European Journal of Physical and Rehabilitation Medicine 2023 February;59(1):32-41
DOI: 10.23736/S1973-9087.22.07725-5

ORIGINAL ARTICLE

Prevalence and determinants of hip pain in non-ambulatory cerebral palsy children: a retrospective cohort study

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ABSTRACT

BACKGROUND: Hip pain is common in cerebral palsy children, particularly at Gross-Motor Function Classification System level IV-V. It is associated to hip displacement and relates to the migration percentage. Recent literature suggested early reconstructive bone surgery, as the best approach to prevent hip luxation, then hip pain. Still, high rates of hip pain are reported.
AIM: To investigate prevalence and determinants of hip pain in an Italian cerebral palsy sample.
DESIGN: Single-center retrospective cohort study.
SETTING: Inpatient and outpatient.
POPULATION: Patients with spastic or dyskinetic cerebral palsy, Gross-Motor Function Classification System level IV or V, age 0-18.
METHODS: A chart review was implemented to report hip pain, as a dichotomous variable (pain/no pain), age, sex, cerebral palsy subtype, Gross-Motor Function level, lumbar scoliosis, migration percentage, previous orthopedic surgery, or botulinum injections, oral or intrathecal baclofen, drug-resistant epilepsy, assistive devices for standing or walking. Descriptive statistics and a multivariate logistic stepwise regression were performed.
RESULTS: A total of 504 subjects were included: 302 level V, 209 females, 432 spastics. The mean length of follow-up was 6 years. The overall prevalence of hip pain was 8.9% (6.3% were at level V) and of hip dislocation was 19% (15.9% were at level V). Just 39% of dislocated hips were painful. Children at spastic subtype and level V were predominantly affected. Botulinum and soft tissue surgery related to lower rates of hip pain, without statistical significance. Age (OR 1.19, 95%CI 1.14-1.25, P value 0.000), sex (OR 1.72, 95%CI 1.18-2.52, P value 0.005), migration percentage (OR 1.02, 95%CI 1.02-1.03, P value 0.000) and lumbar scoliosis (OR 1.32, 95%CI 0.86-2.01, P value 0.200) resulted significant independent determinants of hip pain.
CONCLUSIONS: Hip pain relates with the migration percentage, but not all dislocated hips become painful. Hip pain may be transient and requires a targeted and individualized approach. Children at spastic subtype and level V were predominantly affected. Age and sex are confirmed as determinants. Specific validated measures are to be implemented to assess hip pain.
CLINICAL REHABILITATION IMPACT: Considering severe non-ambulatory cerebral palsy patients, pain and quality of life should be considered as outcomes, in the management of hip luxation.

(*Cite this article as:* Faccioli S, Sassi S, Ferrari A, Corradini E, Toni F, Kaleci S, *et al.* Prevalence and determinants of hip pain in non-ambulatory cerebral palsy children: a retrospective cohort study. Eur J Phys Rehabil Med 2023;59:32-41. DOI: 10.23736/S1973-9087.22.07725-5)

KEY WORDS: Rehabilitation; Orthopedics; Botulinum toxins; Disabled persons; Muscle spasticity.

Pain is a major health issue in cerebral palsy (CP), strongly associated with reduced quality of life.[1] The prevalence of pain in children and young adult affected by CP varies from 14% to 76% according to a recent systematic review by McKinnon *et al.*[2] For subjects with severe communication disability, parents' perception of their child's pain is usually assessed. In a cross-sectional multicenter European study, the parent-reported pain in the previous 4 weeks was 73-77%.[3, 4] It is higher in patients at Gross Motor Function Classification Level (GMFCS) V, females, and older patients.[5] Musculoskeletal pain is common and increases with age.[6] It is mostly related to the feet and knee in ambulatory CP patients, respectively GMFCS I and III, and to the hips in GMFCS level IV-V.[6] Limited to non-ambulatory CP subjects, an overall prevalence of any pain of 27% was reported among children,[7] while a higher prevalence (82.6%) of musculoskeletal pain was reported among adolescents.[5] Specific hip pain prevalence ranged from 9.6% to 27% among non-ambulatory children or adolescents with CP.[7, 8] Hip pain is associated to hip displacement and relates to the Migration Percentage (MP)[9] and the hip morphology.[10] Recent literature stated the importance of surveillance programs[11] and suggested early reconstructive bone surgery,[10, 12] as the best approach to prevent hip luxation, then hip pain. Still, high hip pain prevalence is described among the non-ambulatory CP patients, attending surveillance programs that extensively provide reconstructive surgery.[9, 10, 13] These population-based registry studies reported a prevalence of hip pain of 7.9% among GMFCS IV and 20.5% among GMFCS V patients in the range 4-16 years,[9] and an overall prevalence of 72% among adolescents and young adults with CP.[10]

Italy does not yet have a national surveillance program. Clinical and radiographic monitoring of CP children is performed either at local services or at tertiary referral centers, which deliver surgery, spasticity treatments and postural management, based on individual needs. However, no data have been published so far regarding hip pain prevalence.

