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Performance on Balance Evaluation Systems Test (BESTest) impacts health-related quality of life in Adult Spinal Deformity Patients

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Study Design: Prospective single-center study

Objective: This study investigates how dynamic balance performance complements 2D static radiographic measurements and demographics in terms of understanding health-related quality of life in Adult Spinal Deformity (ASD) patients.

Summary of Background Data: Recent insights suggest that demographic variables have a stronger impact on health-related quality of life than 2D radiographic spinopelvic parameters in ASD patients

Methods:9 Healthy volunteers and 36ASD patients following inclusioncriteria were recruited. Demographics, Scoliosis Research Society Score-22r (SRS-22r), OswestryDisability Index (ODI), Core Outcome Measures Index(COMI),2D radiographic spinopelvic measurements and performance on Balance Evaluation Systems Test (BESTest) and Trunk Control Measurement Scale (TCMS) were determined for each subject. Non-parametric tests, Spearman correlations, univariate and stepwise-like linear multivariate regression analysis were performed.

Results:BESTest and TCMS had significant lower values in the ASD group versus the control group (p=0,000). In the ASD group, Cumulative Illness Rating Scale (CIRS) correlated fair to ODI, COMI (0,441≥r≥0,383, p<0,021) and to SRS-22-r (r=-0,335, p=0,046), Mini Mental State Examination correlated fair to COMI (r=-0,352, p=0,035), 'Pelvic Incidence minus Lumbar Lordosis' correlated fair to ODI (r=0,361, p=0,031), BESTest correlated moderate to ODI and COMI (r≤-0,505; p≤0,002), TCMS correlated fair to ODI (r=-0,356; p=0,033). CIRS and BESTest were significant predictive variables for COMI based on univariate analysis in ASD patients. Multivariate regression analysis including demographics, 2D static radiographic parameters and dynamic balance scales identified BESTest as single independentvariable (p=0,000) to predict COMI (adjusted R^2= 0,285) in ASD patients.

Conclusions:BESTest has a higher potential than demographic and 2D radiographic spinopelvic parameters to predict quality of lifein ASD patients.Further research is necessary to identify the impact of ASD on quality of life.

KeyWords: Adult SpinalDeformity, Balance Evaluation Systems Test, BESTest, Quality of life, Multivariate Regression Analysis

Level of Evidence: 3

Introduction.

Patient status in Adult Spinal Deformity (ASD) is currently typically assessed using Health Related Quality of Life measures (HRQOL) in combination witha set of static 2D radiographic measurements.To quantify HRQOL, general functional outcome scores, as the Oswestry Disability Index (ODI) and Core Outcome Measurement Index (COMI)(1–3)have been introduced, as well as spinal deformity-specific scores,such as SRS-22r (4-5). With regards to 2D radiographic measurements, the SRS-Schwab Classification iscurrently one of the most established classification systems for ASD with demonstrated good inter- and intra-rater reliability (6-8). It provides a coronal description of the curve (Thoracic only, TL/Lumbar only, Double Curve, no major coronal deformity) in combination withsagittal measurements, including Pelvic Incidence minus Lumbar Lordosis (PI-LL), Sagittal Vertical Axis (SVA) and Pelvic Tilt (PT). Next to the SRS-Schwab Classification, other global radiographic spinopelvic parameters like T1 spinopelvic inclination angle (T1 SPI), T1 Pelvic Angle (TPA),Global Sagittal Axis (GSA) have been introduced to quantify global alignment in ASD subjects(9-15).Supported by arange of studiesdemonstrating correlations($r<0,55$) between HRQOL and several spinopelvic radiographic measurements(8-10,16-22), the latter have evolved into the single most important and reliable surgical targetforachieving improvement inHRQOLin adult spinal deformity surgery (23).However, past literature was based on a mixed ASD-population also including iatrogenic deformity with or without previous spinal instrumentation. Arecent paper of Chapman et al. - explicitly excluding any iatrogenic deformity - states that static radiographic parameters only show no to weak correlations with HRQOL-scores (24). Other recent studiesattempting to clarifythe impact of spinal deformityon quality of life in ASD stated that demographic dataas opposed to spinopelvic parameters have the largestinfluence on HRQOL(25-27). As such, these more recent insights suggest that 2D spinopelvic radiographic parameters are not the sole drivers of quality of life in ASD.

