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Head and pelvis are the key segments recruited by adult spinal deformity patients during daily life activities

Elma Ayoub[1,4], Ali Rteil[1,4], Celine Chaaya[1], Rami Rachkidi[1], Maria Saadé[1], Elena Jaber[1], Elio Mekhael[1], Nabil Nassim[1], Rami Rehayem[1], Mohamad Karam[1,2], Aren Joe Bizdikian[1], Ismat Ghanem[1], Wafa Skalli[3], Abir Massaad[1] & Ayman Assi[1,3]

Functional assessment is a key element in evaluating adult spinal deformity (ASD) patients. The multitude of 3D kinematic parameters provided by movement analysis can be confusing for spine surgeons. The aim was to investigate movement patterns of ASD based on key kinematic parameters. 115 primary ASD and 36 controls underwent biplanar radiographs and 3D movement analysis during walking, sit-to-stand and stair ascent to calculate joint and segment kinematics. Principal component analysis was applied to identify the most relevant kinematic parameters that define movement strategies adopted by ASD. Pelvis and head relative to pelvis kinematics were the most relevant parameters. ASD patients adopted four different movement strategies. Class 1: normative head and pelvis kinematics. Class 2: persistent pelvic backward tilt. Class 3: persistent forward shift of the head. Class 4: both pelvic backward tilt and forward shift of the head. Patients in class 3 and 4 presented sagittal malalignment on static radiographs with increased pelvic tilt, pelvic incidence-lumbar lordosis mismatch and sagittal vertical axis. Surprisingly, patients in class 3 had normal pelvic kinematics during movement, showing the importance of functional evaluation. In addition to being key segments in maintaining static global posture, head and pelvis were found to define movement patterns.

Keywords Adult spinal deformity, 3D movement analysis, Functional assessment, Head kinematics, Pelvis kinematics, Daily life activities

Adult Spinal Deformity (ASD) presents a significant burden on public health systems, leading to various comorbidities. Even when treated surgically, complications can appear post-operatively including mechanical problems that affect patient's quality of life. Over the past two decades, substantial progress has been made in understanding the basic principles of spino-pelvic alignment proposed by Duval-Beaupère and Dubousset[1,2]. These advancements have contributed to our knowledge of the compensatory mechanisms enabling ASD patients to maintain an upright posture. Past research mostly relied on static X-rays to explore these mechanisms and reasons for surgical failure.

It is essential to recognize that patients do not remain static during daily life and are dynamic entities, actively engaging in movements that are crucial for their autonomy and social interactions. Until lately, patient movement was qualitatively evaluated in Health-Related Quality of Life (HRQoL) questionnaires. In fact, it has been recently demonstrated that functional assessment through the calculation of joint kinematics during walking can better explain HRQoL scores than classic radiographic evaluation[3]. In the past few years, several studies highlighted the importance of the functional evaluation in patients with spinal deformity[4,5].

In fact, several reports have contributed to providing a comprehensive description of the kinematic limitations experienced by ASD patients during movements such as walking, ascending and descending stairs, and sit-to-stand transition[6–9]. In such evaluation, an exhaustive list of 3D joint and segmental angles of the whole

[1]Laboratory of Biomechanics and Medical Imaging, Faculty of Medicine, Saint Joseph University of Beirut, Beirut, Lebanon. [2]Institute of Physiotherapy, Faculty of Medicine, Saint Joseph University of Beirut, Beirut, Lebanon. [3]Institut de Biomécanique Humaine Georges Charpak, Arts et Métiers, Paris, France. [4]These authors contributed equally: Elma Ayoub and Ali Rteil. ✉email: ayman.assi@usj.edu.lb

body is calculated, including the head, neck, shoulder, thorax, spine segments, pelvis, hip, knee, ankle, and foot, in addition to the classical spatio-temporal parameters such as walking speed, cadence and step length.

While the movement analysis community is used to such parameters, spine surgeons can face challenges in adding all these new parameters to the already long list of radiographic parameters they have to integrate in their clinical reasoning.

Therefore, the aim of this study was to investigate the most relevant kinematic parameters that define ASD movement patterns in order to incorporate patients' functional evaluation in daily-routine clinical practice.

Material and methods

Participants

This is a cross-sectional IRB-approved study (CEHDF1259—Ethical committee of the Hôtel-Dieu de France Hospital) where primary ASD patients were referred by their physicians for a radiographic analysis due to back pain and/or discomfort were enrolled. Patients were older than 20 years old and presented at least one of the following radiographic criteria: pelvic tilt (PT) > 25°, sagittal vertical axis (SVA) > 50 mm, pelvic incidence-lumbar lordosis mismatch (PI-LL) > 10°, thoracic kyphosis (TK) > 60°, and/or coronal Cobb angle > 20°[10,11]. Adult patients who have untreated adolescent idiopathic scoliosis were included.

Patients who had recent spine or lower limb surgery were excluded.

A group of control subjects, comparable in sex distribution and age to the ASD group were enrolled. Subjects in the control group were included based on the following: no prior history of degenerative joint disease, lower limb, spinal surgery or musculoskeletal system diseases.

All participants were informed about the whole procedure and signed a consent form prior to their enrollment. All experiments were performed in accordance with the Declaration of Helsinki. Informed consent for publication of identifying information/images in an online open-access publication that could lead to identification of a study participant were obtained.

Data acquisition

Demographics

Age (year), sex (F/M), height (cm) and weight (kg) were collected for each subject.

Radiographic parameters

All participants underwent low-dose whole-body biplanar radiographs using the EOS® system (ATEK Spine, Inc., CA, USA). Subjects were asked to stand in the free-standing position (Fig. 1a)[12,13].

Following radiographic acquisitions, an experienced operator performed three-dimensional reconstructions of the spine and pelvis using a dedicated software (SterEOS®, ATEK Spine, Inc., CA, USA). The classical spinopelvic parameters were calculated: pelvic tilt (PT), pelvic incidence (PI), lumbar lordosis L1S1 (LL), thoracic kyphosis T1T12 (TK), Cobb angle, sagittal vertical axis (SVA), knee flexion angle and the odontoid to hip axis (ODHA) angle between the vertical line and the line joining the odontoid process with the hip axis[14] (Fig. 1b,c).

In addition, assessment of hip osteoarthritis of all subjects was performed by an orthopedic surgeon using the method described by Kellgren and Lawrence[15].

HRQoL questionnaires

All participants filled out the following HRQoL and disability questionnaires: Visual Analog Scale for pain (VAS), Oswestry Disability Index (ODI), Short Form Health Survey (SF-36): measuring both Physical Component Summary (PCS) and Mental Component Summary (MCS).

Motion analysis

<u>Motion capture.</u> Eight cameras were used (Vero 2.2, Vicon Motion Systems®, Oxford, UK) for the kinematic analysis. In order the investigate whole-body kinematics, a total of 41 markers were placed on the spine and lower limbs according to the Leardini and Davis protocols[16,17] mainly on the head, acromion processes, sternoclavicular joint, xiphoidal process, C7, T2, T10, L1, L3, L5 vertebral spinous processes, anterior superior and posterior superior iliac spines, lateral thigh and shank, internal and medial condyles and malleoli, as well as the calcaneum and the base of the second metatarsal bone (Fig. 2). Women were provided with a sport top to wear during acquisitions that makes anatomical landmarks accessible for marker placement.

<u>Joint angle definition and gait parameters.</u> The following angles were calculated, in all 3 planes, using Nexus and ProCalc (Vicon®, Oxford, UK): head, trunk and pelvis (all relative to the global reference), segmental movements of the spine (L3L5 relative to L1L3, L1L3 relative to T10L1, T10L1 relative to T2T10, T10L3 relative to T2T10, and T2T10 relative to T2C7), L3L5-pelvis (pelvis relative to L3L5), hip (femur relative to pelvis), knee (tibia relative to femur), ankle (foot relative to tibia), and the foot progression (foot relative to global reference).

The kinematic modified ODHA angle (k-ODHA) (angle between the vertical and the line joining the center of the 4 head markers and hip axis), an angle that reflects the radiographic ODHA, was calculated to estimate the sagittal alignment during movement.

Similarly, k-pelvic tilt was calculated to estimate the radiographic pelvic retroversion (PT) during movement, known also as pelvic tilt (forward/backward) during walking. It should be noted that pelvic retroversion increases with increasing radiographic pelvic tilt and decreasing kinematic pelvic tilt, called pelvic backward tilt during movement (Fig. 3).

Mean values and range of motion (ROM) of all kinematic parameters were calculated.