The purpose of the present study was to investigate prevalence and determinants of hip pain in a large cohort of non-ambulatory CP children.

Materials and methods

The present manuscript describes a single-center retrospective (chart review) cohort study, the setting was either outpatient or inpatient.

The study was conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. The study was approved by the Area Vasta Emilia Nord Ethics Board (Chairperson Sebastiano Calandra Buonaura), on 21 April 2020 (200/2020/OSS*/AUSLRE).

Participants

Inclusion criteria were: bilateral spastic or dyskinetic CP, according to Surveillance of CP in Europe (SCPE) Classification;[14] GMFCS level IV or V; age 0-18 years; having attended the Children Rehabilitation Unit at the S. Maria Nuova Hospital, in Reggio Emilia, before March 2020; having at least one pelvic radiography with MP reported or measurable; informed consent of the parents for minors; informed consent of the adult patient if he/she was able to independently subscribe it, or of the support administrator for vulnerable adults. Exclusion criteria were unilateral CP, ataxic subtype,[14] GMFCS level I-III, no pelvic radiography available.

The following information were acquired from the patients' charts.

Clinical and functional assessment:

- report of hip pain at each visit;
- age at the time of the assessment;
- sex;
- CP subtype according to SCPE;[14]
- GMFCS level;
- the presence of drug-resistant epilepsy;
- having undergone botulinum (BoNT-A) injections in hip muscles during the 6 months prior to the assessment;
- having undergone soft tissue or bone surgery during the 12 months prior to the assessment;
- the presence of lumbar scoliosis clinically or radiographically evidenced;
- the use of assistive devices for standing or walking (*i.e.*, standers or walkers with weight relief);
- ongoing treatment with oral baclofen or Intrathecal Baclofen (ITB).

The presence of pain was recorded as a dichotomous variable (pain/no pain), and referring to each hip, right and left. Hip pain was systematically enquired by asking the care givers open questions about the presence, circumstances and sites of pain. Then, close questions were posed, inquiring sleep disturbances and nonverbal indicators of pain (*i.e.*, increased agitation or resistance to movement, increased respiratory and/or heart rate, facial grimaces), observed at rest or in activities that implied hip mobilization, such as toileting or dressing or while transferring the patient. Moreover, explicit pain or indirect signs of discomfort, were enquired during the visit by the physiatrist, by mobilizing the hips and by observing the patient's behavior, while transferring and while sitting in her/his wheelchair or customized device. As in other studies,[5, 7-10] the prevalence of pain related to the patients was firstly described and stratified by GMFCS level and CP subtype. Secondarily, to verify the persistence of hip pain and its determinants, the data were analyzed at the level of the individual hips. Hips having undergone palliative surgery were excluded. Pain was defined as "recurrent" when it persisted at the following visit or was registered at the last or unique evaluation available; it was called "transient" when it was denied at subsequent controls, if available. In case of transient pain, the treatment that had occurred between the two succeeding visits was recorded, since it might have contributed to pain resolution.

Radiographic evaluation:

- MP measure for right and left hip for each acquired radiography.

Whenever the MP value was not reported on the chart, it was newly measured on the pelvic radiography included into the chart or recoverable from the institutional picture archiving system. The MP was calculated on an anterior-posterior radiography of the pelvis, acquired in a supine position with the legs parallel, avoiding either pelvic rotation or anteversion. The MP is calculated as the percentage of ossified femoral head laying lateral to Perkin's line. The Perkin's line is drawn through the lateral acetabular margin and perpendicular to Hilgenreiner's line. The latter one passes through the superior aspect of the triradiate cartilage.[15, 16]

Statistical analysis

Descriptive statistics are presented for baseline demographic and clinical characteristics, for the entire group of patients with GMFCS IV and with GMFCS V, as well as for the hip sample with or without pain. Continuous variables are presented as the number of patients (N), mean, standard deviation (SD), minimum (min), and maximum (max) and compared between subgroups using unpaired Student's *t*-test; categorical variables are presented as frequency (N, percentage [%]) and compared using Pearson's χ^2 Test.