Furthermore, as radiographic spinopelvic parameters quantify postural changes only in an upright, standing posture and not during dynamic activities of daily life (28), no conclusions whatsoever can be drawn with respect to postural control and balance capacities during thesedynamic conditions. Given the primary focus on static radiographic parameters in the literature, only little information is currently available regarding this dynamic impact of ASD. Some earlier studies suggest a multifactorial etiology of impaired balance control (29-33) represented by the line of gravity fallingoutside the base of support, which in turn leads to poor stability in upright standing. In parallel, Dubousset introduced the 'cone of economy' principle, which represents the range in which a body is balanced and stable without external support or excessive energy expenditure (34). Other studies looking into compensation mechanisms in patients with spinal deformity reportedthe use of multiple musculoskeletal compensation strategies to compensate for the abnormal spinal alignment and reorient the gravity line position within their base of support (35-41).

Clinical scales for quantifying balance performance, therefore, have clear potential to deepen our understanding of potential dynamic drivers of HRQOL in adults with spinal deformity.Such balance assessment scaleshave been described in the literature for use in a variety of musculoskeletal and neurological conditions associated with balance impairment (42-50) such as the Berg Balance Scale, Physical Performance Test and modified Physical Performance Test. In e.g. Parkinson disease and stroke, these balance assessment scales evolved into a key clinical assessment tool. However,as these specific scales are primarily targeting lower functioning elderly,the associated ceiling effect makes them lesssuitableto asses balance in community dwelling ASD subjects (51-54). Similarly, the Fullerton Advanced Balance Scale and Trunk Impairment Scale (TIS) do not seemimmediately applicable in ASD, because, respectively, the tested itemsare too demanding in an ASD population which might include subjects with osteoporosis (55,56) or the testdoes not prevent lower limb compensations during trunk control assessment(57-60).On the other hand, certain scales seem more straightforwardly applicable in ASD populations. The Trunk Control Measurement Scale (TCMS) evaluatesthree-planar movements in, but also outside of, the base of support while the patient is sitting without feet support, thuslimiting lower limb compensations(61). However, normative adult TCMS-scoreshave until now not yet been reported in the literature. Finally, the Balance Evaluation Systems Test (BESTest) is a relatively new balance assessment tool used in neurological as well as musculoskeletal disorders (62-63). A specific feature of interest of the BESTestis its use of subscales,allowing to scoreindividual components of the postural system: biomechanical constraints, stability limits/verticality, anticipatory postural adjustments, postural responses, sensory orientation and stability in gait. Furthermore, normative adult BESTest scoresare available in the literature(64-66). Based on the above appraisal, the TCMSand BESTest seem to be the most promising tests to assess balance in ASD (67,68).

Therefore, the objective of this paper is to investigate how dynamic balance performance as quantified by the BESTest and TCMS complements the currently used analysis of 2D static spinopelvic alignment and demographicsin terms of understanding ASD's impact on health-related quality of life scores. We hereby hypothesize that the combined use of 2D spinopelvic radiographic measurements and balance assessment scales hasa higher predictive value towardsHRQOL than each analysis individually.

Material and Methods.

Following ethical approval and informed consent by our institution's ethical committee (S58082), a convenience sample of 36 ASD subjects in a pre-and nonsurgical settingwas recruited and clinically screened for compliancewith following inclusion criteria: adults suffering from a spinal deformity with or without sagittal malalignment, agedbetween 18 and 79 years, Mini mental state examination (MMSE)≥25, able to walk at least 50 meters distance independently, no current history of diagnosed musculoskeletal disorders of the lower extremities affecting motor performance such as severe hip arthrosis with or without flexion contracture, severe knee arthrosis, severe ankle arthrosis, severe leg length discrepancy (> 3 cm), no history of neurological disease affecting balance such as stroke, Parkinson disease or vestibular lesion, no history of spinal fusion surgery. Additionally, 9 asymptomatic adults without major coronal deformity and with non-pathological sagittal alignment were recruited.