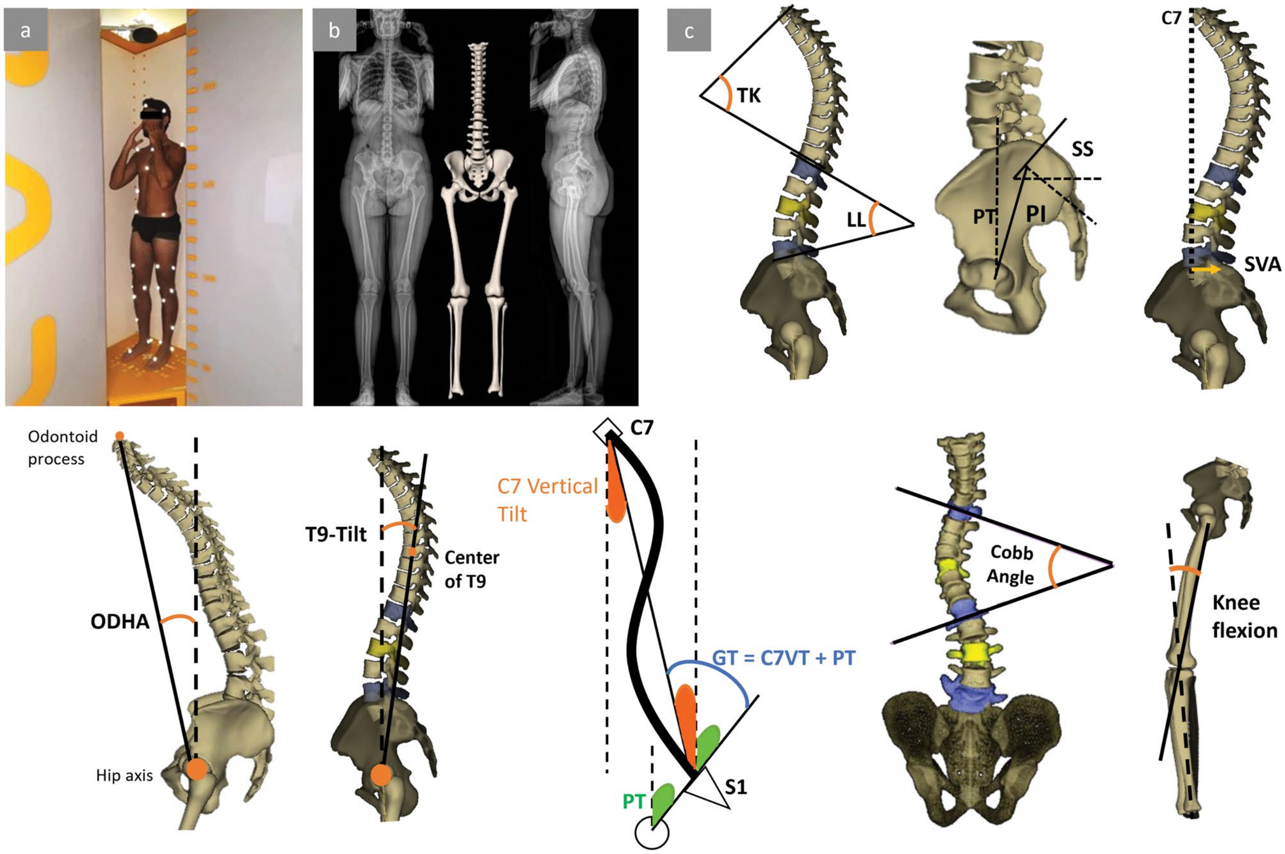

Figure 1. (**a**) Subject in the free-standing position in biplanar radiographs; (**b**) 3D reconstruction of the spine and pelvis; (**c**) Spino-pelvic and postural parameters. TK, thoracic kyphosis T1T12; LL, lumbar lordosis L1S1; PT, pelvic tilt; PI, pelvic incidence; SS, sacral slope; SVA, sagittal vertical axis; ODHA, odontoid to hip axis angle; GT, global tilt; C7VT, C7 vertical tilt.

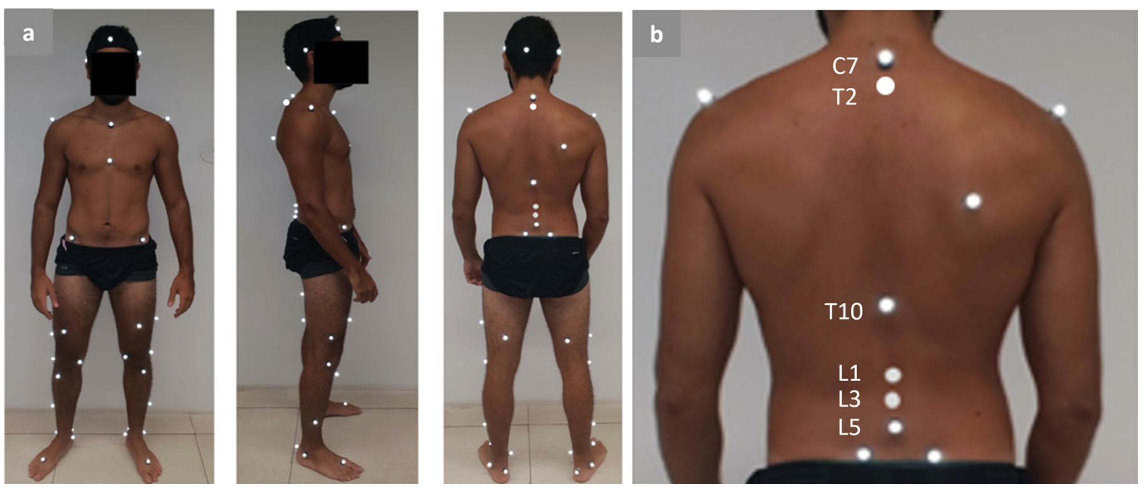

Figure 2. (**a**) Marker placement based on the protocol described by Davis et al.[17]; (**b**) Representation of spine segments as described by Leardini et al.[16].

Additionally, the Gait deviation index (GDI), based on the deviation of pelvic and lower limb gait parameters from the normative database, was calculated[18] to quantify the overall gait alterations.

The following spatio-temporal parameters were computed during walking: walking speed (m/s), cadence (steps/min), foot off (% of walking cycle), double support time (s), step length (m).

Functional tasks. Three functional tasks were studied: walking, sit-to-stand transition, and stair ascent.

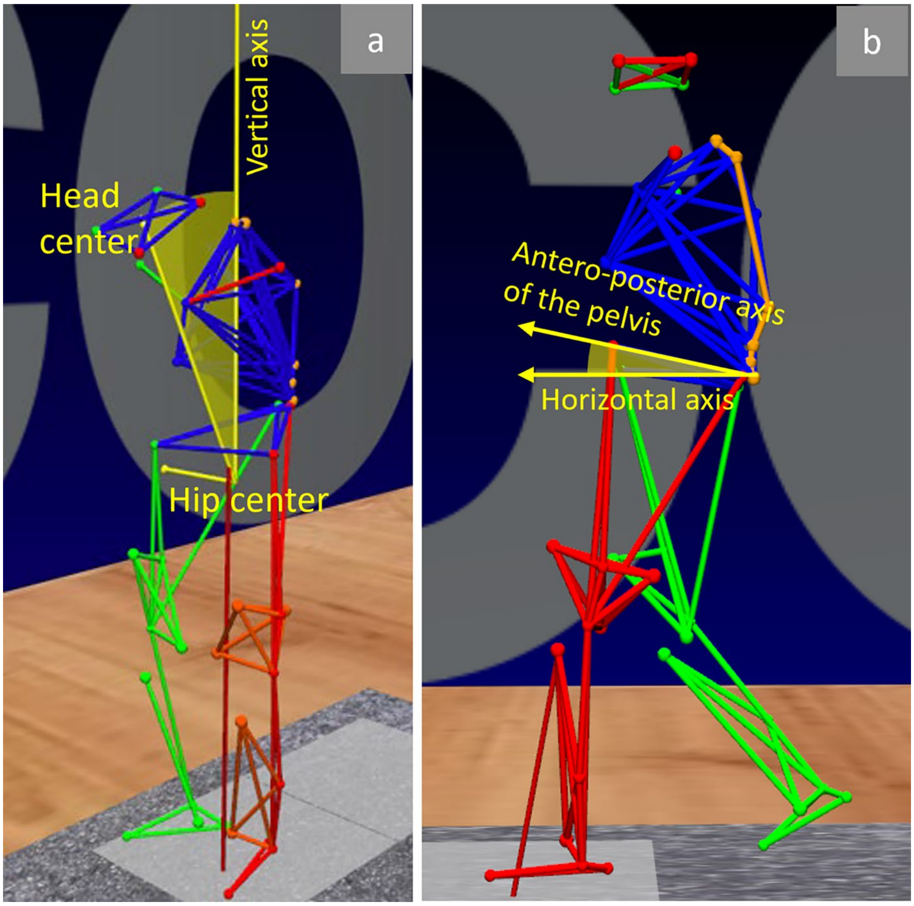

Figure 3. Representation of (kinematic) k-ODHA (**a**) and k-Pelvic tilt (**b**) on 3D models.

For the walking exercise, subjects were asked to walk at a self-selected speed in a 10-m corridor. For the sit-to-stand transition, participants were asked to complete it without using hands for support if possible or while using hands for support on the thighs if required. The stair ascent was performed on a single stair step of a standard height of 16 cm. Movements were normalized between the beginning (0%) and end of each task (100%). The walking cycle begins at the heel strike and finishes at the next heel strike of the same limb. The sit-to-stand cycle begins immediately before rising from the chair and finishes directly when the subject is immobilized after standing. The stair ascent cycle begins immediately before moving the leading foot and finishes when the opposite foot lands on the stair step.

Statistical analysis
In order to define movement patterns developed by ASD during daily life activities, the most relevant kinematic variables were investigated. A principal component analysis (PCA), based on correlation matrix, was performed on 19 variables representing the average during movement of: k-ODHA, head flexion/extension, neck flexion/extension, thorax flexion/extension, shoulder-pelvis axial rotation, flexion/extension of C7T2-T2T10, T2T10-T10L1, T10L1-L1L3, L1L3-L3L5, L3L5-pelvis, pelvic and hip kinematics in the three planes, knee flexion/extension, ankle dorsi/plantar flexion, and foot progression angle. The most strongly correlated variables to the first three components determined by the PCA were then selected depending on their clinical significance.