Some patients regularly attended visits and interventions, while others referred to the investigating unit just for periods, based on individual needs, therefore the follow-up differed among patients. Considering this, to enquire factors potentially influencing hip pain, a multivariate logistic regression analysis was conducted at the level of individual hips, with the corresponding MP and pain assessment, as reported at each visit. A stepwise selection method was used, to identify the prognostic factors between hips with or without pain. The analysis was computed considering pain, as the dependent variable, and the following independent variables: age at the assessment, GMFCS level, sex, CP subtype, drug-resistant epilepsy, dislocated hip, MP, previous BoNT-A or surgery, use of standing or walking devices, oral or intrathecal baclofen, lumbar scoliosis. In the first step, the intercept-only model was fitted and individual score statistics for the potential variables (age, GMFCS level, sex, CP subtype, etc.) were evaluated. A significance level of $P<0.05$ was used to allow a variable into the model. In stepwise selection, an attempt was made to remove any insignificant variables from the model before adding a significant variable to the model. Hosmer and Lemeshow Test was used to evaluate "goodness of fit" in the selection model. Data from the univariate and multivariate logistic regression analyses were expressed as Odds Ratio (OR) and 95% confidence interval (CI). A $P<0.05$ was considered statistically significant.

Based on the multivariate logistic regression, a well-calibrated nomogram was developed for predicting the probability of the hip pain. Independent predictors ($P<0.05$ in the multivariate logistic regression analysis) as well as clinically significant predictors were included in the nomogram construction. The nomogram was validated internally, the internal validation was performed by a calibration method and the area under the receiver operating characteristic (ROC) curve (AUC). The AUC ranged from 0 to 1, with 1 indicating perfect concordance, 0.5 indicating no better than chance, and 0 indicating discordance.

Statistical analysis was performed using STATA® software version 14 (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP.).

Results

As represented in Figure 1, 1208 quadriplegic CP patients attended our Unit between January 2008 and February 2020, according to the hospital log. However, as medical records filed prior to 2015 were not available for consultation, only those of 530 of these patients could be examined. A total of 504 patients gave their informed consent and was included.

Demographic and clinical data of the subjects at the first visit are presented in Table I.

More information about the examined population have been recently published.[17]

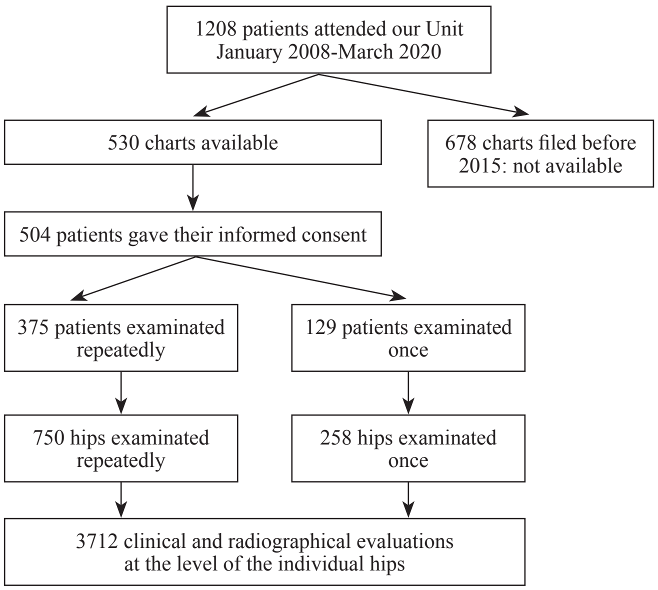

Figure 1.—Flow chart representing the recruitment process.

A total of 375 patients had more than one visit and radiography acquired, with a mean of 3.37 (SD 2.49) evaluations each. The mean length of follow-up was 6 years (0.1 to 17 years; SD 4). Table II reports the interventions and clinical data recorded during the entire follow-up.

A total of 45 patients (8.9%) over the entire population (N.=504) demonstrated hip pain or discomfort, at least once. They were 13 (2.6%) GMFCS IV patients and 32 (6.3%) GMFCS V. Considering CP subtype, just one dyskinetic child at GMFCS level IV complained hip pain. Conversely, the percentage of children who reported hip pain in the other subgroups ranged from 6.5% to 10.9%, being the spastic subtype the most affected. Seventeen patients (3.4%) reported hip pain just once and denied it at the following visits. Conversely, 28 (5.5%) subjects presented recurrent hip pain: 8 (1.6%) were GMFCS IV and 20 (3.9%) were GMFCS V. Among the overall sample of 504 recruited subjects, 96 (19%) showed hip dislocation (MP 91-100): 80 (15.9%) were GMFCS V.

Table I.—*Characteristics of the subjects at the first visit, considering the total sample and stratified by GMFCS level and CP subtype.*

