UNIVERSITEIT GENT

FACULTEIT GENEESKUNDE EN GEZONDHEIDSWETENSCHAPPEN

Revalidatiewetenschappen en Kinesitherapie
Academiejaar 2015-2016

Kinematics and Kinetics of the Ankle-Foot Complex in Women with the Hypermobile Type of Ehler-Danlos Syndrome

A case-control study

Masterproef voorgelegd tot het behalen van de graad van
Master of Science in de Revalidatiewetenschappen en Kinesitherapie

Stefan Vermeulen
Sofie Verstraelen

Promotor: dr. Lies Rombaut
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Table of contents

List of flowcharts, figures and tables

- **Flowcharts**

- **Figures**

- **Tables**

Table 1: Selection criteria.

Table 2: Marker placement Ghent Foot Model.

Table 3: Anthropometric information.

Table 4: Pain locations of the lower limb in EDS-HT (Margolis).

Table 5: Kinematic data of Rearfoot vs Tibia.

Table 6: Kinematic data of Midfoot vs Rearfoot.

Table 7: Kinematic data of Lateral Forefoot vs Midfoot.

Table 8: Kinematic data of Medial Forefoot vs Midfoot.

Table 9: Kinematic data of Hallux vs Medial Forefoot.

Table 10: Kinetic data (ground reaction forces).

Table 11: Pain intensity.

Table 12: Total and domain scores for questionnaires.

List of abbreviations

ABD = Abduction

ADD = Adduction

ADL = Activities of daily life

AP = Antero-Posterior

BMI = Body Mass Index

DF = Dorsal Flexion

EDS-HT = Ehler-Danlos Syndrome Hypermobility Type

EV = Eversion

EXT ROT = External Rotation

FFC = First Foot Contact

FFF = Fore Foot Flat

FFI = Foot Function Index

FMC = First Metatarsal Contact

GFM = Ghent Foot Model

HO = Heel Off

INT ROT = Internal Rotation

INV = Inversion

JHS = Joint Hypermobility Syndrome

LEFS = Lower Extremity Functional Scale

LFC = Last Foot Contact

Med-Lat = Medio-Lateral

N = Number

PF = Plantar Flexion

SD = Standard Deviation

SF-36 = Short Form 36

SPM = Statistical Parametric Mapping

VAS = Visual Analogue Scale

Case-control study

Abstract (English)

Background: The hypermobile type of Ehler-Danlos Syndrome (EDS-HT) is a connective tissue disorder characterized by generalized joint hypermobility and a wide range of musculoskeletal symptoms. Even though these complaints have a considerable impact on daily functioning, only a few quantitative studies have been carried out to investigate the altered movements seen in EDS-HT during walking. Hence, biomechanical gait parameters of the ankle-foot complex can only be hypothesized until now. To better understand the extent of the problem, three-dimensional gait analyses are opportune.

Objectives: To identify differences in kinematics and kinetics of the ankle-foot complex during gait between EDS-HT patients and healthy controls and to assess foot function and pain in these patients.

Study Design: Case-control study.

Methods: Twenty-three women with EDS-HT and twenty-three healthy gender- and age-matched controls participated in this three-dimensional gait analysis. Subjects walked barefoot at self-selected speed on a 12m walkway, while kinematic and kinetic data were collected by using an optoelectronic system, a force and plantar pressure platform. Marker placement was determined by the multi-segmented Ghent Foot Model (GFM). Data about foot function and pain were gathered using Visual Analogue Scale (VAS)-scores, the Margolis Pain Diagram, the Foot Function Index (FFI) and the Lower Extremity Functional Scale (LEFS).

Results: Regarding kinematics, the stance phase showed that EDS-HT patients are characterized by a significantly different position of the ankle and foot in the sagittal plane with less plantar flexion of the rearfoot and forefoot, but a more plantar flexed position at the level of the midfoot. In the frontal plane, a significantly higher value for inversion of the rearfoot and hallux and more eversion of the medial forefoot were found in comparison with the control subjects. Finally, significant more abduction of the midfoot and hallux occurred in the horizontal plane for these patients. Regarding kinetics, significant differences in the horizontal ground reaction force components were found, which reflects a decreased propulsion capacity in these patients. Further, individuals with EDS-HT reported a significantly higher pain distribution and pain intensity at the lower limb together with more foot dysfunction, greater disability and a reduced quality of life.

Conclusion: Altered kinematics and kinetics of the ankle and foot segments during walking could be demonstrated in patients with EDS-HT by using a multi-segmented foot model. Foot dysfunction and pain was shown to be higher in these patients. These findings may suggest that patients with EDS-HT would benefit from an individualized rehabilitation program with a focus on improving muscle strength and optimizing ankle strategy. Another important clinical implication is a recommendation for customized orthoses and chronic pain management.

Keywords: Ehler-Danlos Syndrome Hypermobility Type, kinematics, kinetics, gait, ankle-foot complex.