The selected variables were then coded as normal, if within the normative corridor of mean ± standard deviation (SD) of the control group, or abnormal if outside the normative corridor (Fig. 4). A classification of movement patterns was therefore defined based on the selected variables and their position relative to the normative corridor.

Demographic data, kinematic parameters, radiographic parameters and HRQoL scores were compared between classes of movement patterns using the Analysis of Variance (ANOVA) with a Tukey pairwise comparison or a Kruskall-Wallis U test followed by a Conover-Iman multiple pairwise comparison depending on the normality of the data (Shapiro–Wilk test). Correlations between HRQoL scores, radiographic and kinematic parameters were calculated using either Pearson's or Spearman's correlation coefficient depending on the normality of the data (Shapiro–Wilk test). The association between the movement patterns developed by the patients and the movement performed was evaluated using a Chi-squared test. An example was displayed to illustrate the results.

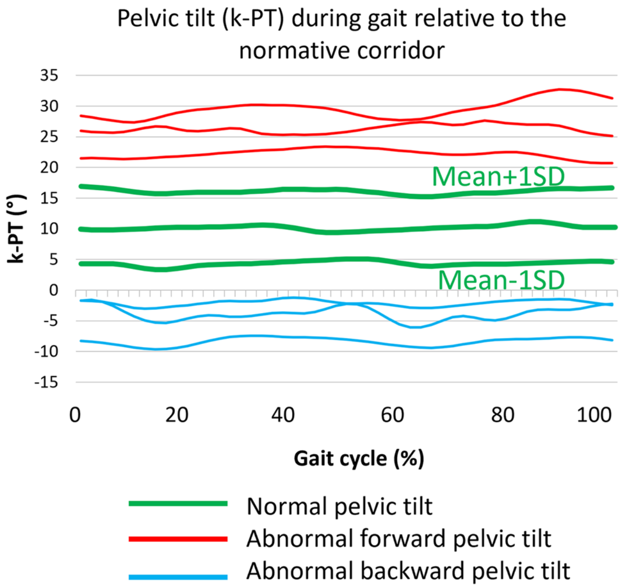

Figure 4. Example of classification of kinematic waveforms as normal or abnormal depending on the corridor of normality.

All statistical analyses were performed using XLSTAT® (Addinsoft, Paris, France; version 2018.3). The significance level was set at 0.05 and adjusted, when necessary, by a Bonferroni correction.

Results

Demographics

In total, 115 ASD [53 ± 19 years old; 86 F; 73 ± 14 kg; 161 ± 10 cm] and 36 controls [50 ± 13 years old: 22 F; 73 ± 11 kg; 165 ± 8 cm] were enrolled. No significant differences in age, and weight distribution between the two groups was noted ($p > 0.05$). ASD subjects were slightly shorter compared to controls ($p < 0.05$).

Functional classification

The PCA analysis showed that the cumulative percentage of total variability ranged from 20% with the first component, 32% with the second component, 40% with the third component and 70% with the seventh component. The most correlated variables to the first, second and third components were k-ODHA, k-PT and hip abduction/adduction respectively with the following factor loading 0.87, 0.80 and 0.79 (Fig. 5). Since hip abduction/adduction is less clinically relevant in the setting of ASD than k-ODHA and k-PT, only the two latter were then selected for further analysis.

Mean and SD of k-ODHA in controls were 4° and 2° respectively; k-ODHA > 6° was considered as an abnormally forwarded head. Mean and SD of k-PT in controls were 13° and 7° respectively; k-PT < 6° was considered as an abnormally backward tilted pelvis.

Thus, four different classes of movement patterns were determined:

ASD in class 1 had normal k-ODHA and k-pelvic tilt (ASD-moderate), those in class 2 had only an increased backward pelvic tilt (Pelvis-backward tilt), ASD patients in class 3 had only an increased k-ODHA (Head-forward), and finally ASD in class 4 had an increased pelvic backward tilt and k-ODHA (Pelvis-backward tilt_Head-forward). Class 0 was attributed to controls.

The percentage of patients in each class for each movement as well as the intra and inter-class variances are presented in (Table 1).

Comparison of the kinematic parameters between the 4 classes

Kinematic waveforms that differed between classes are displayed in Fig. 6 and Table 2.

ASD-moderate (Class 1)

Patients in class 1 showed similar kinematics compared to controls during walking, sit-to-stand transition, and stair ascent.

ASD Pelvis-backward tilt (Class 2)

During walking, patients in class 2 showed an increased pelvic backward tilt (− 2 ± 4° vs. 13 ± 7° in controls; $p < 0.001$), hyperflexion of the L3L5 segment relative to the pelvis (17 ± 9° vs. 1 ± 8° in controls; $p < 0.001$) and a decreased hip flexion (2 ± 6° vs. 18 ± 8° in controls; $p < 0.001$).

During sit-to-stand transition, patients in class 2 exhibited an increased pelvic backward tilt (− 1 ± 6° vs. 15 ± 7° in controls, $p < 0.001$).

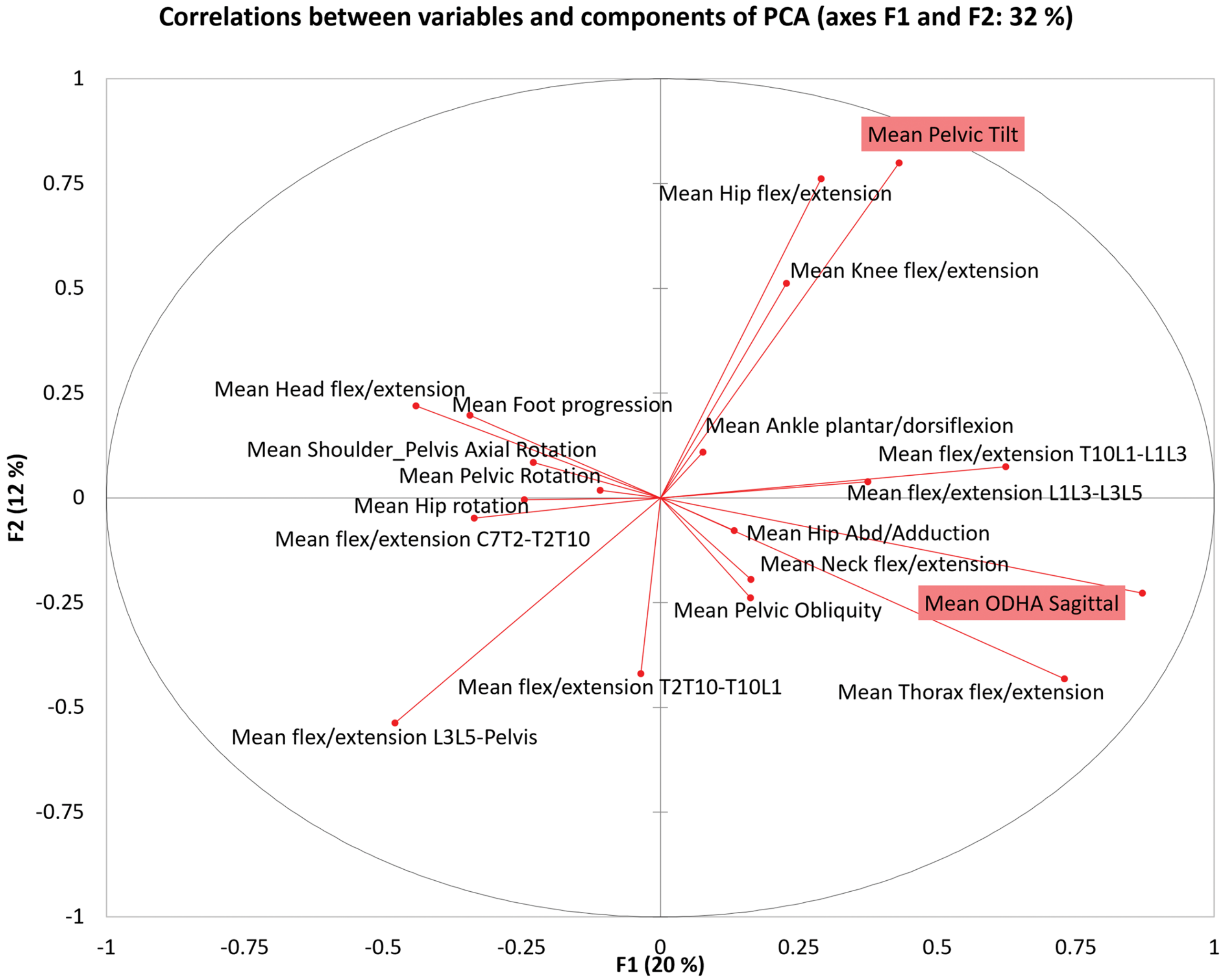

Figure 5. Correlations between kinematic variables and the first two components obtained by PCA.

During the stair ascent movement, patients in this class had a k-ODHA comparable to controls. They had a retroverted pelvis during movement (3 ± 3° vs. 16 ± 6° in controls, $p < 0.001$), with a decreased hip flexion (24 ± 5° vs. 37 ± 10° in controls, $p < 0.001$). They presented an increased knee flexion ROM (89 ± 11° vs. 86 ± 14° in controls, $p = 0.01$).