Characteristics	Total	GMFCS IV			GMFCS V			P value
		Dyskinetic	Spastic	P value	Dyskinetic	Spastic	P value	
Subjects	504	18	184		54	248		0.005
Hip pain#	10 (2.0)	0	3 (1.6)	0.585	1 (1.8)	6 (2.4)	0.802	0.511
Age*	5.0±3.6 (0-17)	4.2±3.2 (0-11)	5.1±3.6 (0-17)	0.308	5.1±4.0 (1-17)	5.0±3.6 (0-15)	0.856	1.00
Male#	295 (58.5)	12 (66.7)	109 (59.2)	0.539	30 (55.6)	144 (58.1)	0.735	0.610
Female#	209 (41.5)	6 (33.3)	75 (40.8)		24 (44.4)	104 (41.9)		
Drug-resistant epilepsy#	40 (8.0)	0	1 (0.5)	0.754	3 (5.5)	36 (14.5)	0.075	<0.001
MP (%)*§	23.2±26.0 (0-100)	12.0±16.3 (0-66)	19.2±20.0 (0-100)	0.141	13.8±19.9 (0-100)	29.0±29.4 (0-100)	<0.001	0.010
Walking device#	162 (32.1)	12 (66.7)	98 (53.3)	0.276	21 (38.9)	31 (12.5)	<0.001	<0.001
Standing device#	216 (42.8)	6 (33.3)	98 (53.3)	0.106	26 (48.1)	86 (34.7)	0.063	0.001
Oral Baclofen#	81 (16.1)	1 (5.5)	16 (8.7)	0.647	6 (11.1)	58 (23.4)	0.045	<0.001
ITB#	5 (1.0)	0	0	-	1 (1.8)	4 (1.6)	0.901	0.066
Lumbar scoliosis#	36 (7.1)	0	4 (2.2)	0.527	3 (5.5)	29 (11.7)	0.184	<0.001

#N. (%); *Mean±SD (range); §mean MP including both right and left hips.

Table II.—*Hip pain, interventions and clinical signs reported in the total sample and stratified by GMFCS level and CP subtype.*

Characteristics	Total	GMFCS IV			GMFCS V			P value
		Dyskinetic	Spastic	P value	Dyskinetic	Spastic	P value	
Subjects	504	18	184		54	248		
Hip pain#	45 (8.9)	1 (0.5)	12 (6.5)	0.873	5 (9.2)	27 (10.9)	0.725	0.108
BTX-A injections#*	100 (19.8)	4 (22.2)	44 (23.9)	0.972	10 (18.5)	42 (16.9)	0.780	0.071
Soft-tissue surgery#§	145 (29.0)	1 (0.5)	57 (31.0)	0.023	7 (13.0)	80 (32.2)	0.005	0.982
Bone surgery#&	22 (4.7)	1 (0.5)	9 (4.9)	0.901	2 (3.7)	10 (4.0)	0.911	0.599
Oral baclofen#	174 (34.5)	3 (1.7)	42 (22.8)	0.549	15 (27.8)	114 (46.0)	0.014	<0.001
ITB#	37 (7.3)	1 (0.5)	5 (2.7)	0.498	6 (11.1)	25 (10.1)	0.821	0.002
Lumbar scoliosis#	36 (7.1)	0	4 (2.2)	0.480	3 (5.5)	29 (11.7)	0.184	<0.001

#N. (%);*single or repeated injections involving muscles around the hip, such as adductors, gracilis, hamstrings, psoas or rectus femuris; §uni or bilateral surgical release of one or more of the following muscles, according to individual features: adductors, gracilis, hamstrings, psoas, rectus femuris; &uni or bilateral reconstructive (femoral or combined) surgery or temporary medial hemiepiphysiodesis of proximal femur.

TABLE III.—*Characteristics of the total hip sample and stratified by GMFCS level.*

Characteristics	Total	GMFCS IV	GMFCS V	P value
	3712	1482	2230	
Hip pain#	130 (3.5)	34 (2.3)	96 (4.3)	0.001
Age*§	7.7±4.1 (0-18)	7.79±4.1 (0-18)	7.6±4.1 (0-18)	0.042
Male#	2132 (57.4)	882 (59.5)	1250 (56.0)	0.037
Female#	1580 (42.6)	600 (49.5)	980 (44.0)	
Dyskinetic CP#	458 (12.3)	122 (8.2)	336 (15.1)	<0.001
Spastic CP#	3254 (87.6)	1360 (91.8)	1894 (84.9)	
Drug-resistant epilepsy#	298 (8.0)	10 (0.7)	288 (12.9)	<0.001
MP (%)*	31.2±28.6 (0-100)	22.8±20.8 (0-100)	36.7±31.6 (0-100)	<0.001
BoNT-A injection in the previous 6 months#	274 (7.4)	132 (8.9)	142 (6.4)	0.004
Soft tissue surgery in the previous 12 months#	343 (9.2)	143 (9.65)	200 (8.9)	0.483
Bone surgery in the previous 12 months#	41 (1.1)	20 (1.3)	21 (0.9)	0.244
Walking device#	1374 (37.0)	992 (66.9)	382 (17.1)	<0.001
Standing device#	1788 (48.2)	882 (59.5)	906 (40.6)	<0.001
Oral Baclofen#	938 (25.3)	222 (14.9)	719 (32.1)	<0.001
ITB#	218 (5.8)	40 (2.7)	178 (7.9)	<0.001
Lumbar scoliosis#	482 (12.9)	108 (7.3)	374 (16.7)	<0.001

#N. (%); *Mean±SD (range); §age at the time of the acquired radiography, corresponding to the MP measurement.