Demographic variables, 2D radiographic parameters (coronal SRS Schwab classification and spinopelvic parameters)and performance on clinical balance assessment scales (BESTest and TCMS) were determined for each study subject (Table 1). Spinopelvic alignment was quantified in each subject through full body bi-planar X-ray images(EOS, EOS imaging, Paris, France) acquired in the SRS free standing position(Figure 1)using IMPAX Data Center viewer (Agfa Healthcare, Mortsel, Belgium) by an adult spinal deformity surgeon experienced in the definition and use of spinopelvic parameters (LM). Health-related quality of life was quantified ineach subject throughvalidated SRS-22r, ODI and COMI questionnaires. Balance performance was quantified in each subject through bothBESTest and TCMS by an experienced physiotherapist (PS), specifically following the guidelines of Horak et al. for the BESTest and Heyrman et al. for TCMS (61,62,69)(Figure 2). The average length of BESTest and TCMS in our cohort of ASD patients, taking respectively 25and 15 minutes to perform, is still within acceptable limits in terms of clinical utility and feasibility of these tests.

First, all variables were statistically compared between the ASD and control group using non-parametric Mann-Whitney U test,exceptfor gender and coronal SRS-Schwab classification (Chi-square test).Significance level was set at p<0,05, including for all further analyses. Next, correlations between HRQOL-scores and demographic variables, 2D radiographic parameters as well as clinical balance assessment scales were calculated within the ASD group(Spearman, r<0,25=little to no correlation, 0,25<r<0.50=fair, 0,50<r<0,75=moderate, and 0,75<r<1,00=high correlation) (51).Finally, both univariate and multivariate linear regression analyses wereconducted to identify significant predictive variables for HRQOL in ASD patients. Justified by the mutual correlations within the collected HRQOL-scores (r>0,80, p<0,001), we selecteda single HRQOL-score as dependent variable to simplify the furtherlinear regression analyses. COMI was selected due toits brevity, favorable psychometric properties and responsiveness to change following treatment being comparable to the disease-specific SRS-22r. Prior to regression analysis, the applicable assumptions were checked (continuous dependent variable, 2 or more independent variables, independence of observations, linear relationship, homoscedasticity, multicollinearity, no significant outliers, high leverage points or highly influential points, normal distribution of residuals). If required for univariate regression analysis,transformation of independent variables was performed.For every original independent and transformed (squared, logistic, square root) independent variable, a univariate linear regression analysis was performed.Next, four stepwise multivariate models were developed with varying input sets of independent variables:

- model 1: only demographic variables(age^2, gender, BMI^2, MMSE^2 and CIRS)
- model 2: adding spinopelvic parameters (PI^2, log(SS), PT^2,PI-LL, SVA, T1 SPI^2, sqrt(TPA), GSA) and SRS-Schwab coronal classification (T,D,L,N) as predictors to model 1
- model 3: adding total score on BESTest(in %) and TCMS^2 as predictors to model 1
- model 4: adding total score BESTest (in %) and TCMS^2 as well as all spinopelvic parameters (PI^2, log(SS), PT^2, PI-LL, SVA, T1 SPI^2, sqrt(TPA), GSA) and SRS-Schwab coronal classification (T,D,L,N) as predictors to model 1

All analyses were carried out using IBM SPSS version 24 (IBM Corporation, New York, USA) and reviewed by a bio-statistician.

Results.

All collected demographic variables, HRQOL-scores,SRS-Schwab coronal classification, spinopelvic radiographic parameters, BESTest and TCMS scoresare listed in Table 1. Spinal alignment in terms of coronal SRS-Schwab classification, PI-LL, SVA and GSA is significantly different between both groups illustrating the presence of spinal malalignment in the ASD group. Performance on TCMS and BESTest is significantly more impaired in the ASD group than in the control group. In terms of demographic correlations with HRQOL-scores, CIRS was found to correlate fairlywith all HRQOL-scores(0,441≥r≥0,335;p<0,046)whereasMMSEonly correlatedfairlywith COMI (r=-0,334; p=0,047).In terms of radiographic correlations with HRQOL, PI-LLwas the only parameter which correlated fairlywith ODI (r=0,361;p=0,031). All other demographic and 2D radiographic variables were not found to correlate with HRQOL-scores (r<0,25).Finally, with regards to the correlations between balance assessment scales and HRQOL, BESTestwas found to show moderate correlations with both ODI and COMI (-0,505≥r≥-0,519; p≤0,002). TCMSon the other hand, only correlated fairlywith ODI(r=-0,356;p=0,033).