ASD Head-forward (Class 3)

During walking, patients in class 3 presented an increased trunk flexion (18 ± 11° vs. 4 ± 5° in controls; $p < 0.001$), head extension (– 16 ± 12° vs. 1 ± 11° in controls; $p < 0.001$) and a reduced dynamic lumbar lordosis (L1L3–L3L5: – 5 ± 9° vs. – 12 ± 6° in controls; $p < 0.001$). They also showed a reduced hip ROM (38 ± 9° vs. 46 ± 6° in controls; $p < 0.001$) and knee ROM (55 ± 5° vs. 60 ± 6° in controls; $p < 0.001$) in the sagittal plane throughout the gait cycle. Concerning the spatio-temporal parameters, these patients walked slowly (0.8 ± 0.3 m/s vs. 1.2 ± 0.2 m/s in controls; $p < 0.001$), with a longer double support time (0.4 ± 0.2 s vs. 0.2 ± 0.1 s in controls; $p < 0.001$) and a shorter step length (0.5 ± 0.1 m vs. 0.6 ± 0.1 m in controls; $p < 0.001$).

During sit-to-stand transition, they had, by definition, an increased k-ODHA (22 ± 4° vs. 13 ± 4° in controls, $p < 0.001$). In addition, they had an increased trunk flexion (31 ± 8° vs. 14 ± 6° in controls, $p < 0.001$) and C7T2-T2T10 flexion (27 ± 8° vs. 18 ± 7° in controls, $p < 0.001$).

During stair ascent, patients in class 3 exhibited an increased k-ODHA (19 ± 8° vs. 8 ± 4° in controls, $p < 0.001$), coupled with an increased trunk flexion (24 ± 9° vs. 5 ± 6° in controls; $p < 0.001$), as well as a reduced dynamic lumbar lordosis (L1L3–L3L5: – 7 ± 11° vs. – 14 ± 8° in controls; $p = 0.002$). Pelvis and lower limbs kinematics were comparable to controls.

ASD Pelvis-backward tilt_Head-forward (Class 4)

During walking, patients in class 4 presented the most altered gait deviation index compared to controls (76 ± 7° vs. 94 ± 11° in controls; $p < 0.001$) and walked with an increased pelvic backward tilt (– 3 ± 4° vs. 13 ± 7° in controls; $p < 0.001$), k-ODHA (13 ± 5° vs. 4 ± 2° in controls; $p < 0.001$), head extension (– 13 ± 8° vs. 1 ± 11° in controls; $p < 0.001$), as well as trunk flexion (23 ± 10° vs. 4 ± 5° in controls; $p < 0.001$). They showed a reduced flexion of

	Controls (N = 36)	**ASD (N = 115)**				***p*-value**	**Controls vs. Class 1**	**Controls vs. Class 2**	**Controls vs. Class 3**	**Controls vs. Class 4**	**Class 1 vs. Class 2**	**Class 1 vs. Class 3**	**Class 1 vs. Class 4**	**Class 2 vs. Class 3**	**Class 2 vs. Class 4**	**Class 3 vs. Class 4**
	Class 0	**Class 1**	**Class 2**	**Class 3**	**Class 4**											
Walking																
N (%)		56	12	25	7											
Age (years)	53 ± 8	47 ± 20	51 ± 14	66 ± 13	65 ± 14	**< 0.001**			*			*	*	*		
Weight (Kgs)	73 ± 11	70 ± 13	72 ± 15	78 ± 15	73 ± 17	0.17										
Height (cm)	165 ± 8	162 ± 9	162 ± 8	160 ± 12	161 ± 16	0.12										
Inter/Intra-class variance (%)		72%/28%														
Sit to Stand																
N (%)		68	7	19	6											
Age (years)	47 ± 14	49 ± 20	48 ± 21	61 ± 16	67 ± 8	**0.001**			*	*		*				
Weight (Kgs)	72 ± 12	71 ± 15	68 ± 18	75 ± 12	75 ± 7	0.33										
Height (cm)	167 ± 7	162 ± 9	164 ± 11	160 ± 9	153 ± 12	**0.002**	*		*	*						
Inter/Intra-class variance (%)		85%/15%														
Stair ascent																
N (%)		50	10	30	10											
Age (years)	50 ± 13	46 ± 19	44 ± 19	65 ± 14	64 ± 12	**< 0.001**			*	*		*	*	*	*	
Weight (Kgs)	72 ± 12	71 ± 16	70 ± 15	76 ± 11	70 ± 17	0.16										
Height (cm)	167 ± 7	163 ± 11	165 ± 7	161 ± 9	158 ± 10	**0.004**			*	*						
Inter/Intra-class variance (%)		80%/20%														

Table 1. Comparison of demographic parameters (mean ± SD) between classes of movement patterns during walking, sit to stand and stair ascent. *and bold: significant *p*-value.

the L3L5 segment relative to the pelvis (8 ± 12° vs. 1 ± 8° in controls; $p < 0.001$). They also exhibited a lack of hip flexion (5 ± 8° vs. 18 ± 8° in controls; $p < 0.001$), with reduced knee ROM during all of the gait cycle (51 ± 9° vs. 60 ± 6° in controls; $p < 0.001$). They presented with slower walking pace (0.8 ± 0.2 m/s vs. 1.2 ± 0.2 m/s in controls; $p < 0.001$), a longer double support time (0.4 ± 0.2 s vs. 0.2 ± 0.1 s in controls; $p < 0.001$) and a shorter step length (0.5 ± 0.1 m vs. 0.6 ± 0.1° in controls; $p < 0.001$).

During sit-to-stand, patients in class 4 had similar kinematic alterations as class 3, with the addition of a significantly backward tilted pelvis (4 ± 3° vs. 15 ± 7° in controls, $p < 0.001$).

During stair ascent, patients in class 4 exhibited overall positive alignment during movement marked by an increased k-ODHA (18 ± 6° vs. 8 ± 4° in controls, $p < 0.001$), pelvic backward tilt (1 ± 4° vs. 16 ± 6° in controls, $p < 0.001$) and consequent limitation of hip flexion (23 ± 11° vs. 37 ± 10° in controls, $p < 0.001$).

Comparison between classes

Pelvic incidence was comparable between the 4 classes ($p > 0.05$).

During walking, ASD-moderate patients (class 1) showed only an increased Cobb angle (23 ± 19° vs. 6 ± 6° in controls; $p < 0.001$).

ASD Pelvis-backward tilt patients (class 2) showed mostly an increased PT (24 ± 9° vs. 11 ± 6° in controls; $p < 0.001$).

ASD Head-forward patients and ASD Pelvis-backward tilt_Head-forward patients (class 3 and 4) showed a significant increase of radiographic PT (Class 3: 24 ± 10°, Class 4: 32 ± 16° vs. 11 ± 6° in controls; $p < 0.001$), ODHA (Class 3: 7 ± 6°, Class 4: 5 ± 3° vs. 3 ± 2° in controls; $p < 0.001$), SVA (Class 3: 85 ± 60 mm, Class 4: 88 ± 84

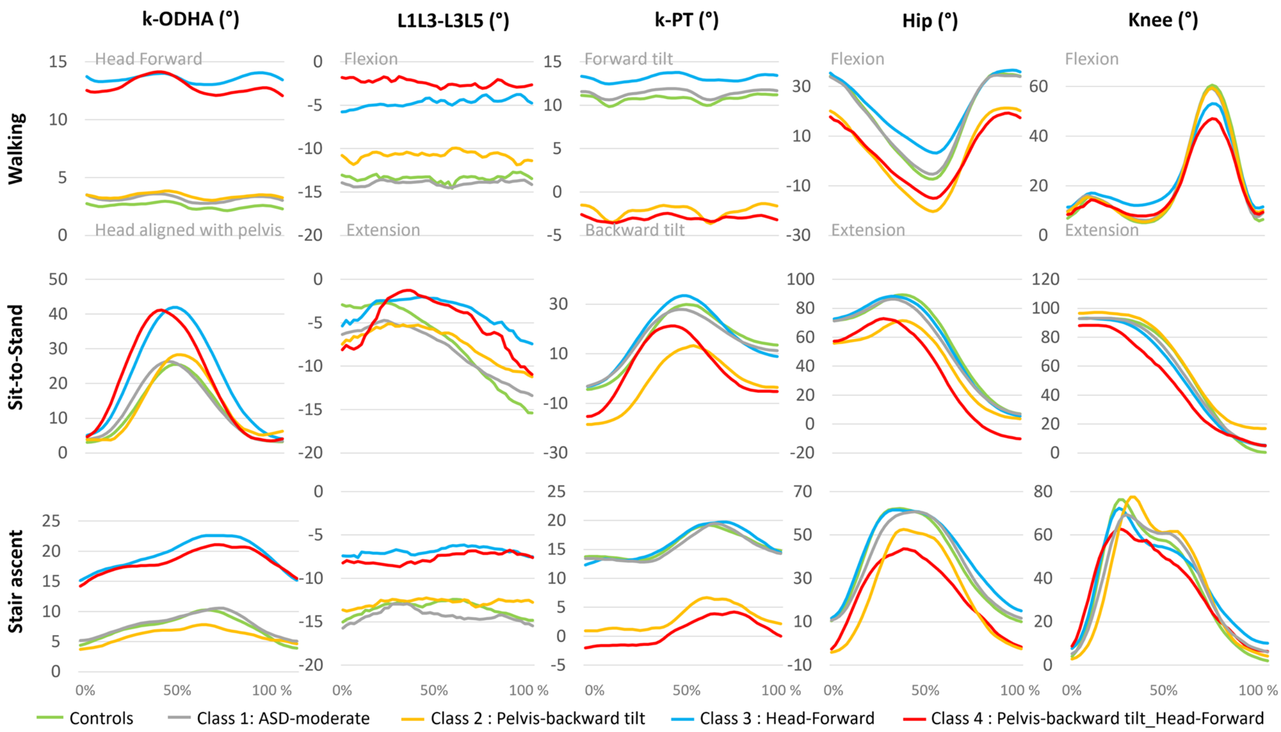

Figure 6. Average kinematic waveforms for each subgroup during walking, sit-to-stand transition, and stair ascent for k-ODHA, L1L3-L3L5, k-pelvis, hip and knee in the sagittal plane. Movement cycles were normalized between 0 and 100%.

mm vs. − 2 ± 22 mm in controls; $p < 0.001$), PI-LL mismatch (Class 3: 13 ± 22°, Class 4: 25 ± 34° vs. − 11 ± 8° in controls; $p < 0.001$), and knee flexion angle (Class 3: 11 ± 10°, Class 4: 12 ± 14° vs. 1 ± 7° in controls; $p < 0.001$).