Abstract (Dutch)

Achtergrond: Het hypermobiele type van het Ehler-Danlos Syndroom (EDS-HT) is een bindweefselaandoening die gekenmerkt wordt door veralgemeende hypermobiliteit en een breed spectrum van musculoskeletale symptomen. Ondanks de impact van deze klachten op het dagelijks functioneren, zijn er slechts enkele kwantitatieve studies die de verschillen tijdens het stappen bij EDS-HT hebben onderzocht. Hierdoor kunnen tot op heden enkel biomechanische gangparameters van het enkel-voetcomplex worden verondersteld. Om de omvang van het probleem beter in kaart te brengen, zijn driedimensionale ganganalyses noodzakelijk.

Doelstellingen: Het identificeren van de verschillen in kinematica en kinetica van het enkel-voetcomplex tijdens het stappen tussen patiënten met EDS-HT en een gezonde controlegroep en het onderzoeken van de voetfunctie en –pijn in deze patiëntenpopulatie.

Onderzoeksdesign: Patiënt-controle onderzoek.

Methode: Drieëntwintig vrouwen met EDS-HT en drieëntwintig gezonde controles, gematcht op geslacht en leeftijd, namen aan deze driedimensionale ganganalyse deel. De testpersonen stapten blootsvoets aan een zelfgekozen snelheid op een 12m lange wandelweg, terwijl kinematische en kinetische data werden verzameld door een optoelektronisch systeem, een kracht- en een drukplatform. De plaatsing van de markers werd bepaald aan de hand van het multi-segmentaal Ghent Foot Model (GFM). Data betreffende voetfunctie en pijn werden verworven door gebruik te maken van Visueel Analoge Schaal (VAS)-scores, het Margolis Pijndiagram, de Foot Function Index (FFI) en de Lower Extremity Functional Scale (LEFS).

Resultaten: Wat betreft de kinematica werden EDS-HT patiënten in de standsfase gekenmerkt door een significant verschillende positie van de enkel en voet in het sagittale plan met een verminderde plantairflexie van de achter- en voorvoet en een toegenomen plantairflexie ter hoogte van de middenvoet. In het frontale vlak werd in vergelijking met de controlegroep een significant hogere waarde voor inversie in de achtervoet en grote teen, alsook een toegenomen eversie in de mediale voorvoet waargenomen. Ten slotte vond er in het horizontale vlak significant meer abductie in de middenvoet en hallux plaats bij deze patiënten. Wat betreft de kinetica werd een significant verschil opgemerkt in de horizontale grondreactiekracht componenten, wat wijst op een verminderd afduwvermogen bij deze patiënten. Verder rapporteerden individuen met EDS-HT een significant hogere pijnverdeling en pijnintensiteit ter hoogte van het onderste lidmaat, alsook een grotere functiestoornis van de voet, meer beperkingen en een verminderde levenskwaliteit.

Conclusies: Door gebruik te maken van een multi-segmentaal voetmodel kon deze studie de verschillen in kinematica en kinetica van het enkel-voetcomplex tijdens het gaan aantonen bij patiënten met EDS-HT. Verder werd meer pijn en disfunctie van de voet vastgesteld bij deze patiënten. De bevindingen benadrukken het belang van een geïndividualiseerd revalidatieprogramma met aandacht voor het verbeteren van de spierkracht en optimaliseren van enkelstrategie bij deze patiënten. Een andere belangrijke klinische implicatie is het advies rond aangepaste orthesen en chronisch pijnmanagement.

Trefwoorden: Het hypermobiele type van Ehler-Danlos Syndroom**,** kinematica**,** kinetica, gang, enkel-voetcomplex.

Introduction

The hypermobile type of Ehler-Danlos Syndrome (EDS-HT), clinically similar to Joint Hypermobility Syndrome (JHS), is a heterogeneous group of heritable connective tissue disorders caused by defects in biosynthesis and secretion of fibrillar collagen molecules (Beighton et al., 1997; Celletti et al., 2012; Murray et al., 2012; Rombaut et al., 2012). The pathogenesis as well as the exact prevalence is still unclear, but it is remarkable more common in the female gender (Steinmann et al., 2002; Castori et al., 2010).

The revised Villefranche criteria are used to clinically diagnose this syndrome. Generalized joint hypermobility, objectified by a Beighton score of ≥5/9, together with skin hyper extensibility or skin fragility are the major criteria. Recurrent joint dislocations, chronic musculoskeletal pain and positive family history belong to the minor criteria of this diagnostic tool (Beighton et al., 1997).