Subsequent univariate linear regression analysis in ASD only identified CIRS and BESTest as significant predictive variables. Although MMSE, PI-LL and TCMSindividually demonstrated significant correlations with HRQOL-scores, these variables were not identified as significant predictive variables (Table 2).

Thenastepwiselinear multivariate regression analysis using the selected independent variables based on the aforementioned univariate analysis was performed.The first and second multivariate model identified comorbidity (CIRS) as independent predictive variable for COMI (p=0,019) (adjusted R^2= 0,126). Forthe third and fourth model BESTestwas twice retained as the only independent predictive variable (p<0,001)for predicting COMI(adjusted R^2= 0,285) (Table 2), rejecting our mainhypothesis.

Discussion.

With regard to our study objective, we hypothesized that the combined use of 2D spinopelvic radiographic measurements and balance assessment scales would better explain variations in HRQOL in ASD than their individual explanatory abilities.Therefore, we explored the potential valueto combinedynamic balance assessment scales with 2D radiographic and demographic variables in a stepwise multivariate regression analysis(model 4) to predict health-related quality of life in our ASD population. Balance performance on BESTest was retained as the only independent variable (p<0,001) for predicting COMI in model 4 and explains nearly 30% of the variance of COMI in our ASD patients.However, model 3, which includes balance assessment scales combined with demographic variables, seems to provide equally significant predictive value for HRQOL in comparison to model 4. Based on these conclusions and very much to our surprise, we have to reject our hypothesisthat combined use of 2D spinopelvic radiographic measurements and balance assessment scales has a higher predictive value towards HRQOL than each analysis individually, since model 4 does not demonstrate an increased predictive power for COMI compared to single use of dynamic balance assessment scales on a demographic background (model 3).As we observed a high correlation between all HRQOL-scores, the results of our multivariate regression analysis can be extrapolated to ODI and SRS-22-r. Furthermore, this multivariate regression analysis shows that TCMS seems less appropriate to use as predictor for COMI in ASD compared with BESTest.

To compare our multivariate regression analyses including dynamic balance assessment scales (model 3 and 4) to the standard model in literature (25-27),model 2 also analyzed the predictive power for HRQOL in ASD using 2D spinopelvic radiographic parameters combined with demographic variables. The multivariate regression model 2 identifies comorbidity (CIRS) as unique significant predictive variable with nearly 13% explained variance for COMI which is less than half the number of explained variance for COMI in model 3 and 4 (Figure 3). This illustrates that dynamic balance assessment scales have the potential to deepen our understanding in the drivers of HRQOL in ASD.To improve insights, into the influence of a spinal deformity on balance performance this study conducted a comparison between both study groupswhich confirms impaired balance performance in ASD patients(Table 1). Analysis of subscale scores illustrates that ASD subjects score lower on dynamic items in TCMS and all items in BESTest. As demographic variables like age, BMI and cognitive impairment (MMSE) which have been identified in the literature as factors to negatively influences balance performance (70-72) were not significantly different between both study groups, these variables do not explain worse performance in the ASD group. As potential diseases affecting balance performance were excluded from this study, we believe that the decreased performance of ASD patients on BESTest is associated with the presence of spinal deformity.

In accordance with past literature (25,26), multivariate regression analysis model 2, which uses 2D spinopelvic radiographic parameters combined with demographic variables, confirms that demographic variables have a stronger impact on health-related quality of life than 2D radiographic spinopelvic parameters.However, in contrast to previous papers which identify also other demographic variables as predictors for HRQOL in ASD, model 2 identifies comorbidity (CIRS) as unique significant predictive variable. Our older ASD study group (±10 years older compared to other studies) may explain this difference with past literature.

