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Early signs of gait deviation in Duchenne muscular dystrophy

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Background. **Most analytical studies found in literature only focus on specific aspects of Duchenne muscular dystrophy (DMD) gait and posture (joint range of motion, standing balance, variations of gait spatial-temporal parameters). Some of them analyze single cases and do not provide a comprehensive evaluation of locomotion. There are few studies about DMD gait patterns, most of them concerning small groups of patients, sometimes not homogeneous, in which the clinical manifestations of the next stages of DMD were present.**
Aim. **The goal of our study was to analyze the characteristics of gait patterns in early stage patients, when clinical and functional evaluation do not allow to quantify initial walking worsening or to identify the changes adopted to compensate for muscle weakness.**
Setting. **Gait Analysis Laboratory by using a six-camera motion capture system (Vicon, Oxford Metrics, UK), set at a sampling rate of 60 Hz. Subjects were asked to walk barefoot at their usual cadence, along a 10-m walkway, where one force platform (Kistler, Switzerland), embedded in the middle portion of the pathway, measured the foot-ground reaction forces. Retroreflective markers were placed on the subjects according to the protocol described in Davis *et al.***
Population. **A group of 15 patients aging from 5 to 6.8 years was compared with a similar age control group composed of 9 healthy children.**
Results. **Spatial and temporal parameters showed significant differences between the two groups: cadence was increased and step length was decreased significantly in the DMD group. We found a significant increase in the range of anterior-posterior pelvic tilt and in pelvic rotation. In the frontal plane there was a tendency for an increased pelvic obliquity. Dynamic range of motion in sagittal plane showed a significant difference at the ankle, with an increased plantarflexion in swing in the dystrophic patients. Maximum dorsiflexion was reduced in the DMD group. Kinetic analysis showed significant differences in power generation and absorption at the hip joint and at the ankle joint. At knee there was a reduced flexor moment in mid-stance. Ankle showed a reduced dorsiflexor moment in terminal stance and pre-swing with a consequent reduction in the peak-to-peak excursion.**
Conclusion and clinical rehabilitation impact. **It was shown that instrumented gait analysis, being more sensitive than other clinical and functional assessment methods, allowed to quantify the very early modifications characterizing locomotion worsening in the first stage of the DMD.**

KEY WORDS: Gait - Posture - Muscular dystrophy, Duchenne - Biomechanics.

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Duchenne muscular dystrophy (DMD) is an hereditary muscular disease, caused by a defect in the gene located on the X-chromosome that codes for dystrophin, a protein normally located in muscle membrane. Dystrophin deficiency causes a progressive degeneration of muscle fibers and subsequently severe muscular weakness.[1] Early manifestation of the pathology may start at the age of 3 years. Progressive muscle weakness demands for compensatory strategies to be adopted by the patient in order to walk. Nevertheless, worsening of gait occurs which finally leads to loss of walking ability, usually at the beginning of the second decade of life.

The early occurrence of compensatory strategies may reveal that muscle weakness is beginning to produce the first functional abnormalities.

In children with slight symptoms of the disease, clinical/functional tests may not be sensitive enough to detect early compensatory strategies acted by the child. The quantitative testing of muscle strength has been shown to be more sensitive at this stage.[1] Even though, there is however a gap between the muscle strength assessment and the effects of muscle weakness on gait ability. Our goal was to identify the gait analysis features that have an early tendency to change during walking in DMD patients, and to perform a quantitative assessment of such gait abnormalities. Instrumented gait analysis was adopted to this purpose and DMD patients exhibiting only slight reductions of muscular strength or functional performance were analyzed.

Materials and methods

A pathologic group, composed of 15 subjects aged from 5 to 6.8 years (mean 6.1±0.7 years), was selected among a larger population of DMD patients examined at our institute, on the basis of a relative homogeneity of motor conditions clinically assessed. Patients diagnosis was confirmed by genetic analysis and by the absence of dystrophin in muscle biopsy. Inclusion criteria, aimed at selecting subjects with minimal functional alterations, were the following: no reduction of passive range of motion, capability to walk 10 m without assistance, ability to get up from the floor from lying position (Gowers' sign) in less than 4 seconds, capability to climb and descent staircases alternating left and right feet without external support. The exclusion criteria were: age lower than 5 years, surgical or pharmacological treatment before the observation period and additional pathological conditions.