Capsuloligamentous structures, muscles and tendons contain large portions of these affected collagen molecules and this explains the high prevalence of musculoskeletal problems seen in this subgroup of Ehler-Danlos Syndrome. Rombaut et al. (2010) investigated this important clinical manifestation and displayed the occurrence of musculoskeletal complaints in particular. Remarkably, all patients reported joint pain and the majority of the study group described joint dislocations as well. These findings can be incorporated within the characteristic joint hypermobility of this population. A significant part of these musculoskeletal complaints was located in the lower extremity, with a 77,8% prevalence of ankle and foot pain. On a structural level, EDS-HT patients seem to have more foot anomalies such as asymptomatic pes planus, hallux valgus and claw toe (Beighton and Horan, 1969; Tompkins and Bellacosa, 1997; Pau et al., 2013). These foot alterations together with muscle pain in the lower limb and difficulties with transmitting muscle force, result in an insufficient functioning of the ankle-foot complex as the first link of the kinetic chain in walking (Beighton and Horan, 1969; Tompkins and Bellacosa, 1997; Voermans et al., 2009; Tinkle et al., 2010; Galli et al., 2011; Rombaut et al., 2012; Granata et al., 2013; Pau et al., 2013).

The introduced impairments in structure and body function have a relevant and negative impact on activities of daily life (ADL) and influence participation at school, work or during leisure time activities (Murray et al., 2012; De Wandele et al., 2013). Rombaut et al. (2012) reported a poorer physical function in patients with EDS-HT in contrast to healthy controls. Moreover, the greatest physical impairment was observed in walking and bending. Additionally, psychosocial factors such as psychological distress, depression and anxiety contribute to the restrictions seen in ADL (Baeza-Velasco et al., 2011; Murray et al., 2012).

The observation of walking as one of the greatest physical impairments in patients with EDS-HT is crucial because it is an essential and automatic activity in daily life. Important influencing factors for walking could be muscle weakness, generalized joint laxity, foot deformities and fear of falling. This fear of falling has been shown to be clinically important in a study of Rombaut et al. (2011), in which about 80% of the patients with EDS-HT experienced some fear of falling in daily life. More explicit, the highest scores for anxiety were observed when taking a walk in the study of Cimolin et al. (Cimolin et al., 2011; Galli et al., 2011; Rombaut et al., 2011; Rigoldi et al., 2012).

A systematic review was performed in November 2014 and an update was done in October 2015 with no relevant new articles found. Until then, only a few studies investigated gait in patients with EDS-HT. Most studies investigated spatio-temporal parameters and kinematics during forward walking in EDS-HT. Concerning these spatio-temporal parameters, it is likely that patients with EDS-HT walk with a reduced gait velocity, step length and stride length (Cimolin et al., 2011; Galli et al., 2011; Rombaut et al., 2011; Rigoldi et al., 2012).

Regarding kinematics, it is probable that patients with EDS-HT show other joints positions and kinematics of the pelvis, hip, knee and ankle during the different phases of gait (Cimolin et al., 2011; Galli et al., 2011; Celletti et al., 2013). For the ankle and foot region, the feet of EDS-HT patients are placed more in plantar flexion during initial contact and at toe-off (Cimolin et al., 2011; Galli et al., 2011). The general laxity of the joints, together with pain and weakness of the muscles could lead to these abnormal joint positions during the step cycle.

Limited evidence exists for kinetics, including plantar pressure, ground reaction forces, moments and power. Only one study investigated plantar pressure patterns in EDS-HT and showed that these patients would have larger plantar pressure peaks in the forefoot, with a smaller forefoot contact area for static and dynamic conditions (Pau et al., 2013).

Celletti et al. (2012) concluded a negative correlation between the intensity of fatigue and the maximum vertical ground reaction force in patients with EDS-HT. As these patients report a greater level of fatigue before, immediately after and one minute after a muscle endurance test, a lower vertical ground reaction force can be expected (Rombaut et al., 2012).

Finally, the reduced calf muscle strength would explain why these patients walk with a restricted peak of ankle plantar flexor moment and power during terminal stance (Cimolin et al., 2011; Galli et al., 2011; Rigoldi et al., 2012).

After all, Booshanam et al. (2010) states that the biomechanical consequences of the joint hypermobility on the movement pattern are complex and still poorly understood.

In summary, only a few quantitative studies have been carried out to investigate the altered movements seen in EDS-HT during walking. More specific, the impact of the foot dysfunction and pain on biomechanics at different segments of the ankle-foot complex can only be hypothesized. Three-dimensional gait analyses are needed to better understand the extent of the problem and the impact on activities in daily life and can be of help to develop evidence-based therapy guidelines.

Based on the existing knowledge in literature and the clinical manifestations on the musculoskeletal structures in patients with EDS-HT, significant differences in kinematics and kinetics can be hypothesized when comparing EDS-HT with healthy persons. More specific, the presence of joint hypermobility, reduced muscle strength and lower endurance capacity could result in a decreased ability of stabilizing the foot. This, in turn, could result in an excessive and/or prolonged eversion in the frontal plane during walking which could increase the contact area of the foot significantly. Pain and the presence of fatigue could be two factors which reduce vertical ground reaction force.

Therefore, the primary purpose of this case-control study is to identify differences in kinematics and kinetics of the ankle-foot complex during gait between EDS-HT and healthy age-matched controls by using three-dimensional gait analysis. The secondary objective of this study is to assess foot function and pain in these patients.

Method

1. Study design

Case-control study.