The explained variance for COMI in model 2, 3 and 4 is however lower than the nearly 40% explained variance for ODI by other demographic variablesin the study of Boissière et al. (26), which includes a larger group of subjects (n=755) with lower mean value of age and BMI and without including comorbidity and dynamic balance assessment scales. We assume that the difference in explained variance and number of variables between our study and past literature can be attributed to thesmaller ASD study group (n=36). This brings us to the first study limitation, i.e. a from a clinical point of view relatively small sample size. Before start of the study, a power analysis wasperformedin function of the Mann-Whitney U tests between ASD and control group.As advanced Parkinson disease often involves spinal deformity and data in the non-neurologic ASD population is not readily available, we based this analysis onreported data of BESTest in a Parkinson population with ≤ 1 fall (BESTest-score=76,4% (SD=13,6%) versus normal population (BESTest-score= 91,4% (SD=3,4%) in age cohort 60-69 years old using a power $1-\beta=80\%$ and level of significance $\alpha=0{,}05$ (65,73). Post hoc power analysis on our study data for the Mann-Whitney U test using BESTest confirmed sufficient power ($1-\beta=0{,}985$)and sample size of the current study in function of the associated conclusions. Given the relatively small sample size, we furthermore choose to use the stepwise approach in our regression analysis instead of forward or backward analysis. Furthermore, a minimum of 2 subjects per independent variable for adequate estimation of regression coefficients, standard errors and confidence intervals and 10 subjects per significant independent variable for adequate power of the adjusted R^2 value is suggested in literature (74,75). In view of the 2 resulting significant variables, it can be concluded that the 36 samples in our study providedsufficient power for all performed tests.Another limitation of the study is thestatisticaldifferencein co-morbidity (CIRS) between our total ASD group versus our control group which could have influencedthe reported difference in balance performance between both groups. Despite these limitations, we believe to have shown that dynamic balance assessment scaleshave a huge potential and surpass demographic and static 2D radiographic parameters in terms of understanding the potential drivers of health-related quality of life in ASD.

Conclusion.

To our knowledge this is the first study to report the use of clinical postural tests in the ASD population. The BESTesthas a higher potentialto predict HRQOL in the primary ASD population than demographic variables and 2D radiographic spinopelvic measurements.Further research is necessary to identify additional drivers of quality of lifein ASD, toexplore the potential of balance performance scales to enhance risk assessment for Proximal Junctional Kyphosis (76) and to offerimproved insights intowhat extent different types of spinal deformity and their surgical correction can impact balance performance as quantified by BESTest and its subscales. From these insights, noveltreatment algorithmscan be developed, including more targeted rehabilitation programs - as e.g. has been demonstrated in other balance-related pathologies like stroke and Parkinson disease (69, 77) - to address impaired balance control in the non-surgical, pre-and postsurgical treatment phase. As such the future clinical introduction of these tests provides a clear opportunity to integrate dynamic function in novel treatment pathwaysin view of the in this study documented key rolein the ASD patient'squality of life.

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Figure legend 1:

Left side: Subject standing in SRS-free standing finger-on-clavicle position during force plate instrumented 2D stereoradiographic acquisition of full body images (Iso=Isocenter, GL= Gravity Line projection,

Mean GL= Mean Gravity Line Projection).

Rightside: Schematic presentation of all measured sagittal Spinopelvic Parameters (PI=Pelvic Incidence, PT=Pelvic Tilt, SS=Sacral Slope, LL= Lumbar Lordosis from T12 to S1, TK=Thoracic Kyphosis from T1 to T12, SVA=Sagittal Vertical Axis, T1 SPI= T1 Spinopelvic Inclination, TPA= T1 Pelvic Angle, GSA= Global Sagittal Axis