The patient group was characterized by a body mass and height of 20.6±4.4 kg and 1.14±0.08 m, respectively. A control group, composed of 9 healthy males aged 7.5±1.2 years was also analyzed. While their body mass and height were higher than in DMD patients (27.7±5.2 kg and 1.31±0.1 m, respectively), the body mass index (mass/height^2) was fairly the same in both groups (15.8±2.4 kg/m^2 DMD group, control 16.0±2.0 kg/m^2).

Muscle strength was tested manually and bilaterally in all subjects of both groups and scored according to Medical Research Council.[12] In this scale strength is classified between 0 (no force) and 5 (normal force). In addition the marks "+" or "-" are usually used to increase the score sensibility. For averaging purposes, because this is a non-parametric scale, grades were converted to ordinal numbers in decimal base, "+" marks being assumed as +0.33 and "-" marks assumed as -0.33 as reported in Armand S *et al*.[6]. Functional assessment was also performed by the Hammersmith Motor Ability Score,[13] which has 20 scored activities, the timed Gowers test, and the 10-meter timed walk.

Motion analysis was performed in the Gait Analysis Laboratory at the G. Gaslini Institute by using a six-camera motion capture system (Vicon, Oxford Metrics, UK), set at a sampling rate of 60 Hz. Subjects were asked to walk barefoot at their usual cadence, along a 10-m walkway, where one force platform (Kistler, Switzerland), embedded in the middle portion of the pathway, measured the foot-ground reaction forces. Retroreflective markers were placed on the subjects according to the protocol described in Davis *et al*.[2] Absolute and relative angles of each of the segments considered were obtained. Force signals collected simultaneously to segments motion were processed as to obtain the joint moments and joint powers along the recorded stride. Anthropometric parameters necessary to estimate inertial characteristics of the lower leg segments were measured on each individual. The elaboration procedure used the models implemented in Vicon Clinical Manager, an estimation of joint centers based on Davis' anthropometric model [2] and an inverse dynamics solution of joint kinetics. Joint moments and powers were normalized by body weight. Kinematic and kinetic data (pelvic and lower limb joint angles,