2. Participants

In total, 46 subjects participated in the study, of whom 23 patients diagnosed with EDS-HT and 23 healthy control subjects. In 2014, 24 patients diagnosed with EDS-HT and 7 healthy controls were examined. However, data of one patient with EDS-HT was not applicable because of the absence of a static trial. A year later, completion of the examination took place by testing the remaining 16 healthy controls. This resulted in a final group of 23 patients with EDS-HT and 23 individually matched healthy controls.

Patient selection was performed in the Centre for Medical Genetics at the Ghent University Hospital based on the revised Villefranche Criteria for EDS-HT, which include the presence of generalized joint hypermobility (Beighton score ≥5/9) and skin hyperextensibility/fragility, in combination with recurring joint dislocations, and/or chronic musculoskeletal pain, and/or a positive family history (Beighton et al., 1997).

The control subjects were healthy volunteers, individually matched with the EDS-HT patients for gender, age and ethnicity. They were recruited on a voluntary basis after verbal advertisement and a corresponding letter.

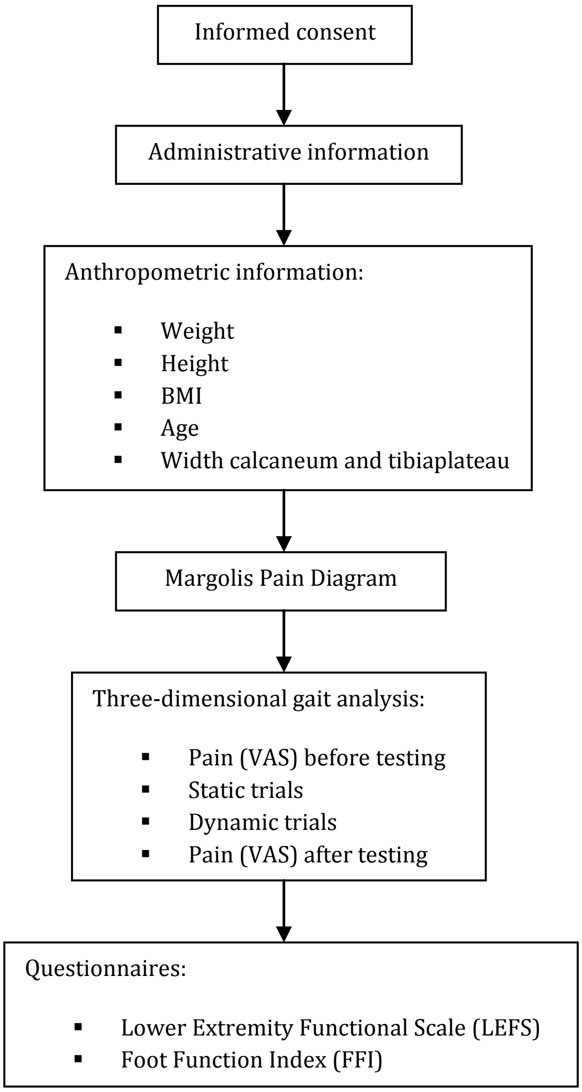
In this case-control study, only women were included because they represent the vast majority of the patient population (Beighton et al., 1997). Other inclusion and exclusion criteria for the patient and control group are summarized in Table 1.

Table 1: Selection criteria.

	Inclusion	**Exclusion**
EDS-HT	▪ Woman ▪ Beighton ≥ 5/9 ▪ Diagnose of EDS-HT based on revised Villefranche Criteria	▪ Current injury of the lower extremities or in the past 6 months ▪ System disease(s) with potential impact on feet and/or gait pattern (e.g. diabetes mellitus or rheumatic disorders) ▪ Not able to walk barefoot and without a walking device for 5m ▪ Pregnancy
Healthy control	▪ Woman ▪ Beighton ≤ 3/9	▪ Musculoskeletal complaints of the trunk or lower limb ▪ Musculoskeletal disorders or surgery of the lower limb in the past year ▪ Prior history of cardiovascular or neurological disorders ▪ System disease(s) with potential impact on the lower limb ▪ Walking device ▪ Obvious gait abnormalities ▪ Pregnancy

3. Procedure

The study was approved by the Ethical Committee of the Ghent University Hospital. Written informed consent together with administrative information was obtained from all the participants before examining. Each participant was individually evaluated using a standardized protocol (see Flowchart 1). For this investigation, subjects had to visit the Ghent University Hospital at the department of Rehabilitation Sciences and Physiotherapy.



Flowchart 1: Testing protocol.

3.1. Anthropometric measurements

3.1.1. Weight, height, BMI, Age

Participants were asked to fill in an administration form where among others weight, height and date of birth were registered. Body Mass Index (BMI) and age were derived from the collected data.

3.1.2. Width calcaneum/tibiaplateau

The width of the calcaneum and the tibial plateau was measured on both sides by using a calliper. The measurements were always carried out by the same examiner to minimize the potential inter-tester differences. The tibial plateau width was measured from anterior, just distally of the articular space, where the tibia is at its widest. Whereas the calcaneum was measured posterior at its thickest part. These data were used in the data processing in Visual 3D (Visual 3D v5, C-motion, Germantown, MD) at a later stage of the study.