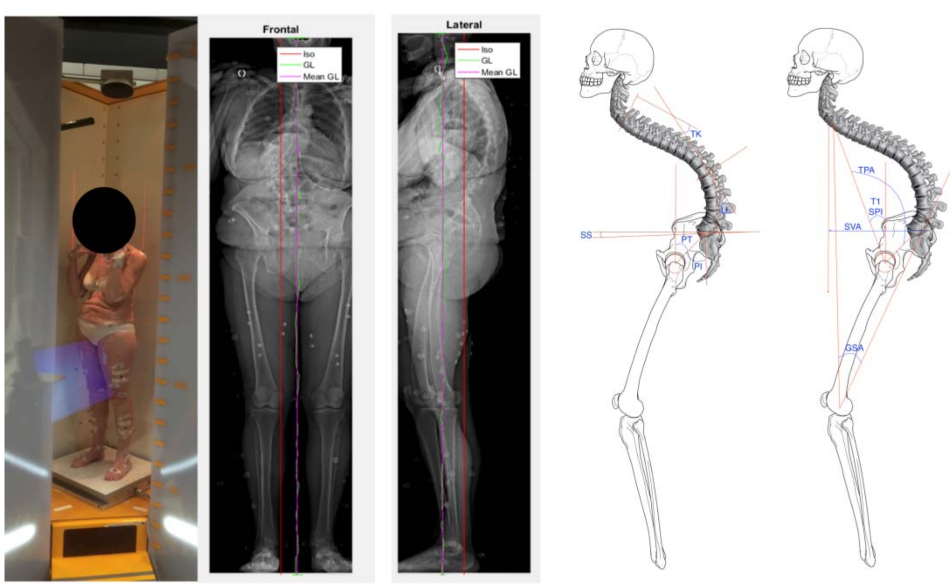
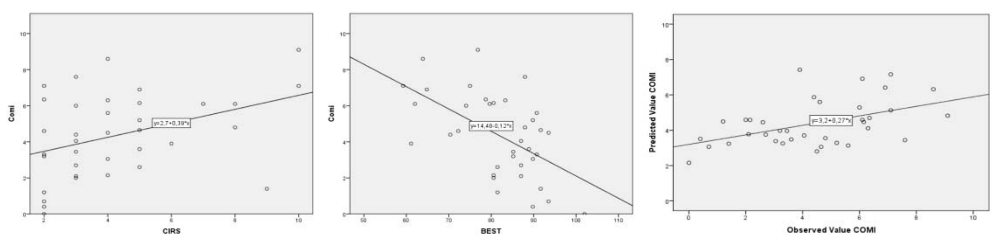


Figure legend 2: Subject performing dynamic tasks in BESTest (first row) and TCMS (second row).

Figure legend 3: Scatterplot of stepwise multivariate regression analysis with COMI as dependent variable showing the regression line in model 1 and 2 (left) with slope = 0,388, the regression line in model 3 and 4 (middle) with slope= -0,124 and linear relationship between observed COMI versus predicted COMI in model 3 and 4 (right). COMI: Core Outcome Measures Index; CIRS: Cumulative Illness Rating scale; BESTest: Balance Evaluation Systems Test.



IN	Model 1	Model 2	Model 3	Model 4		**ASD Group (n = 36)**	**Control Group (n=9)**	**P-value**
					Demographics			
					Age (years)	62,42(± 9,31)	55,44(± 10,33)	0,083
					Body height (cm)	161,25(± 9,05)	168,01(± 5,02)	0,026 *
					Body weight (kg)	67,79(± 11,14)	68,93(± 8,79)	0,410
					Body Mass Index	26,07(± 3,55)	24,38(± 2,53)	0,222
					Gender (M/F)	6/30	4/5	0,073
					Mini Mental State Examination	28,78(± 1,36)	29,22(± 0,83)	0,501
					Cumulative Illness Rating Scale	4,28(± 2,33)	1,44(± 1,59)	0,001 *
					2D spinopelvic radiographic parameter			
					Pelvic Incidence	58,55(± 13,61)	61,20(± 15,00)	0,766
					Sacral Slope	33,98(± 9,58)	41,51(± 8,78)	0,033 *
					Pelvic Tilt	24,80(± 11,38)	19,69(± 8,68)	0,245
					Pelvic Incidence minus Lumbar Lordosis	16,17(± 23,18)	-1,178(± 6,282)	0,012 *
					Sagittal Vertical Axis	41,43(± 49,71)	8,133(± 18,90)	0,032 *
					T1-Spinopelvic Inclination	-2,35(± 5,78)	-5,022(± 1,90)	0,152
					T1 Pelvic Angle	22,45(± 12,52)	14,667(± 8,22)	0,063
					Global Sagittal Axis			0,006 *
					SRS-Schwab coronal			