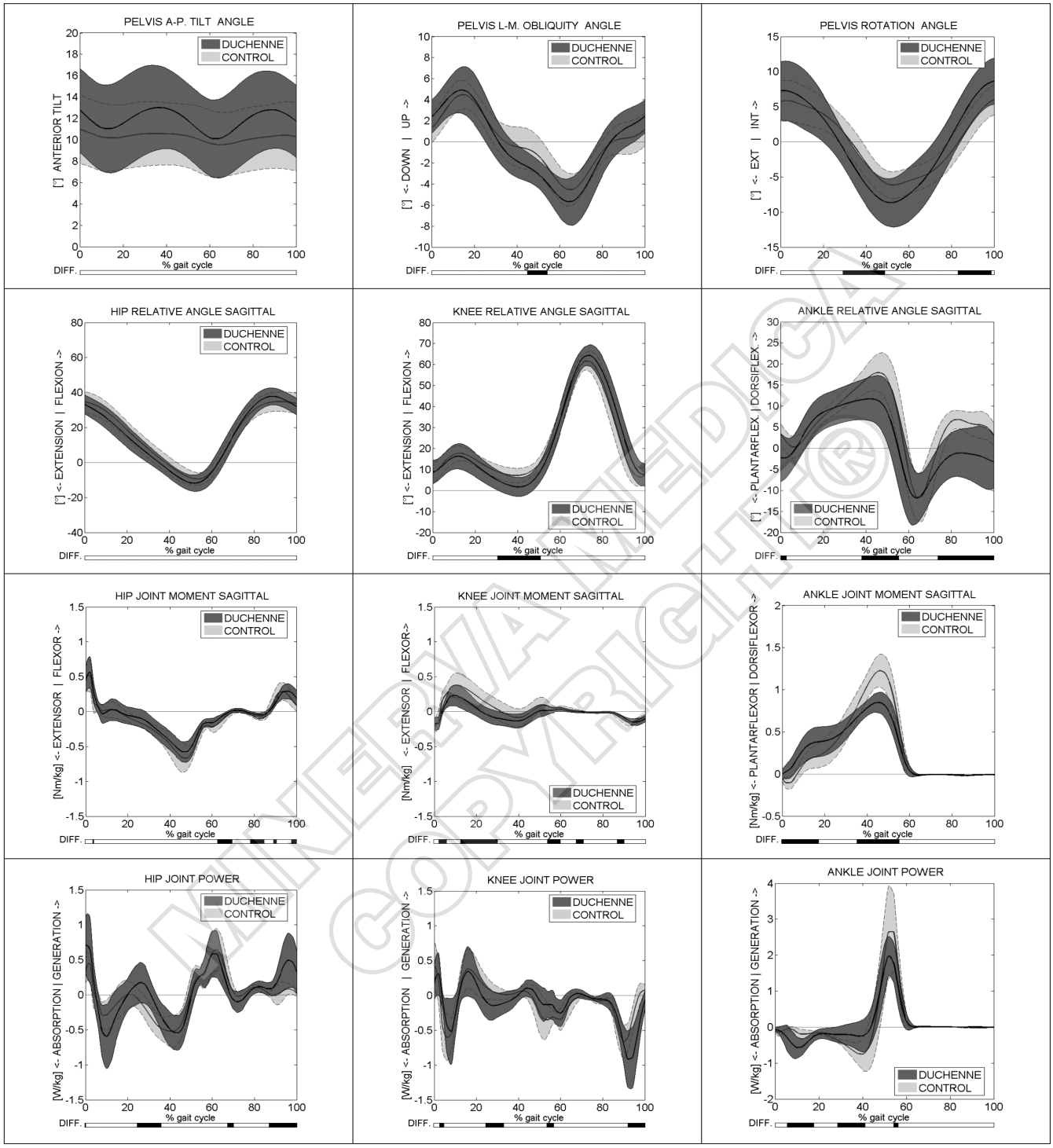

Figure 1.—Average traces of kinematic and kinetic variables (mean values and bands representing ±1 standard deviation) for DMD patients group (dark gray) and control group (light gray) are presented over the gait cycle. The black bars in the bottom of each graphic represent the intervals of the gait cycle where differences between both groups reached statistical significance for P<0.05.

external joint moments and powers) both from the pathologic and the control groups were then compared for statistical analysis of the differences. At least five trials for each side were performed. All kinematic and kinetic variables were time normalized at 100% of the stride duration.

Differences between the pathologic and the control groups were quantitatively assessed, using custom written routines in Matlab (MathWorks, Inc), in two ways: 1) by analyzing the overall time course of each kinematic and kinetic variable; and 2) by statistically analyzing the main parameter extracted from the stride cycle (stride and temporal parameters, minimum and maximum peaks of the curves, range of variation of each variable).

After time normalization the mean curve and standard deviation was obtained for each kinematic and kinetic variable and for each group. When averaging the individual data, a check for outliers was performed to test the homogeneity of the subjects data: no outliers were found between the subjects composing each group. Then, comparisons between the curves of the pathologic group and those of the control group were done by a paired Student's t-Test performed at every 1% of the gait cycle. So the statistical significance of the point to point difference of the curves was ascertained. The results were reported in the form of black horizontal bars at the bottom of each graphic (Figure 1), showing the time intervals of the gait cycle where the differences between the two average curves were significant at $P<0.05$.

Maximum, minimum and the range of excursion were obtained for each curve and for each subject, independently of the instant at which the peaks occurred. Afterwards, these values were averaged for subjects belonging to each group (the normal distribution was verified by means of the Kolmogorov-Smirnov Test) and the comparison between groups was performed through the Student's t-Test. The same approach was used to compare the temporal and stride parameters as well.