They also had a higher grade of hip osteoarthritis (Class 3: 1.9, Class 4: 1.4 vs. 1.0 in controls; $p < 0.001$).

Results of radiographic parameters in each class of patients during sit-to-stand transition and stair ascent were comparable to those during walking (Table 3, Fig. 7).

All ASD patients showed a deteriorated HRQoL compared to controls. This deterioration was more pronounced in ASD Head-forward patients and ASD Pelvis-backward tilt_Head-forward patients for the ODI (Class 3: 42 ± 17, Class 4: 43 ± 15 vs. 15 ± 12 in controls; $p < 0.001$) and the PCS of SF-36 (Class 3: 34 ± 6, Class 4: 38 ± 11 vs. 51 ± 6 in controls; $p < 0.001$) (Table 4).

Correlations

During walking, the k-ODHA was positively correlated to the VAS for pain and ODI (ρ = 0.28, r = 0.47, respectively; $p < 0.001$).

During the sit-to-stand transition, the k-ODHA angle was positively correlated to the grade of hip osteoarthritis (ρ = 0.38, $p < 0.001$), VAS for pain, and ODI (ρ = 0.28, r = 0.33; $p < 0.001$, respectively).

Finally, during stair ascent, k-ODHA angle was positively correlated with the radiographic pelvic tilt (r = 0.49, $p < 0.001$) and positively correlated with ODI (r = 0.41; $p < 0.001$) (Fig. 8).

The association analysis showed that 13% of the patients adopted the same kinematic strategy in all 3 performed movements ($p = 0.9$).

Clinical case presentation

The clinical case presented in Fig. 9 shows a 71-year-old female patient with a PI of 59°, SVA of 31 mm, PT of 36°, LL of 33° and TK of 54°. This patient adopted 3 different movement patterns during the studied functional tasks. She walked with a backward tilted pelvis which would correspond to class 2. She went from a sitting position to a standing position with a forward head and therefore identifies as a class 3 patient. She ascended the stair step with the head forward and the pelvis backward tilted which would be the movement pattern of class 4.

Discussion

Recent studies have shown the importance of functional assessment in patients with adult spinal deformity and not to rely solely on static standing radiographs. Daily life activities are essential for maintaining patients' autonomy that reflects on their quality of life. This study showed that the kinematic global alignment of the head above the pelvis, and the kinematic pelvic tilt are the key parameters that define four different movement patterns adopted by ASD patients during daily life activities.

Parameters	Controls (N = 36)	Class 1	Class 2	Class 3	Class 4	*p*-value	Controls vs. Class 1	Controls vs.Class 2	Controls vs.Class 3	Controls vs. Class 4	Class 1 vs. Class 2	Class 1 vs. Class 3	Class 1 vs. Class 4	Class 2 vs. Class 3	Class 2 vs. Class 4	Class 3 vs. Class 4
Walking																
Gait Deviation Index (GDI)	94 ± 11	93 ± 13	80 ± 9	82 ± 14	76 ± 7	**< 0.001**		*	*	*	*	*	*			
Mean k-ODHA Sagittal (°)	4 ± 2	3 ± 2	3 ± 2	14 ± 6	13 ± 5	**< 0.001**			*	*		*	*	*	*	
Mean Head flex/ext (°)	1 ± 11	0 ± 10	3 ± 12	− 16 ± 12	− 13 ± 8	**< 0.001**			*	*		*	*	*	*	
Mean Trunk flex/ext (°)	4 ± 5	3 ± 9	4 ± 7	18 ± 11	23 ± 10	**< 0.001**			*	*		*	*	*	*	
Mean Trunk axial rot (°)	0 ± 0	0 ± 0	0 ± 1	0 ± 1	0 ± 1	0.55										
Mean flex/ext L3L5-Pelvis (°)	1 ± 8	3 ± 10	17 ± 9	− 4 ± 11	8 ± 12	**< 0.001**		*			*	*		*		*
Mean flex/ext L1L3-L3L5 (°)	− 12 ± 6	− 14 ± 10	− 11 ± 9	− 5 ± 9	− 2 ± 10	**< 0.001**			*			*	*			
Mean flex/ext C7T2-T2T10 (°)	26 ± 7	29 ± 9	32 ± 9	27 ± 9	21 ± 10	**0.02**										
Mean Pelvic Tilt (°)	13 ± 7	11 ± 5	− 2 ± 4	13 ± 7	− 3 ± 4	**< 0.001**		*		*	*		*	*		*
Mean hip flex/ext (°)	18 ± 8	17 ± 7	2 ± 6	22 ± 10	5 ± 8	**< 0.001**		*		*	*		*	*		*
ROM hip flex/ext (°)	46 ± 6	44 ± 6	42 ± 6	38 ± 9	39 ± 9	**< 0.001**			*			*				
Mean hip Abd/Add (°)	0 ± 4	0 ± 5	0 ± 3	0 ± 5	0 ± 2	0.96										
Mean Knee flex/ext (°)	21 ± 5	22 ± 6	21 ± 6	23 ± 7	22 ± 7	0.91										
ROM knee flex/ext (°)	60 ± 6	50 ± 11	57 ± 8	55 ± 5	51 ± 9	**< 0.001**			*	*		*				
Walking Speed (m/s)	1.2 ± 0.2	1.0 ± 0.2	1.0 ± 0.2	0.8 ± 0.3	0.8 ± 0.2	**< 0.001**	*		*	*		*		*		
Cadence (step/min)	113.7 ± 13.4	105.5	106.5 ± 9.2	94.8 ± 15.3	97.0 ± 15.1	**< 0.001**	*		*	*		*		*		
Single Support (s)	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	**0.01**			*							
Step Length (m)	0.6 ± 0.1	0.6 ± 0.1	0.6 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	**< 0.001**	*		*	*		*		*		
Double Support (s)	0.2 ± 0.1	0.3 ± 0.1	0.3 ± 0.1	0.4 ± 0.2	0.4 ± 0.2	**< 0.001**			*	*		*		*		
Sit-To-Stand																
Mean k-ODHA Sagittal (°)	13 ± 4	13 ± 4	14 ± 3	22 ± 4	20 ± 24	**< 0.001**			*	*		*	*	*	*	
Mean Head flex/ext (°)	9 ± 14	6 ± 12	5 ± 15	− 11 ± 15	− 6 ± 11	**< 0.001**			*	*				*		*
Mean Trunk flex/ext (°)	14 ± 6	16 ± 7	20 ± 10	31 ± 8	38 ± 10	**< 0.001**			*	*		*	*	*	*	
Mean Trunk axial rot (°)	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0.58										
Mean flex/ext L3L5-Pelvis (°)	5 ± 8	8 ± 10	15 ± 7	6 ± 11	11 ± 18	0.06										
Mean flex/ext L1L3-L3L5 (°)	− 7 ± 7	− 78 ± 7	− 7 ± 5	− 4 ± 9	− 1 ± 13	0.34										
Mean flex/ext C7T2-T2T10 (°)	18 ± 7	23 ± 10	23 ± 5	27 ± 8	14 ± 8	**< 0.001**			*	*			*			
Continued																

Parameters	Controls (N = 36)	Class 1	Class 2	Class 3	Class 4	*p*-value	Controls vs. Class 1	Controls vs.Class 2	Controls vs.Class 3	Controls vs. Class 4	Class 1 vs. Class 2	Class 1 vs. Class 3	Class 1 vs. Class 4	Class 2 vs. Class 3	Class 2 vs. Class 4	Class 3 vs. Class 4
Mean Pelvic Tilt (°)	15 ± 7	15 ± 6	− 1 ± 6	17 ± 8	4 ± 3	**< 0.001**		*		*	*		*	*		*
Mean hip flex/ext (°)	86 ± 11	82 ± 12	73 ± 23	86 ± 13	88 ± 16	0.22										
ROM hip flex/ext (°)	8 ± 4	9 ± 5	8 ± 4	9 ± 4	9 ± 3	0.73										
Mean hip Abd/Add (°)	19 ± 7	22 ± 11	20 ± 12	27 ± 12	32 ± 21	0.11										
Mean Knee flex/ext (°)	94 ± 7	90 ± 11	82 ± 25	89 ± 11	84 ± 18	0.15										
ROM knee flex/ext (°)	60 ± 9	59 ± 9	65 ± 11	56 ± 11	52 ± 9	0.13										
Stair ascent																
Mean k-ODHA Sagittal (°)	8 ± 4	8 ± 5	6 ± 3	19 ± 8	18 ± 6	**< 0.001**			*	*		*	*	*	*	
Mean Head flex/ext (°)	− 8 ± 20	− 11 ± 14	− 8 ± 17	− 31 ± 14	− 32 ± 17	**< 0.001**			*	*		*	*	*	*	
Mean Trunk flex/ext (°)	5 ± 6	6 ± 6	4 ± 4	24 ± 9	26 ± 7	**< 0.001**			*	*		*	*	*	*	
Mean Trunk axial rot (°)	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0.68										
Mean flex/ext L3L5-Pelvis (°)	− 2 ± 10	2 ± 10	13 ± 9	1 ± 12	15 ± 12	**< 0.001**		*		*	*		*	*		*
Mean flex/ext L1L3-L3L5 (°)	− 14 ± 8	− 14 ± 10	− 13 ± 4	− 7 ± 11	− 8 ± 9	**0.002**			*			*				
Mean flex/ext C7T2-T2T10 (°)	25 ± 8	30 ± 10	33 ± 8	29 ± 10	29 ± 10	**0.03**										
Mean Pelvic Tilt (°)	16 ± 6	15 ± 5	3 ± 3	16 ± 6	1 ± 4	**< 0.001**		*		*	*		*	*		*
Mean hip flex/ext (°)	37 ± 10	36 ± 9	24 ± 5	40 ± 10	23 ± 11	**< 0.001**		*		*	*		*	*		*
ROM hip flex/ext (°)	56 ± 8	57 ± 8	60 ± 7	56 ± 8	54 ± 8	0.50										
Mean hip Abd/Add (°)	− 1 ± 6	0 ± 5	− 3 ± 3	− 1 ± 5	0 ± 5	0.27										
Mean Knee flex/ext (°)	36 ± 8	37 ± 9	37 ± 5	39 ± 8	36 ± 9	0.76										
ROM knee flex/ext (°)	86 ± 14	85 ± 10	89 ± 11	77 ± 13	82 ± 10	**0.01**			*			*		*		