classification (T, D, L, N)	4,37(± 4,87) 0T,10D,20 L,6N	0,678(± 1,77) 0T,0D,0L, 9N	0,000 *
Dynamic Balance Scores			
TCMS total score (0-58)	49,00(± 4,80)	55,00(± 2,40)	0,000 *
Static (0-20)	19,28(± 1,11)	19,78(± 0,67)	0,121
Dynamic (0-28)	21,19(± 3,80)	25,89(± 2,32)	0,001 *
Reaching (0-10)	8,53(± 1,70)	9,33(± 0,87)	0,197
BESTest total score (%)	81,82(± 10,38)	94,96(± 6,26)	0,000 *
Biomechanical Constraints	75,23(± 19,47)	96,30(± 6,76)	0,000 *
Stability limits/Verticality	80,55(± 13,15)	95,24(± 5,83)	0,000 *
Transitions & Anticipatory postural adjustments	82,11(± 19,89)	96,30(± 6,21)	0,015 *
Reactive postural responses	72,18(± 17,42)	88,89(± 13,32)	0,006 *
Sensory orientation	88,75(± 15,86)	98,52(± 2,94)	0,009 *
Stability in gait	78,76(± 15,75)	95,24(± 7,14)	0,000 *
OUT			
HRQL scores			
COMI	4,36(± 2,32)	0,47(± 1,05)	0,000 *
SRS-22r questionnaire	3,35(± 0,60)	4,64(± 0,18)	0,000 *

ODI	29,08(± 17,31)	1,56(± 3,13)	0,000 *

Table1: Comparison in demographics, HRQOL scores, 2D radiographic parameters and Dynamic Balance Scores for ASD group vs control group. Mean and standard deviations are reported. *Significance level = $p<0,05$

Univariate Analysis with COMI as dependent variable			
Variables	**Regression coefficient**	**95,0% Confidence Interval**	**P-Value**
Demographic variables			
Age^2	2,702E-05	-0,001, 0,001	0,939
Gender	0,712	-1,416, 2,839	0,501
BMI^2	0,003	-0,001, 0,007	0,140
CIRS	0,388	0,067, 0,709	0,019*
MMSE^2	-0,010	-0,020, 0,000	0,054
2D Spinopelvic radiographic parameters			
PI^2	0,000	0,000, 0,001	0,331
log(SS)	0,844	-3,891, 5,579	0,720
PT^2	0,001	-0,001, 0,002	0,320
PI-LL	0,014	-0,020, 0,049	0,413
SVA	0,003	-0,014, 0,019	0,750
T1 SPI^2	0,003	-0,013, 0,018	0,709
sqrt(TPA)	0,254	-0,400, 0,908	0,435
GSA	0,043	-0,122, 0,209	0,599
SRS-Schwab Coronal Curve Classification	-0,322	-1,233, 0,590	0,478
Balance Tests (total score)			
BESTest	-0,124	-0,189,-0,059	0,000*

TCMS²	-0,002	-0,003,0,000	0,061

Multivariate Analysis with COMI as dependent variable

Variables	Regression coefficient	95,0% Confidence Interval	P-Value	R²-Value	Adjusted R²-Value
Model 1 & 2					
(Constant)	2,700	1,143, 4,257	0,001 *		
CIRS	0,388	0,067, 0,709	0,019 *	0,151	0,126

Model 3 & 4					
(Constant)	14,482	9,124, 19,840	<0,001*		
BESTest	-0,124	-0,189, -0,059	<0,001*	0,306	0,285

Table2: Uni- and multivariate linear regression with COMI as dependent variable.
^{2}: square transformation, log: logistic transformation, sqrt: square root transformation. Significant p-valuesare marked with *.