3.2. Pain

Pain location and pain intensity were assessed by self-completion of the Margolis Pain Diagram and the Visual Analogue Scale (VAS), respectively.

The **Margolis Pain Diagram** uses two body outlines, front and back, in which subjects have to shade the body parts were they felt pain lasting for more than 24 hours in the past 4 weeks (see Figure 1). Templates that contained the 45 different areas as defined by Margolis (1986) were used to interpret the pain drawings. A score of 1 was assigned if the subjects drawing indicated pain, for each of the 45 areas, and weights were assigned to the different body areas equal to the covering body surface percentage, resulting in a weighted score that reflected the total percentage of body surface shaded as painful. In patients with chronic low-back pain, inter-rater reliability was high with minimal training of the examiners (Margolis et al., 1986).

Foot, ankle and lower leg pain were assessed by a **VAS** for pain before and after the gait analysis, where a score of 0 indicates no pain and a score of 10 indicates unbearable pain (see Figure 2).

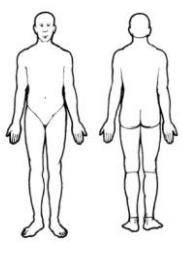


Figure 1: Margolis Pain Diagram.

Figure 2: Visual Analogue Scale.

3.3. Three-dimensional gait analysis

A three-dimensional, full-equipped gait analysis set up was used to obtain kinematics (joint angles) and kinetics (ground reaction forces and plantar pressure) during walking.

Kinematics were registered using an 8-camera optoelectronic system (Oqus 3 and 4 cameras, Qualisys, Sweden, 500Hz) while subjects walked barefoot on an instrumented walkway. In the 12m walkway, a force platform (AccuGait, AMTI, Watertown USA, 49x49cm, 500 Hz) and plantar pressure platform (Footscan, RSscan, Belgium, 50x50cm, 500Hz) were embedded at a 6m distance from the starting point. The AccuGait and Footscan were respectively used to measure ground reaction forces and plantar pressure. The three devices were synchronized.

3.3.1. Marker placement

For capturing the required data, a standardized marker placement was used. Therefore, the Ghent Foot Model (GFM) was applied (De Mits et al., 2012). Passive markers were placed on anatomical bony reference points or as tracking markers (see Figure 3 and Table 2). Palpation and its corresponding marker placement were always carried out by the same examiner to minimize the potential inter-tester differences.

Figure 3: Marker placement Ghent Foot Model on the right leg (frontal, dorsal, medial and lateral).

Table 2: Marker placement Ghent Foot Model (De Mits et al., 2012).

Segment	**Markers**
Lower leg	▪ Upper rim medial condyle tibia ▪ Head fibulae ▪ Tuberositas tibia ▪ Midway medial side tibia ▪ Malleolus medialis ▪ Malleolus lateralis
Rearfoot	▪ Upper part bisection posterior aspect calcaneum ▪ Lower part bisection posterior aspect calcaneum ▪ Sustentaculum tali ▪ Tuberculum peronei
Midfoot	▪ Naviculare ▪ Cuboid ▪ Dorsum foot (between tendons extensor digitorum longus and extensor hallucis longus)
Medial forefoot	▪ Base metatarsal 1 ▪ Shaft metatarsal 1 ▪ Lateral side head metatarsal 1
Lateral forefoot	▪ Lateral side base metatarsal 5 ▪ 3 plate-mounted markers placed on dorsal aspect metatarsal 2-5 ▪ Head metatarsal 2 ▪ Lateral side head metatarsal 5
Hallux	▪ Proximal end hallux ▪ Shaft hallux ▪ Distal end hallux

3.3.2. Static trial

Firstly, a static trial was measured. The participant was asked to stand in tandem stance position for five seconds with the tested foot placed in the middle of the force platform. A tandem stance position is defined by the position in which the body weight is divided over the two legs and the knee of the tested leg is flexed until the lower leg is perpendicular to the floor (De Mits et al., 2012).

This procedure was repeated until at least one good static trial could be recorded. A static trial was considered to be useful if each passive marker was visual on the Qualisys software (Qualisys Track Manager, Qualisys, Sweden).

3.3.3. Dynamic trial

For the dynamic trials, the participant was instructed to walk at self-selected speed over the walkway while looking forward.

Dynamic foot–ground contact parameters were synchronized and registered together with their corresponding kinematic data during these dynamic trials.

This procedure was repeated until at least ten well-performed dynamic trials for each leg could be recorded. A dynamic trial was considered to be good if the force and plantar pressure measurement platform was touched by only one foot in the middle of the platform without targeting.

3.4. Questionnaires

The Lower Extremity Functional Scale (LEFS) and the Foot Function Index (FFI) were used to evaluate the impact of EDS-HT on foot function and pain.