Twenty-one patients, with at least one luxated hip, complained hip pain and it was recurrent (just three were GMFCS IV). They corresponded to 4.2% over the 504 recruited children and just 39% over the subgroup with dislocated hip.

Since the regression analysis was computed at the level of the individual hips and 750 hips were examined almost twice, a total of 3712 MP measurements was included (Table III). Six hips were excluded from the analysis after having undergone palliative surgery (3 subjects at GMFCS V, 1 subject at GMFCS IV).

The overall prevalence of painful hips in the sample was 3.5%: 2.2% in GMFCS IV subgroup and 4.3% in GMFCS V. The prevalence of painful hips increased with age, reaching the highest values at 13-15 years. But painful hips were also found at younger age, since the age of 2 years. To represent the prevalence of hip pain related to the MP, reference MP ranges were established: <20%, 21-30%, 31-40%, 41-50%, 51-60%, 61-90%, 91-100%. Low rates of pain were observed at any MP range. But a trend increasing with the MP was noticed, with a peak at 91-100 MP range. The prevalence of pain related to age (A) and to MP ranges (B) is represented in Figure 2.

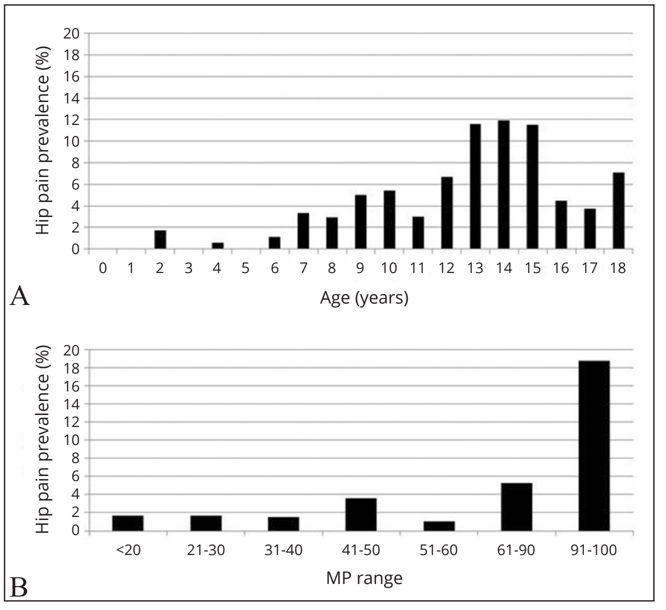

Figure 2.—Hip pain prevalence related to age (A) and to hip migration percentage range (B).

Pain was recurrent in 2.5% and transient in 1% of the overall hip sample. Prevalence of recurrent or transient hip pain is described in Table IV, related to the following MP ranges: 0-30%, 31-90%, 91-100%.

The rate of recurrent painful hips reached the higher values in the range MP 91-100%. Considering that, among the hips in the range 91-100, just 3 over 62, had a MP<100 (91-92%), this range may be assumed as representative of dislocated hips. With MP>30% the prevalence of painful hips, and recurrent painful hips was higher in GMFCS IV level, than in GMFCS V. In case of transient pain, the treatment that had occurred between the two succeeding visits was reported: 2 oral baclofen, 5 ITB, 15 soft tissue surgery, 4 bone surgery.

Descriptive statistics for hips with or without pain and univariate logistic regression analysis are presented in Table V.

TABLE IV.—*Prevalence of recurrent or transient pain among hips, related to MP ranges and stratified by GMFCS level; treatments temporally associated with transient pain.*

Characteristics	Total	MP 0-30%		MP 31-90%		MP 91-100%	
		GMFCS IV	GMFCS V	GMFCS IV	GMFCS V	GMFCS IV	GMFCS V
	3712	1050	1177	399	757	33	296
Mean age*#	11±3	11±3	11±3	13±3	10±3	10±3	11±4
Painful hips§	130 (3.5)	13 (1.2)	24 (2)	12 (3)	19 (2.5)	9 (27.2)	53 (17.9)
Recurrent painful hips§	93 (2.5)	9 (0.8)	19 (1.6)	9 (2.3)	12 (1.6)	5 (15)	39 (13.2)
Transient painful hips	37 (1)	4 (0.4)	5 (0.4)	3 (0.7)	7 (0.9)	4 (12.1)	14 (4.7)
Oral baclofen	2	-	1	-	-	1	-
ITB	5	-	-	2	-	-	3
Soft tissue surgery	15	2	5	1	3	1	2
Bone surgery	4	-	-	-	-	2	2

*Age at the time of the evaluation; #±SD (year); (%); §N. (%).