Results

The measured range of motion during walking exhibited no difference between pathological and control groups. This was consistent with the fact that patients included in the DMD group had no reduction of range of motion either when tested manually. From manual muscle testing performed in both groups (Table I), a strength reduction was found in 86% of the patients in the DMD group that was statistically significant for tibialis anterior, peroneus, hip adductors and biceps femoris muscles. The time required to rise from the floor (Gowers' time) was 3.2±0.8s in patients 2.1±0.5s in the control group; the difference was statistically significant ($P<0.01$). The "10-meters walking" time was 4.4±3.2 s in DMD patients, and 3.4±0.6s in the control group; the difference was significant at a P level of 0.05. As expected, the Hammersmith score (which can be at maximum 40) was also significantly different between the DMD group (37.7±1.9, $P<0.05$) and the control group (39.3±0.9).

Concerning the gait analysis results, temporal and stride parameters showed significant differences between the two groups (Table II): cadence increased and step length decreased in the DMD patients ($P<0.01$). Walking velocity was instead not significantly different.

The pelvis orientation showed significant differences: pelvis obliquity and pelvis horizontal rotation differed significantly at the double support phase (Figure 1), while the peaks were not statistically different (Table III). Pelvis tilt exhibited larger oscillations in DMD patients compared to normal control group, although the point to point difference was not significant in any phase of the gait cycle. Only the range of the pelvis tilt was significantly different between DMD group and control group ($P<0.01$, Table III).

The hip joint flexion appeared to be increased, but the difference between the average curves was not significant. Only the range of motion was significantly increased in the DMD group by 5° ($P<0.05$). At the knee joint the range of motion in the sagittal plane showed a significant difference due to a mild hyperextension observed in DMD patients at terminal stance (1.0°±4.5°), while in the same phase the control group showed a flexion peak (5.4°±4.0°; $p<0.05$). At the ankle joint, plantarflexion was observed in swing phase in the dystrophic patients (-1.86°±5.9°) while in control group dorsiflexion occurred (7.5°±2.2°). Maximum dorsiflexion in terminal stance was less in the patient group (12.9°±4.9°) than in control group (18.3°±4.3°; $p<0.05$).

Concerning kinetics, the knee joint exhibited a smaller than normal flexion moment during the

TABLE I.—*Manual and Functional test (Manual Muscle Testing scored according to Medical Research Council,[12] Hammersmith, Gowers and 10 m walk times).*

Manual muscle testing	DMD Mean±SD	Control Mean±SD	Diff.
Glutei	4.60±0.35	4.68±0.40	
Rectus femoris	4.71±0.30	4.87±0.17	
Abb	4.64±0.40	4.72±0.46	
Add	4.36±0.33	4.77±0.23	P<0.01
Biceps	4.79±0.30	5.00±0.00	P<0.05
Tibialis anterior	4.55±0.31	4.96±0.11	P<0.01
Peroneus	4.65±0.34	5.00±0.00	P<0.01
Triceps	4.70±0.40	4.96±0.11	
Mean±S.D.	4.63±0.25	4.87±0.13	P<0.05
Gowers' time [s]	3.2±0.8	2.1±0.5	P<0.01
10 m Walk time [s]	4.4±3.2	3.4±0.6	P<0.05
Hammersmith score	37.7±1.9	39.3±0.9	P<0.05

first half of stance phase (Figure 1), difference that appeared to be significant also at the single peaks analysis (0.24±0.13 Nm/kg *versus* 0.39±0.17 Nm/kg; P<0.05). Ankle joint missed the initial plantarflexor moment at the beginning of stance phase, and showed a smaller dorsiflexor moment in terminal stance (Figure 1). The latter, in particular, and the range from maximum to minimum joint moment, proved to be significantly reduced in DMD (0.86±0.11 Nm/kg; 1.24±0.20 Nm/kg in control group; P<0.01).

Significant differences were also observed in power production and absorption at hip and knee joints in mid stance, terminal stance and terminal swing; at the ankle joint a bigger absorption was observed at loading response, and a smaller production at terminal stance: the maximum peak of power production was 2.14±0.58W/kg in the DMD group, and 2.95±1.10 W/kg in the control group (P<0.05).

Discussion

Most analytical studies found in literature only focus on specific aspects of DMD gait and posture (joint range of motion, standing balance, variations of gait spatial-temporal parameters).[3-5] Some of them analyze single cases and do not provide a comprehensive evaluation of locomotion. There are few studies about DMD gait patterns, most of them concerning small groups of patients, sometimes not homogeneous, in which the clinical manifestations of the next stages of DMD were present.[6-8] Instead, the aim of our study was to analyze the characteristics of gait patterns in early stage patients, when clinical and functional evaluation do not allow to quantify initial walking worsening nor to identify the changes adopted to compensate for muscle weakness. Therefore, some of differences found in the present study, which proved to be statistically significant in our groups, were not previously reported as typical of the early stage.