When using the **LEFS,** participants need to answer 20 questions about their abilities to perform everyday tasks such as walking between two rooms. For each item, a score from 0 (extreme difficult/unable to perform activity) to 4 (not difficult) is given. The lower the total score, the greater the disability.

Binkley et al. (1999) showed excellent reliability in patients with lower extremity musculoskeletal dysfunction and the LEFS had higher sensitivity to change in comparison with the Short Form 36 (SF-36) in this patient population.

The **FFI** measures the impact of foot pathology on function in terms of pain, disability and activity restriction. For each of the 23 questions, a score on a visual analogue scale from 0 to 10 is given. A high total score corresponds to severe pain, foot dysfunction and reduced quality of life due to foot pathology.

In a cohort of 87 patients with rheumatoid arthritis, test-retest reliability, internal consistency and validity of the FFI were good (Budiman-Mak et al., 1991).

4. Post-processing

The acquired kinematic and kinetic data were analyzed in the Qualisys (Qualisys Track Manager, Qualisys, Sweden) and Visual 3D software (Visual 3D v5, C-motion, Germantown, MD), according to the GFM. Euler rotations (X-Y-Z, representing respectively dorsi-/plantar flexion, eversion/inversion and ab-/adduction) were used to calculate motion between the defined segments in the different planes (see Figure 4).

Duration of stance was derived from the kinetic data. Five key moments were defined within this phase, based on the plantar pressure data (De Mits et al., 2012). First Foot Contact (FFC) happened at 0% of stance, First Metatarsal Contact (FMC) at 8%, Fore Foot Flat (FFF) at 38%, Heel Off (HO) at 64% and Last Foot Contact (LFC) at 100% (De Cock et al., 2005).

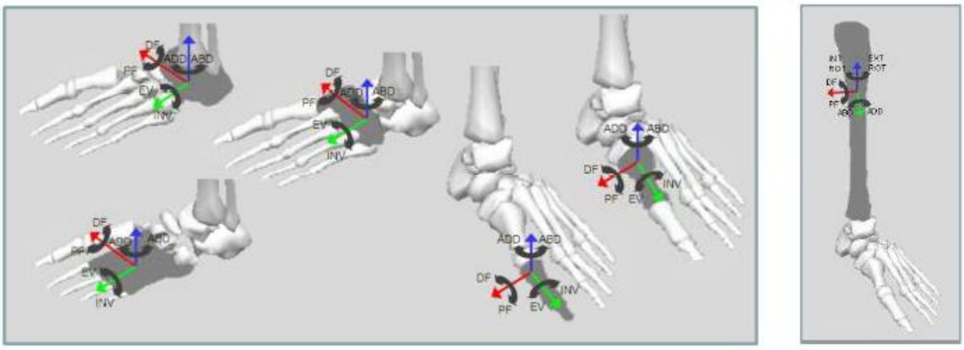


Figure 4: Axes of rotation and motions at the different ankle and foot segments (De Mits et al., 2012).

5. Statistical analysis

This analysis was performed in the software package IBM SPSS statistics 23. Descriptive data are shown as mean ± standard deviation (SD). As the data fulfilled the assumptions of normal distribution, independent t-tests were used to compare age, weight, height, BMI, pain scores, and the questionnaires' total and domain scores. This statistical test was also conducted to compare the kinematic and kinetic data between patients and healthy subjects at the five key points of the curves. The level of significance was set at P = 0,05.

Results

1. Subject characteristics

The anthropometric properties of the included participants are represented in Table 3. For weight, length, BMI and age, no significant differences between groups were observed. However, BMI had a tendency to be higher in the patient group.

The Margolis Pain Diagram revealed a significantly higher mean body percentage of pain in the patient group (P<0,001). Patients with EDS-HT felt pain at 37,46% of the total body surface, whereas healthy controls only at 1,02%. Further, 91,30% of the patients reported pain at the lower limb. The relative and absolute frequencies of pain at different locations of the lower limb in EDS-HT are shown in Table 4.

Table 3: Anthropometric information. Values are expressed as mean ± SD.

	EDS-HT	**Control**	***P***
Number	23	23	-
Weight (kg)	72,1 ± 19,27	66,4 ± 10,80	0,222
Length (cm)	165 ± 9,0	166 ± 5,4	0,706
BMI (kg/m^2)	26,4 ± 6,69	24,1 ± 3,57	0,149
Age (years)	41 ± 11,0	41 ± 11,5	0,958

EDS-HT, Ehler-Danlos Syndrome Hypermobility Type; BMI, Body Mass Index.

Table 4: Pain locations of the lower limb in EDS-HT (Margolis).

Pain location	**EDS-HT % (N)**
Lower limb	91,30 (21)
Thigh	69,57 (16)
Shank	73,91 (17)
Foot	69,57 (16)
Hip joint	39,13 (9)
Knee joint	69,57 (16)
Ankle joint	60,87 (14)

EDS-HT, Ehler-Danlos Syndrome Hypermobility Type; %, percentage; N, number.