TABLE V.—*Logistic regression with hip pain as dependent variable.*

Characteristics		Total	Hip pain: No	Hip pain: Yes	P value	OR 95%CI	P value
		3712	3582	130			
Age*		7.7±4.1 (0-18)	7.6±4.1 (0-18)	11.1±3.4 (2-18)	<0.001	1.21 (1.16-1.26)	<0.001
GMFCS#	IV	1482 (39.9)	1448 (40.4)	34 (26.1)	0.001	ref.	
	V	2230 (60.1)	2134 (59.6)	96 (73.8)		1.91 (1.28-2.84)	0.001
Sex#	Male	2132 (57.4)	2082 (58.1)	50 (38.5)	<0.001	ref.	
	Female	1580 (42.6)	1500 (41.9)	80 (61.5)		2.22 (1.55-3.18)	<0.001
CP subtype#	Spastic	3254 (87.6)	3146 (87.8)	108 (93.1)		ref.	
	Dyskinetic	458 (12.3)	436 (12.2)	22 (16.9)	0.106	1.46 (0.91-2.35)	0.108
Drug-resistant epilepsy#	No	3414 (91.9)	3298 (92.1)	116 (89.2)	0.242	ref.	
	Yes	298 (8.0)	284 (7.9)	14 (10.7)		1.40 (0.79-2.47)	0.244
MP*	(%)	31.2±28.6 (0-100)	30.0±27.4 (0-100)	63.7±38.7 (0-100)	<0.001	1.03 (1.02-1.03)	<0.001
BoNT-A injection#	No	3438 (92.6)	3313 (92.5)	125 (96.1)	0.117	ref.	
	Yes	274 (7.4)	269 (7.5)	5 (3.8)		0.49 (0.19-1.21)	0.124
Soft tissue surgery#	No	3369 (90.8)	3250 (90.7)	119 (92.5)	0.755	ref.	
	Yes	343 (9.2)	332 (9.3)	11 (8.5)		0.90 (0.48-1.69)	0.755
Bone surgery#	No	3671 (98.9)	3543 (98.9)	128 (98.5)	0.630	ref.	
	Yes	41 (1.1)	39 (1.1)	2 (1.5)		1.41 (0.33-5.94)	0.632
Walking device#	No	2338 (62.9)	2224 (62.1)	114 (87.7)	<0.001	ref.	
	Yes	1374 (37.0)	1358 (37.9)	16 (12.3)		0.22 (0.13-0.38)	<0.001
Standing device#	No	1924 (51.8)	1820 (50.8)	104 (80.0)	<0.001	ref.	
	Yes	1788 (48.2)	1762 (49.2)	26 (20.0)		0.25 (0.16-0.39)	<0.001
Oral baclofen#	No	2774 (74.7)	2698 (75.3)	76 (58.5)	<0.001	ref.	
	Yes	938 (25.3)	884 (24.7)	54 (41.5)		2.16 (1.51-3.09)	<0.001
ITB#	No	3494 (94.1)	3380 (94.4)	114 (87.7)	0.001	ref.	
	Yes	218 (5.8)	202 (5.6)	16 (12.3)		2.34 (1.36-4.03)	0.002
Lumbar scoliosis#	No	3230 (87.0)	3146 (87.8)	84 (64.6)	<0.001	ref.	
	Yes	482 (12.9)	436 (12.2)	46 (35.4)		3.95 (2.72-5.73)	<0.001

*mean±SD (range); #N. (%).

Several factors appeared to significantly relate to hip pain at the univariate analysis: age, GMFCS level, sex, MP, oral baclofen, ITB and lumbar scoliosis. Conversely, CP subtype did not result a significant determinant. Walking and standing devices, with weight relief and trunk support whenever needed, were related to the absence of hip pain. Nonetheless they were excluded from the multivariate analysis, as confounder, because in the clinical practice their use was suspended in case of hip pain. Botulinum and soft tissue surgery related to lower rates of hip pain, without statistical significance. They were then excluded from the multivariate analysis.

At the multivariate logistic regression, GMFCS, oral baclofen and ITB resulted confounders and were excluded. The best multivariate logistic regression model, with hip pain as dependent variable, included: age (OR 1.19,

