conclusions. Secondly, the PROMIS can only be utilized for patients older than or equal to 5 years. With continued future efforts, domains may be developed which can be applied to younger patients, but at this time we were not able to include outcomes in the younger children. Lastly, this study characterized functional status at a single time point. Future investigations are needed to determine how scores on these tested domains change, if at all, over was one point in time.

Despite these limitations, however, the current study provide important baseline patient-reported outcome data for both amyoplasia and distal arthrogryposis patients. This information will allow for meaningful comparisons of nonoperative and surgical treatment outcomes in the future.

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