2. Three-dimensional gait analysis

2.1. Kinematics

2.1.1. Rearfoot vs Tibia

Patients with EDS-HT walked with a significantly lower plantar flexion at the talocrural joint during the whole stance phase. Significantly higher values for inversion were present during the whole stance phase for the left and at FFC, FMC and LFC for the right foot (see Figure 5, Figure 6 and Table 5).

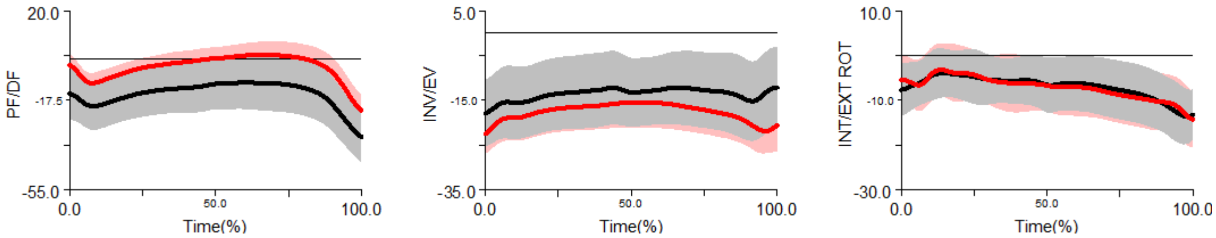


Figure 5: Rearfoot vs Tibia during stance phase (left). - EDS-HT - Control

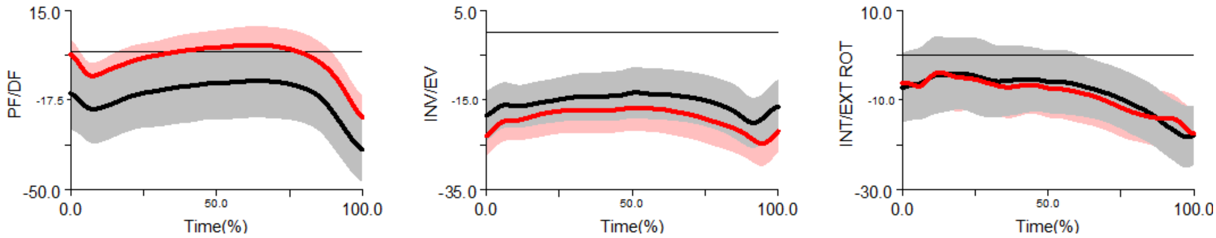


Figure 6: Rearfoot vs Tibia during stance phase (right). - EDS-HT - Control

Table 5: Kinematic data of Rearfoot vs Tibia. Values are expressed as mean ± SD.

		Left			Right		
		EDS-HT	**Control**	***P***	**EDS-HT**	**Control**	***P***
PF/DF	FFC	-2,8 ± 4,74	-14,8 ± 11,54	**<0,001***	-0,8 ± 5,11	-14,0 ± 13,01	**<0,001***
	FMC	-10,2 ± 4,06	-20,3 ± 10,53	**<0,001***	-8,7 ± 4,83	-19,7 ± 12,20	**0,001***
	FFF	-1,9 ± 4,56	-12,5 ± 11,00	**<0,001***	0,4 ± 5,73	-11,3 ± 13,10	**0,001***
	HO	1,2 ± 5,51	-10,2 ± 11,88	**<0,001***	2,9 ± 6,42	-9,3 ± 13,22	**0,001***
	LFC	-21,9 ± 6,52	-32,8 ± 10,74	**<0,001***	-23,3 ± 7,31	-35,0 ± 11,82	**<0,001***
INV/EV	FFC	-22,5 ± 4,54	-17,2 ± 7,81	**0,008***	-22,8 ± 4,42	-18,5 ± 5,79	**0,007***
	FMC	-19,0 ± 4,99	-14,5 ± 8,41	**0,035***	-19,4 ± 4,39	-16,1 ± 5,14	**0,024***
	FFF	-16,4 ± 5,17	-11,9 ± 8,61	**0,040***	-17,2 ± 5,03	-14,2 ± 5,70	0,075
	HO	-16,1 ± 5,35	-11,4 ± 8,41	**0,029***	-17,3 ± 5,19	-14,0 ± 5,99	0,053
	LFC	-20,8 ± 5,94	-11,5 ± 9,34	**<0,001***	-21,9 ± 4,51	-16,5 ± 6,45	**0,002***
INT/EXT ROT	FFC	-5,3 ± 5,65	-8,1 ± 5,82	0,108	-6,3 ± 6,29	-9,1 ± 6,29	0,148
	FMC	-5,6 ± 6,14	-5,9 ± 4,94	0,844	-6,0 ± 5,73	-7,6 ± 6,83	0,401
	FFF	-6,1 ± 6,61	-6,1 ± 4,86	0,971	-6,9 ± 7,04	-7,1 ± 6,11	0,896
	HO	-7,1 ± 6,59	-6,9 ± 6,17	0,891	-8,7 ± 6,93	-8,9 ± 5,78	0,934
	LFC	-14,0 ± 6,21	-13,7 ± 5,43	0,858	-17,4 ± 5,48	-19,6 ± 4,63	0,175

EDS-HT, Ehler-Danlos Syndrome Hypermobility Type; PF/DF, Plantar Flexion/Dorsal Flexion; INV/EV, Inversion/Eversion; INT/EXT ROT, Internal Rotation/External Rotation; FFC, First Foot Contact; FMC, First Metatarsal Contact; FFF, Fore Foot Flat; HO, Heel Off; LFC, Last Foot Contact. All numbers are expressed as degrees.