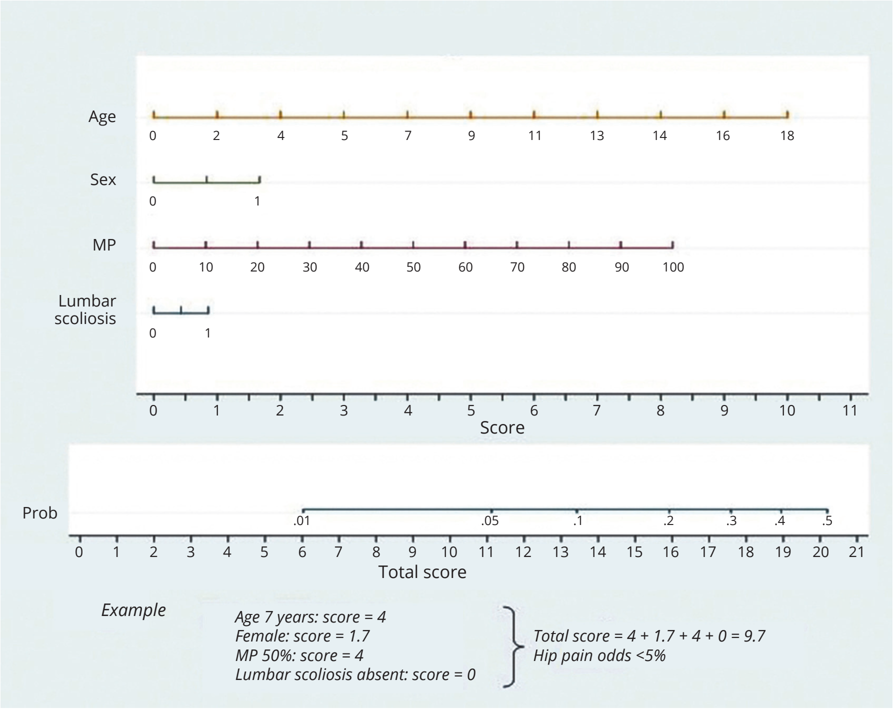

Figure 3.—Nomogram predicting the probability of hip pain.

95%CI 1.14-1.25, P value 0.000); sex as females (OR 1.72, 95%CI 1.18-2.52, P value 0.005), MP (OR 1.02, 95%CI 1.02-1.03, P value 0.000) and lumbar scoliosis (OR 1.32, 95%CI 0.86-2.01, P value 0.200).

Based on regression model and clinical significance, the best independent predictors for hip pain were selected and included in a well-calibrated nomogram to predict the probability of hip pain (Figure 3).

Discussion

To our knowledge, this is the largest sample of Italian non-ambulatory CP patients that has been described on this topic.

In the study population, 8.9% children complained hip discomfort, or showed a behavior attributable to hip pain, at least once. This value is similar to findings by Poirot et al,[7] who found a 9.6% prevalence of hip pain. The authors reported joint mobilization as the first source of pain and muscle pain or cramps as the second, with no details regarding hip management. Conversely, hip pain prevalence in the present study resulted lower than what reported by other authors: 72% in Wawrzuta *et al.*,[10] 27% in Penner *et al.*,[8] 7.9% among GMFCS IV patients and 20.5% among GMFCS V in Marcstrom *et al.*[9]

Several aspects might contribute to explain the gap, compared to the present study.

First, the older age of the population examined by Wawrzuta *et al.*[10] (15-24 years) might justify higher rates of hip pain. Closer, still higher, prevalence values were reported by Marcstrom *et al.*[9] based on a population with an age range (4-16 years) comparable to the present sample (0-17 years). A longer follow-up might register higher rates of hip pain. In fact, it is known and confirmed also by our results, the positive correlation among hip pain and age.

tThird, there are differences among the studies, relative to the recruitment method. Marcstrom *et al.*[9] reported data systematically recorded from a population-based registry study in Sweden. Conversely, Penner *et al.*,[8] described a single tertiary rehabilitation center cohort. Similarly, the present sample was recruited among the patients attending or having attended the investigating Unit, not from a surveillance program of the general CP population in Italy. Nonetheless, children referred to this Unit, as a tertiary referral center, may have presented a more severe or complicated clinical situation than that of the general quadriplegic CP population.

Finally, differences in pain prevalence might rely on the management of hip luxation and of hip pain itself. This remains an open question, because only comparative prospective studies might draw reliable conclusions. Nevertheless, it is worthy sharing some considerations.

Previous authors[9, 10, 12, 13] suggested extensive and early reconstructive surgery to prevent hip luxation, then hip pain. This approach revealed to be effective in preventing hip dislocation, but the rates of hip pain remain high.[13] Conversely, just a few patients at GMFCS level V underwent reconstructive surgery, in the present sample.[17] This led to higher rates of dislocation, but lower rates of hip pain were reported, involving just 39% of subjects with luxated hip. Present data confirm that the prevalence of hip pain increases with the MP, though, only a part of chronic dislocations progresses to become painful.[17, 21] Persisting of hip pain in reconstructed hips, may be due to contractures or spasticity, or to hip dysplasia. In this case, a complete luxation might reduce the risk of hip pain, provided that the limited range of motion is accepted in ADL. As suggested by Chung *et al.*,[22] hip morphology is often underestimated on anterior-posterior or axial radiographies. A relationship between pain and altered hip morphology was confirmed by Wawrzuta *et al.*,[10] who, conversely, concluded recommending reconstructive surgery, because operated patients showed a better hip morphology, according to the Melbourne Classification.[23] In case of MP≥50% spontaneous MP reduction may not be expected[24] and reconstructive surgery is to be considered. Nonetheless, in our opinion, it should be proposed with caution in severe non-ambulatory CP children because most of them, particularly at GMFCS level V, have a clinical and emotional precarious equilibrium, as Children with Medical Complexity (CMC).[25-27] This equilibrium might be overwhelmed by a surgical event, with disadvantages overcoming the benefits, in particular in case of repeated surgery, considering the high rates of recurrence in these patients.[28, 29]