Table 2. Comparison of kinematic parameters (mean ± SD) between classes of movement patterns during walking, sit to stand and stair ascent. *and bold: significant *p*-value. Only clinically important kinematic variables were included.

During gait, control subjects walked with a pelvic forward tilt, as the head was maintained above the hips as shown by the k-ODHA parameter. During the sit-to-stand transition, they performed simultaneous flexion of the hip and the lumbar spine resulting in an initial anterior projection of the trunk. This was followed by an extension of the lower limbs and spine to achieve an erect standing position. An increased lumbar lordosis coupled with a forward tilt of the pelvis were required to complete the stair ascent.

Patients in the ASD-moderate group (class 1) adopted normal kinematic strategies when completing the three studied functional tasks, including the pelvis and the head kinematics. However, they showed a slight deterioration of their quality of life, which might be related to their primary frontal skeletal deformity, estimated by an increased radiological Cobb angle. This is in accordance with previous studies that showed an alteration of HRQoL but normal kinematics in patients with isolated frontal spine deformity[19]. It should be noted that patients in this class were younger than the remaining classes (47 ± 20 vs. 53 ± 8 years in controls; $p < 0.001$). Subjects in this class might originally be adolescent idiopathic scoliosis patients.

Patients in the Pelvis-backward tilt group (class 2) presented a pelvic backward tilt during the three studied tasks, while maintaining a normal head position with respect to their pelvis. Simply retroverting the pelvis appeared to be sufficient to ensure the alignment of the head above the pelvis (estimated by a normal k-ODHA)

Radiographic parameters	Controls (N = 36)	Class 1	Class 2	Class 3	Class 4	*p*-value	Controls vs. Class 1	Controls vs. Class 2	Controls vs. Class 3	Controls vs. Class 4	Class 1 vs. Class 2	Class 1 vs. Class 3	Class 1 vs. Class 4	Class 2 vs. Class 3	Class 2 vs. Class 4	Class 3 vs. Class 4
Functional classification of patients during Walking																
Cobb angle (°)	6 ± 6	23 ± 19	22 ± 20	19 ± 19	16 ± 12	**< 0.001**	*	*	*	*						
PI (°)	51 ± 9	51 ± 12	59 ± 13	52 ± 10	56 ± 8	**0.03**										
PT (°)	11 ± 6	15 ± 9	24 ± 9	24 ± 10	32 ± 16	**< 0.001**		*	*	*	*	*	*			
SS (°)	40 ± 8	36 ± 11	35 ± 12	28 ± 11	24 ± 18	**< 0.001**			*	*		*				
L1S1 (°)	61 ± 9	59 ± 18	60 ± 16	39 ± 21	32 ± 34	**< 0.001**			*	*		*		*		
L1L5 (°)	46 ± 11	46 ± 15	49 ± 16	27 ± 22	14 ± 37	**< 0.001**			*	*		*	*	*	*	
PI-LL (°)	− 11 ± 8	− 8 ± 15	− 1 ± 15	13 ± 22	25 ± 34	**< 0.001**			*	*		*	*			
T1T12 (°)	47 ± 10	52 ± 20	60 ± 17	54 ± 20	47 ± 25	0.11										
T4T12 (°)	43 ± 9	47 ± 21	55 ± 19	51 ± 21	49 ± 25	0.12										
C2–C7 (°)	3 ± 12	9 ± 15	15 ± 17	19 ± 16	6 ± 20	**< 0.001**			*							
ODHA 3D angle (°)	3 ± 2	3 ± 2	3 ± 2	7 ± 6	5 ± 3	**< 0.001**			*			*		*		
T9-tilt (°)	13 ± 3	14 ± 5	17 ± 5	12 ± 7	16 ± 10	**0.01**		*						*		
Global Tilt (°)	9 ± 9	13 ± 13	25 ± 11	35 ± 17	45 ± 26	**< 0.001**		*	*	*	*	*	*			
SVA (mm)	− 2 ± 22	6 ± 31	12 ± 33	85 ± 60	88 ± 84	**< 0.001**			*	*		*	*	*		
Hip Osteoarthritis grade	1.0 ± 0.8	1.0 ± 1.0	0.9 ± 1.0	1.9 ± 0.9	1.4 ± 0.7	**< 0.001**			*			*		*		
Knee flexion (°)	1 ± 7	4 ± 10	2.2 ± 8	11 ± 10	12 ± 14	**< 0.001**			*	*		*		*		
Functional classification of patients during sit to stand																
Cobb angle (°)	6 ± 6	22 ± 20	17 ± 12	22 ± 18	21 ± 18	**< 0.001**	*		*							
PI (°)	51 ± 9	51 ± 10	55 ± 11	52 ± 15	52 ± 10	0.76										
PT (°)	11 ± 6	16 ± 10	23 ± 11	21 ± 10	35 ± 15	**< 0.001**	*	*	*	*			*			
SS (°)	40 ± 8	36 ± 10	3 ± 10	31 ± 12	18 ± 21	**< 0.001**			*	*						
L1S1 (°)	61 ± 9	57 ± 17	55 ± 19	51 ± 26	27 ± 38	0.15										
L1L5 (°)	46 ± 11	43 ± 18	37 ± 21	40 ± 21	12 ± 43	0.23										
PI-LL (°)	− 11 ± 8	− 5 ± 18	0 ± 23	1 ± 19	26 ± 34	**0.02**				*						
T1T12 (°)	47 ± 10	51 ± 20	58 ± 13	59 ± 19	50 ± 30	0.11										
T4T12 (°)	43 ± 9	46 ± 19	54 ± 12	56 ± 24	50 ± 29	0.06										
C2–C7 (°)	3 ± 12	10 ± 15	11 ± 22	14 ± 17	22 ± 13	**0.02**				*						
ODHA 3D angle (°)	3 ± 2	4 ± 3	4 ± 2	5 ± 6	6 ± 6	0.12										
T9-tilt (°)	12 ± 4	13 ± 5	18 ± 4	15 ± 7	17 ± 9	**0.002**		*								
Global Tilt (°)	9 ± 8	16 ± 14	23 ± 14	25 ± 18	46 ± 24	**< 0.001**	*	*	*	*		*	*			
SVA (mm)	− 2 ± 22	13 ± 44	14 ± 40	51 ± 51	83 ± 73	**< 0.001**			*	*		*	*			
Hip Osteoarthritis grade	1.0 ± 0.8	1.0 ± 1.0	0.9 ± 0.8	1.9 ± 1.0	1.7 ± 0.5	**< 0.001**			*			*				
Knee flexion (°)	1 ± 7	3 ± 8	6 ± 7	11 ± 13	14 ± 18	**0.005**			*			*				
Functional classification of patients during stair ascent																
Cobb angle (°)	6 ± 6	25 ± 19	16 ± 13	16 ± 16	19 ± 18	**< 0.001**	*		*							
PI (°)	51 ± 9	52 ± 11	52 ± 9	51 ± 13	56 ± 8	0.49										
PT (°)	11 ± 6	14 ± 10	21 ± 7	22 ± 11	29 ± 11	**< 0.001**		*	*	*		*	*			
SS (°)	40 ± 8	38 ± 9	31 ± 9	29 ± 13	27 ± 9	**< 0.001**			*	*		*	*			
L1S1 (°)	61 ± 9	59 ± 14	57 ± 15	46 ± 27	44 ± 26	0.05										
L1L5 (°)	46 ± 11	46 ± 14	46 ± 12	32 ± 25	28 ± 27	**0.02**						*				
PI-LL (°)	− 11 ± 8	− 7 ± 16	− 5 ± 15	5 ± 23	12 ± 28	**0.01**										
T1T12 (°)	47 ± 10	51 ± 20	57 ± 16	55 ± 19	59 ± 23	0.19										
T4T12 (°)	43 ± 9	46 ± 19	49 ± 16	53 ± 20	59 ± 25	0.05										
C2–C7 (°)	3 ± 12	9 ± 13	11 ± 18	17 ± 18	19 ± 19	**0.003**			*							
ODHA 3D angle (°)	3 ± 2	3 ± 2	5 ± 2	6 ± 5	21 ± 53	**0.004**			*							
T9-tilt (°)	12 ± 3	12 ± 5	18 ± 4	14 ± 6	18 ± 6	**< 0.001**		*		*	*		*			
Global Tilt (°)	9 ± 8	14 ± 13	18 ± 9	29 ± 21	35 ± 16	**< 0.001**			*	*		*	*			
SVA (mm)	− 2 ± 22	12 ± 36	− 11 ± 23	60 ± 70	61 ± 51	**< 0.001**			*	*		*	*	*	*	
Continued																