TABLE II.—*Temporal and stride parameters.*

	DMD group (N:=15)	Control group (N.=9)	Statistical difference
Walking Speed (m/s)	1.06±0.17	1.07±0.18	NS
Cadence (steps/min)	145.7±14.9	121.2±16.2	P<0.01
Stride Time (s)	0.84±0.07	1.01±0.16	P<0.01
Stride Length (m)	0.87±0.10	1.05±0.11	P<0.01
Step Time (s)	0.42±0.04	0.51±0.08	P<0.01
Step Length (m)	0.43±0.05	0.52±0.05	P<0.01
Opposite Foot Off (%)	10.77±1.82	11.19±1.37	NS
Opposite Foot Contact (%)	49.69±0.88	50.02±0.25	NS
Single Support (%)	38.87±2.18	38.30±1.68	NS
Double Support (%)	21.84±3.31	22.49±2.81	NS
Foot Off (%)	60.75±1.67	61.46±1.45	NS

The mean walking velocity in our DMD patients was similar that of the control group; however, among the first signs of alteration, we identified a gait pattern characterized by shorter but faster steps. In effect, DMD patients cadence increased as a compensation for the reduced step length that they naturally adopted.

Increased pelvic anteversion, just appreciable also in the static posture, can be related to a strategy adopted to compensate for the initial gluteus weakness and fatigue. During gait, anteroposterior pelvic tilt exhibited larger oscillations in DMD group, with a "double bump" pattern that has been similarly observed in other pediatric neurological pathologies as cerebral palsy.[10] That emphasizes the under-use of gluteus muscles during gait, which was not correlated with the manual strength test, but may suggest the presence of a reduced muscle activation as a possible mean to reduce fatigue.

TABLE III.—*IVUS findings in NOBORI 1 Clinical Trial at 9 Months.*

	DMD group (N.=15)	Control group (N.=9)	Statistical difference
PELVIC MOTION			
Sagittal plane pelvic anterior/posterior tilt angle (°)			
Max peak	13.5±3.9	11.2±3.2	NS
Min peak	9.9±3.6	9.2±2.9	NS
Range	3.6±1.1	2.0±1.0	P<0.01
Coronal plane pelvic elevation (rise)/depression (drop) Medial-lateral obliquity angle (°)			
Max peak	5.1±2.0	4.6±1.3	NS
Min peak	-5.8±2.1	-4.6±1.5	NS
Range	10.9±4.1	9.2±2.7	NS
Transverse plane pelvic internal/external Rotation angle (°)			
Max peak	9.2±3.7	6.8±2.5	NS
Min peak	-9.2±3.5	-6.5±1.8	P<0.05
Range	18.4±6.5	13.3±4.3	P<0.05
HIP			
Sagittal plane hip flexion/extension angle (°)			
Max peak	38.5±5.2	35.4±5.8	NS
Min peak	-11.9±4.7	-9.8.±3.6	NS
Range	50.5±6.8	45.2.±4.0	P<0.05
Sagittal plane hip flexor/extensor moment/body weight (Nm/kg)			
Max peak	0.57±0.21	0.58±0.17	NS
Min peak	-0.60±0.14	-0.69±0.19	NS
Range	1.17±0.32	1.27±0.34	NS
Hip power/body weight (W/kg)			
Max peak (generation)	0.86±0.35	0.69±0.30	NS
Min peak (absorption)	-0.78±0.33	-0.57±0.19	NS
Range	1.65±0.61	1.27±0.47	NS
KNEE			
Sagittal plane knee flexion/extension angle (°)			
Max peak	64.8±4.8	62.3±4.4	NS
Min peak	1.0±4.5	5.4±4.0	P<0.05
Range	63.7±7.2	56.8±3.9	P<0.05
Sagittal plane knee flexor/extensor moment/body weight (Nm/kg)			
Max peak	0.24±0.13	0.39±0.17	P<0.05
Min peak	-0.23±0.07	-0.25±0.07	NS
Range	0.47±0.16	0.64±0.20	P<0.05
Knee power/body weight (W/kg)			
Max peak (generation)	0.44±0.33	0.57±0.32	NS
Min peak (absorption)	-1.04±0.45	-0.73±0.27	NS
Range	1.48±0.68	1.30±0.55	NS
ANKLE			
Sagittal plane ankle dorsiflexion/plantarflexion angle (°)			
Max peak	12.9±4.9	18.3±4.3	P<0.05
Min peak	-12.3±6.4	-12.5±5.7	NS
Range	25.2±3.9	30.7±5.2	P<0.01
Sagittal plane ankle dorsiflexor/plantarflexor moment/body weight (Nm/kg)			
Max peak	0.86±0.11	1.24±0.20	P<0.01
Min peak	-0.04±0.03	-0.11±0.07	P<0.01
Range	0.90± 0.12	1.35± 0.20	P<0.01
Ankle power/body weight (W/kg)			
Max peak (generation)	2.14±0.58	2.95±1.10	P<0.05
Min peak (absorption)	-0.74±0.22	-0.86±0.39	NS
Range	2.88± 0.69	3.82± 1.45	P<0.05