As several authors reported, pain in CP children may be caused by comorbidities[1, 30, 31] and requires a targeted and individualized approach. Pain localized at hips by care givers, might not be due to sub-luxation, but related to either muscle spasms or contractures or sustained uncomfortable postures.[7] In these cases, spasticity treatments, soft tissue surgery and/or postural management, are effective to solve the pain. The positive role of baclofen and botulinum to reduce the hip pain is confirmed by other authors.[19, 32, 33] Marcstrom *et al.*[9] reported a significant association between pain and limited ROM. This supports the rationale in favor of soft tissue release, if the limited ROM is based on muscle contracture. Moreover, pain may be associated with being moved in adolescents with severe motor impairment,[30] then instructions to care givers are needed, to correctly mobilize the patient in ADL, without forcing the hip range of motion (ROM).

Hip pain may be transient, as confirmed by the present data, in 28.5% of cases over total painful hips. Oral analgesics administration, as paracetamol or non-steroidal anti-inflammatory drugs (NSAID), is firstly recommended.[7] In case of recurrence, intra-articular injections of anesthetic, steroids and hyaluronate may be considered, with ultrasound guidance. This procedure is also useful to confirm the suspect of hip pain, in non-communicating patients. True articular hip pain may be managed with repeated intra-articular injections, at interval based on individual needs, and it often disappears when complete dislocation occurs. Conversely, the hips refractory to conservative pain management, are to be addressed to palliative surgery.

The multivariate logistic regression identified the following independent determinants of hip pain, based on the examined sample: older age, being a female, higher MP, lumbar scoliosis. These findings confirm data from previous studies, about age and sex.[2, 5] Nonetheless, an independent role of GMFCS level was not found, differently from McKinnon *et al.*,[2] even though hip pain prevalence was higher in GMFCS V children than in GMFCS IV. This may be related to the fact that GMFCS IV patients are more active, exposing their hips to more stress, than GMFCS V subjects, who usually are more static and need the caregiver to transfer and position them. By correctly instructing the care givers on how mobilizing the most severe patients, pain may often be avoided. A significant association between scoliosis and hip pain was observed, as reported by Poirot *et al.*[7] This aspect is probably due to sustained positions and localized overload in limited skin area, constrained by the scoliotic deformity. Finally, a significant association between pain and MP was evidenced, even though pain was observed also at the lowest MP levels. This confirms that hip pain may have several causes, other than articular inflammatory response. Moreover, the MP correlates with pain, but does not result a significant determinant of health-related quality of life (HR-QoL), as measured with the Caregiver Priorities and Child Health Index of Life with Disabilities (CPCHILD), being the GMFCS level more significant.[34-36]

Limitations of the study

The reporting of hip pain was limited to a dichotomous measure, as validated tools were not systematically used.

The age range of the present sample was limited to under-18 years, because older patients referred to adults' services. A longer follow-up might register higher rates of hip pain.

The results of the present study should be interpreted with caution as they derive from a retrospective design.

Only spastic or dyskinetic CP were included because they are the most exposed to hip luxation, conversely, the ataxic subtype is rarely affected.[12-37]

Conclusions

The development of specific validated questionnaires is desirable, to assess hip pain in non-verbal subjects.

Pain in CP may be caused by comorbidities or several musculoskeletal factors, then it requires a targeted and individualized approach.

Considering severe non-ambulatory CP patients, the impact on hip pain, of early reconstructive surgery versus a more conservative approach, should be studied in deep. Future research is advisable, considering pain and HR-QoL as primary outcomes.

Age, sex, MP, and lumbar scoliosis resulted independent determinants of hip pain in the examined sample.

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Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' contributions.—Silvia Faccioli: conceptualization, methodology, writing-original draft. SS: conceptualization; Adriano Ferrari: supervision; Elena Corradini and Francesca Toni data extraction; Shaniko Kaleci: statistical analysis, writing-original draft. Francesco Lombardi: supervision; Alessandro Picelli and Maria G. Benedetti: writing-review & editing. All authors read and approved the final version of the manuscript.

Acknowledgements.—We thank Maurizio Mori, Valentina Montemaggiori and Francesco Pelillo for sharing their expertise in the orthopedic management of CP children.

History.—Article first published online: December 12, 2022. - Manuscript accepted: November 22, 2022. - Manuscript revised: November 8, 2022. - Manuscript received: September 16, 2022.