Radiographic parameters	Controls (N = 36)	Class 1	Class 2	Class 3	Class 4	*p*-value	Controls vs. Class 1	Controls vs. Class 2	Controls vs. Class 3	Controls vs. Class 4	Class 1 vs. Class 2	Class 1 vs. Class 3	Class 1 vs. Class 4	Class 2 vs. Class 3	Class 2 vs. Class 4	Class 3 vs. Class 4
Hip Osteoarthritis grade	1.0 ± 0.8	1.0 ± 1.0	0.7 ± 0.9	1.6 ± 1.0	1.5 ± 0.8	**0.005**						*		*		
Knee flexion (°)	1 ± 7	3 ± 9	1 ± 6	10 ± 12	7 ± 12	**0.002**			*			*				

Table 3. Comparison of radiographic parameters (mean ± SD) between classes of movement patterns during walking, sit to stand and stair ascent. *and bold: significant *p*-value.

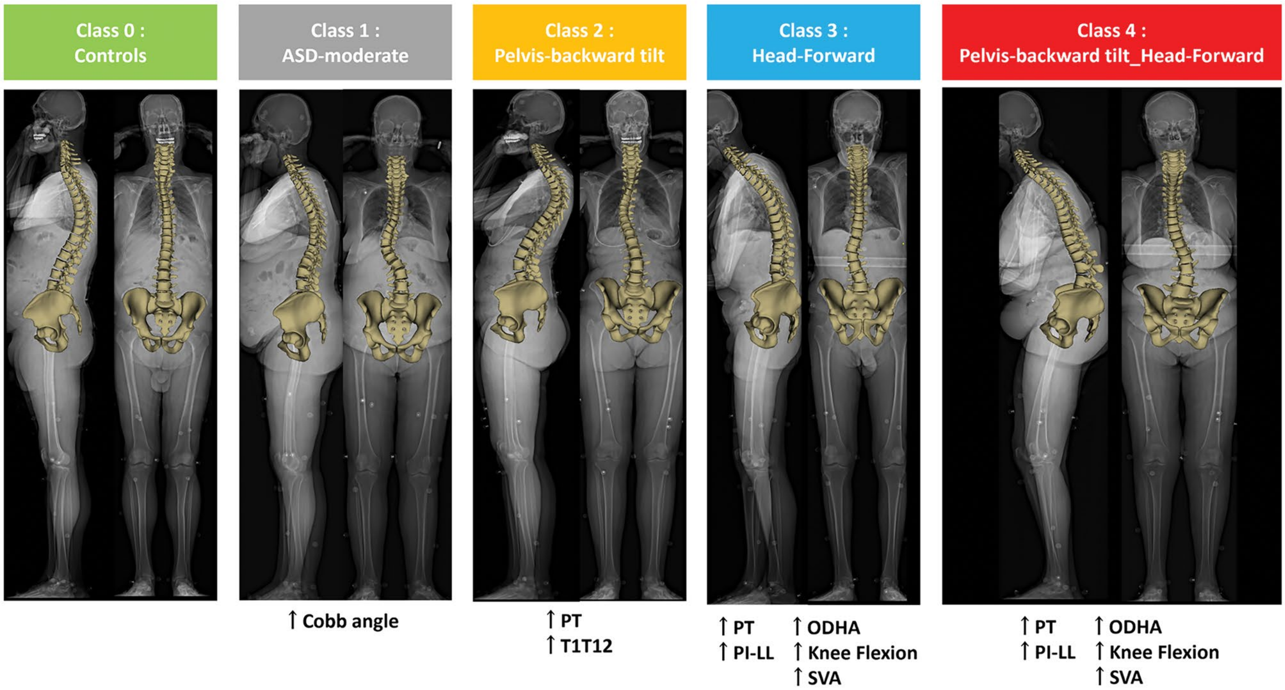

Figure 7. Examples of patients in each class with their most important radiographic features. (↑: increased, ↓: decreased).

Parameters	Controls	Class 1	Class 2	Class 3	Class 4	*p*-value	Controls vs. Class 1	Controls vs. Class 2	Controls vs. Class 3	Controls vs. Class 4	Class 1 vs. Class 2	Class 1 vs. Class 3	Class 1 vs. Class 4	Class 2 vs. Class 3	Class 2 vs. Class 4	Class 3 vs. Class 4
Functional classification of patients during Walking																
VAS/10	2 ± 1	6 ± 3	6 ± 3	7 ± 2	8 ± 2	**< 0.001**	*	*	*	*						
ODI/100	4 ± 6	27 ± 19	27 ± 16	42 ± 17	43 ± 15	**< 0.001**	*		*	*		*		*		
SF36-PCS	49 ± 8	41 ± 9	40 ± 8	34 ± 6	38 ± 11	**< 0.001**	*	*	*	*		*				
SF36-MCS	55 ± 7	51 ± 8	52 ± 9	50 ± 9	46 ± 12	0.07										
Functional classification of patients during sit to stand																
VAS/10	2 ± 1	6 ± 3	6 ± 3	7 ± 2	8 ± 2	**< 0.001**	*			*						
ODI/100	4 ± 6	28 ± 18	24 ± 21	37 ± 18	45 ± 14	**< 0.001**	*	*	*	*						
SF36-PCS	49 ± 8	40 ± 9	42 ± 10	34 ± 5	39 ± 11	**< 0.001**	*		*			*				
SF36-MCS	55 ± 7	51 ± 8	49 ± 11	49 ± 11	45 ± 13	0.08										
Functional classification of patients during stair ascent																
VAS/10	2 ± 1	6 ± 3	5 ± 3	7 ± 2	8 ± 2	**< 0.001**	*	*	*	*			*		*	
ODI/100	4 ± 6	29 ± 18	21 ± 14	34 ± 19	40 ± 19	**< 0.001**	*	*	*	*						
SF36-PCS	49 ± 8	40 ± 10	44 ± 6	36 ± 7	36 ± 8	**< 0.001**	*		*	*		*		*		
SF36-MCS	55 ± 7	51 ± 8	51 ± 8	51 ± 9	46 ± 12	0.07										

Table 4. Comparison of health-related quality of life scores (mean ± SD) between classes of movement patterns during walking, sit to stand and stair ascent. *and bold: significant *p*-value.

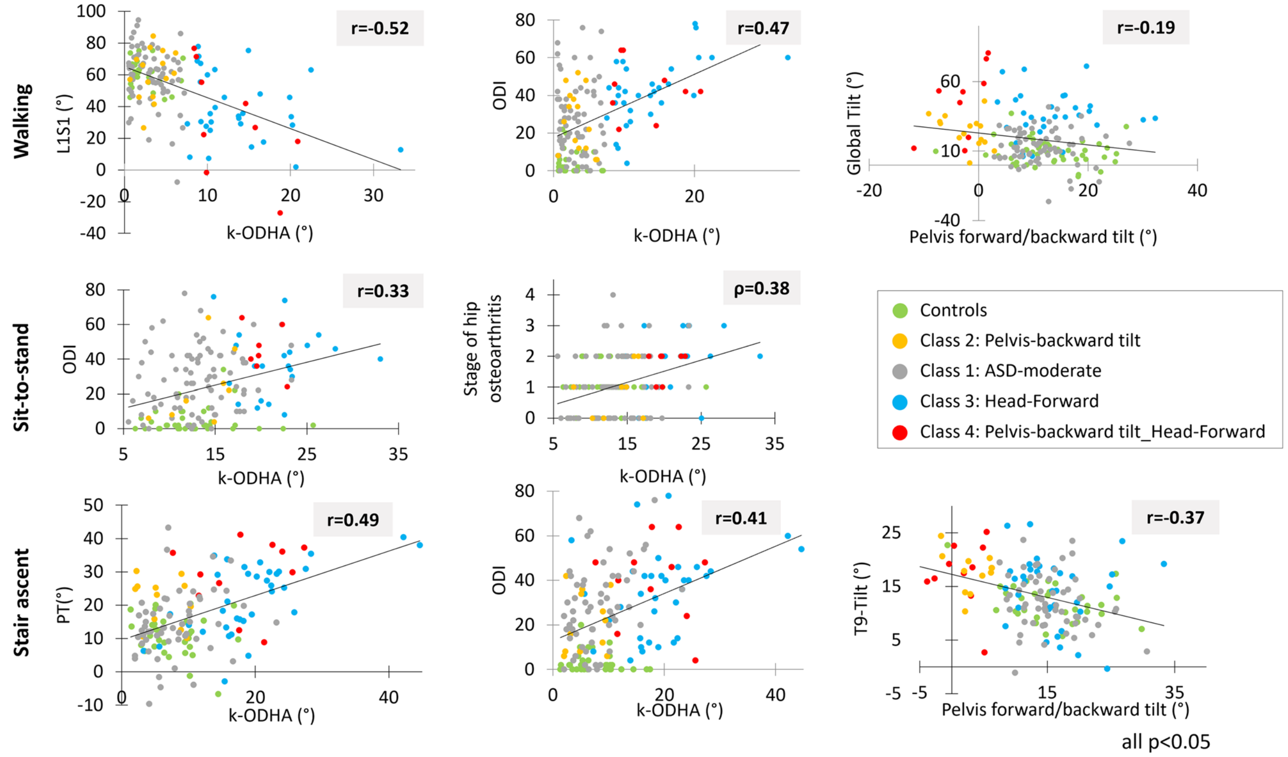

Figure 8. Correlations between altered kinematic parameters, radiographic parameters and health-related quality of life (HRQoL) scores. The most clinically relevant correlations were displayed.