Increased pelvic rotation in transverse plane may be interpreted as a useful strategy adopted to improve step length.

The over extension of the knee at mid/terminal stance is not a specific alteration at this stage but has to be related to the reduced dorsiflexion at the ankle. In fact, the difficult development of the second rocker and the minor dorsiflexion of the ankle in terminal stance reduce the forward progression of the shank, producing a greater extension of the knee. From the kinetics analysis, a significant increase of the knee extensor moment in mid-stance was observed, which was consistent with a stiff-knee gait pattern.

The ankle showed an increased plantarflexion in swing phase and also, consequently, at initial contact. The compensation for this plantarflexion pattern resulted in greater than normal hip and knee flexion and in the slight elevation of the pelvis which appears at late swing (although not statistically significant).

The ankle showed a dorsiflexor moment at initial contact that, in relation to controls, was increased at loading response and reduced at push-off. This pattern is consistent with dynamic equinus foot: in effects, this is a dynamic adaptation that allows an optimal relation of the ground reaction force to proximal joints, especially the knee, to be maintained.[11]

Looking at the joint powers, significant differences were evident at the ankle at loading response (higher absorption) and in pre-swing (lower production). These results show that during loading response the ankle joint yields under the body weight while in pre-swing the power production is reduced because of muscle weakness.

With reference to the work of Sutherland *et al*.[9] the determinants of the DMD gait that were confirmed in our analysis are mainly two: the reduced dorsiflexion in swing and the increased anterior pelvic tilt. At difference with that work, in our DMD patients, cadence was not decreased but increased. Probably, this was due to the fact that in our study only patients in the early stage of the disease were included, and consequently only subtle gait changes had to be expected. In addition to the above mentioned determinants, other small but meaningful changes have been identified in our results. The most relevant of them, from the functional point of view, were: pelvis movement characterized by a "double bump" pattern, similar to that observed by D'Angelo *et al*.[8] in more advanced stages of the dystrophy, increased hip flexion in swing, tendency to knee hyperextension, reduced dorsiflexion in late stance, reduced moments and powers at push off.

Conclusions

These quantitative observations could be relevant to design proper rehabilitation interventions and to support the indications for physiotherapy. On this basis an intervention plan can be aimed at maintaining a proper relation between cadence and step length, the correct balance between flexor and extensor muscles, reducing the increased stiffness that prevents ankle dorsiflexion. For example, at the hip joint, it could be useful to try to keep the proper length of the flexors and increase the strength of the extensors (gluteus maximus). At the ankle joint early stretching exercises could be considered in order to maintain the range of motion. The use of casting could also be decided to help the foot support and to facilitate the toe clearance in swing.

In this respect the sensitivity of the gait analysis is essential in order to assess, characterize, and quantify early signs of modifications. This is particularly useful when applied in the first stages of the pathology, situation in which other clinical and functional assessment methods fail to clearly distinguish between specific alterations that are developing during the progressive worsening of locomotion.

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