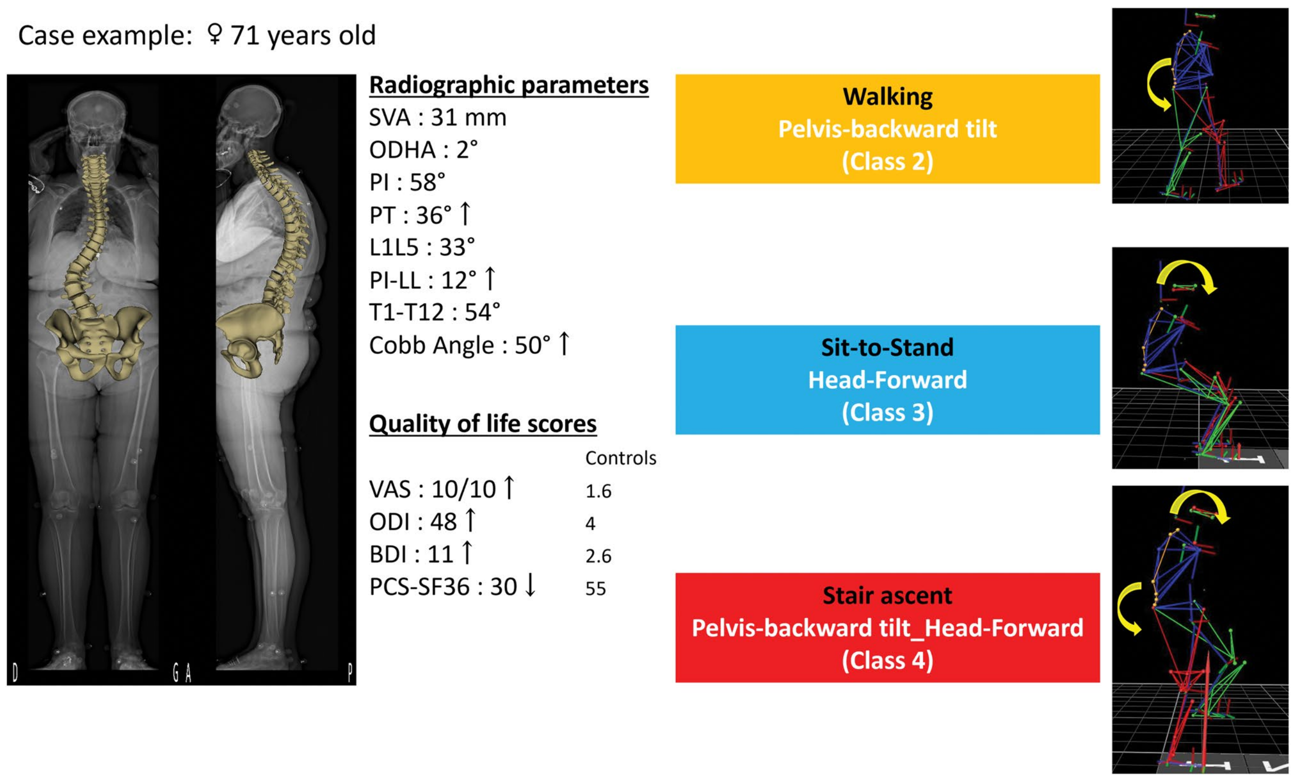

Figure 9. Case example of a patient adopting different kinematic strategies during the three performed tasks. (↑: increased, ↓: decreased).

in these patients. This was noticed during walking and the sit-to-stand transition, even though these patients presented with an increased radiographic SVA, thoracic kyphosis and global tilt. This latter was correlated with pelvic backward tilt while walking. However, during the stair ascent, patients in this class might have increased their hip abduction as a compensatory mechanism, most probably in an attempt to increase the area of their support polygon. Furthermore, these subjects exhibited the least significant deviations in their HRQoL among other subjects, most probably due to their relatively younger age (50 ± 14 vs 53 ± 8 years in controls; $p < 0.001$). Nonetheless, they showed an overall alteration of their gait profile (decreased GDI).

Patients in the Head-forward group (class 3) presented with an increased anterior head shift when completing the different daily life tasks while maintaining normal pelvic kinematics, despite their increased radiographic pelvic tilt.

During the three studied functional tasks, these patients presented an exaggerated flexion of the trunk coupled with an excessive extension of the head as well as a reduced dynamic lumbar lordosis in order to maintain horizontal gaze. This might explain the excessive flexion of the knees during gait, to compensate for the increased flexion of the trunk and thus avoid a forward fall. Patients in this class had altered spatio-temporal parameters, as they walked slowly with a longer double support time and shorter step length. Although they showed a normal pelvis and hip kinematics during sit-to-stand and stair ascent, they had the highest grade of hip osteoarthritis, which was correlated to the k-ODHA and also might explain the deterioration of their quality of life[20].

Patients in the Pelvis-backward tilt_Head-forward group (class 4) had similar characteristics compared to those in class 3 in addition to a persistent pelvic backward tilt during movement. In the static position, patients in class 4 had the same deformities and compensatory mechanisms as patients in class 3.

During walking, these patients had the most decreased GDI indicating the most altered gait profile, that could predict a higher risk of fall[21].

During sit-to-stand, these patients exhibited excessive forward projection of the trunk leading to head extension in order to maintain a horizontal gaze. In addition, the kinematics at the level of the knee showed a reduced extension velocity during this movement (slower extension movement on the kinematic waveforms, Fig. 6). This could underline a weakness of the extensor apparatus, which is in accordance with what has been reported by Ferrero et al. regarding fat infiltration and muscle weakness in ASD patients[22,23]. Furthermore, this group was composed of the oldest subjects (65 ± 14 vs. 53 ± 8 years in controls; $p < 0.001$), probably having sarcopenia and muscle weaknesses consequent to age[24,25].

They ascended a stair step with the head extremely projected forward defining a positive sagittal alignment and a pelvic backward tilt, thus preventing the hip from flexing adequately. The pelvic backward tilt was correlated to a higher T9-Tilt which is in harmony with a shifted-forward center of mass present in these patients. The kinematics of the lower limbs were altered since the flexion of the knee was not sufficient to tackle the stair step. An underlying muscular deficit, in particular of the extensor apparatus of the spine, might largely contribute to the development of the compensatory kinematic strategies in the studied population. Both muscular and kinematic alterations might lead to physical restrictions. In fact, the dynamic projection of the head observed in the three studied functional tasks was correlated to deterioration of the quality-of-life score, in particular the ODI, measuring the disability level. Further studies taking into account muscular component are needed[22,23].

It was important to note that only 13% of patients adopted the same movement patterns during the 3 tasks, and 87% of the patients adopted a different kinematic strategy for each of the three functional tasks. This result indicates that ASD patients are able to recruit different movement patterns while completing daily life tasks, regardless of their skeletal deformities. In fact, this recruitment is task-oriented, where they aim to achieve it with a minimum energy consumption, in terms of muscle activation.

The clinical case presented in Fig. 9 is a perfect example of how ASD patients adopt the most suitable movement pattern to perform a specific movement.

This study has few limitations. The major one is related to the uncertainty on kinematic parameters due to soft tissue artefact (STA), especially in over-weighted patients. In the future, a FEM method will be applied in order to reduce STA artefacts[26]. Moreover, a 3D translation vector, calculated form biplanar X-rays, could have been applied to the center of the head markers in order to calculate the exact ODHA angle during movement. However, the calculated k-ODHA remains highly representative of the exact ODHA angle. When the ODHA was calculated based on both the odontoid processus and the center of head markers, no systematic error was found (mean = 0°, SD = 1.5°) and a homoscedasticity was shown on the Bland and Altman graphs, with a correlation coefficient of 0.986 between the two measurements.

In conclusion, recent studies have shown that the kinematic alterations of ASD patients depend on their radiographic static deformity. This is the first study to describe 4 different movement patterns developed by ASD patients during daily life tasks, based on two key kinematic parameters: the alignment of the head above the pelvis and the pelvic tilt during movement. While these two parameters were always known to be essential in studying patient malalignment on static standing radiographs, it was remarkable to find that these parameters were the key variables in defining the movement patterns adopted by patients during functional tasks. Future studies will focus on establishing a functional score to classify patients according to their kinematic limitations.

Data availability

Data is available and can be provided upon request by the corresponding author through a specific secured link on the data server of the institution.

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Author contributions

E.A., A.R., C.C. wrote the main manuscript. E.A. prepared the figures. E.A., A.R., C.C., R.R.1, M.S., E.J., E.M., N.N., R.R.2 were responsible of data collection and processing. M.K., A.J.B., I.G., W.S., A.B., A.A. were responsible of data interpretation and project supervision. I.G., A.A. were responsible of the funding of the project. A.A., R.R.1, A.M., M.K., A.J.B. reviewed the manuscript.

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Competing interests

The authors declare no competing interests.

Additional information

Correspondence and requests for materials should be addressed to A.A.

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