2.1.2. Midfoot vs Rearfoot

At the Chopart's joint, there was a plantar flexed position in EDS-HT in contrast with the dorsal flexed position in controls during the whole stance phase. At FFC, FMC, FFF and HO, there was significantly more abduction in patients with EDS-HT for the left foot. For the right foot, the increased abduction was only significant later in the stance phase, at FFF and HO (see Figure 7, Figure 8 and Table 6).

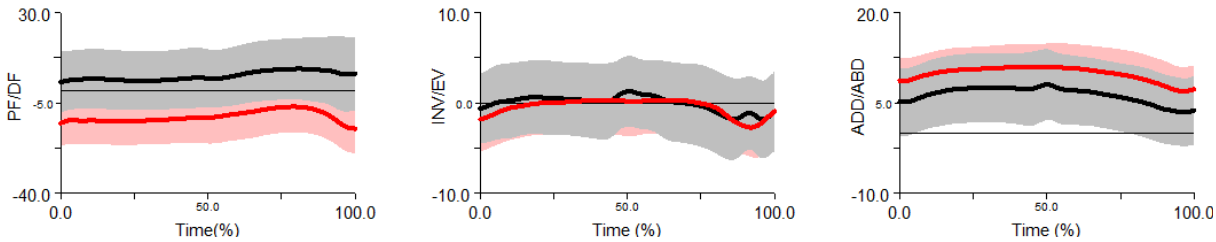


Figure 7: Midfoot vs Rearfoot during stance phase (left). - EDS-HT - Control

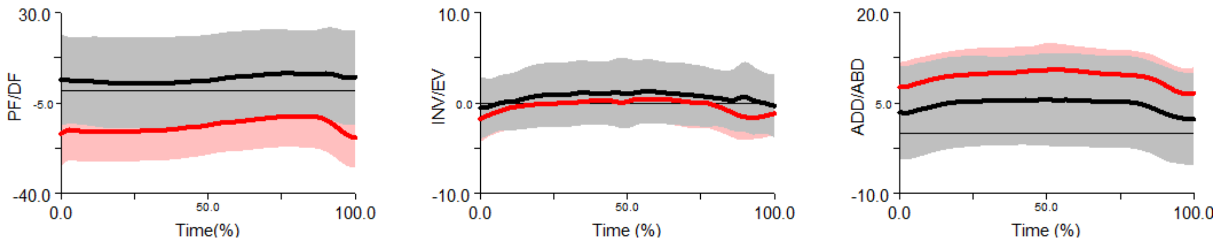


Figure 8: Midfoot vs Rearfoot during stance phase (right). - EDS-HT - Control

Table 6: Kinematic data of Midfoot vs Rearfoot. Values are expressed as mean ± SD.

		Left			**Right**		
		EDS-HT	**Control**	***P***	**EDS-HT**	**Control**	***P***
PF/DF	FFC	-12,9 ± 9,11	4,5 ± 12,77	**<0,001***	-16,8 ± 12,59	3,5 ± 18,09	**<0,001***
	FMC	-12,0 ± 9,33	5,6 ± 12,59	**<0,001***	-15,8 ± 11,99	3,4 ± 16,91	**<0,001***
	FFF	-11,4 ± 9,56	5,2 ± 12,43	**<0,001***	-15,1 ± 12,01	2,6 ± 17,63	**<0,001***
	HO	-8,8 ± 10,24	7,9 ± 12,52	**<0,001***	-11,7 ± 11,75	5,3 ± 17,44	**<0,001***
	LFC	-15,0 ± 9,81	7,5 ± 15,26	**<0,001***	-18,1 ± 11,87	5,1 ± 18,43	**<0,001***
INV/EV	FFC	-1,5 ± 3,37	-1,1 ± 4,24	0,726	-1,8 ± 2,54	-1,0 ± 3,29	0,367
	FMC	-0,3 ± 3,39	-0,4 ± 4,41	0.973	-0,9 ± 2,28	-0,2 ± 2,96	0,420
	FFF	0,8 ± 3,56	-0,6 ± 4,39	0,487	0,2 ± 2,48	0,7 ± 3,36	0,599
	HO	0,7 ± 3,40	-0,1 ± 4,57	0,458	0,1 ± 2,65	0,6 ± 3,28	0,544
	LFC	-0,5 ± 3,99	-1,4 ± 4,66	0,507	-1,1 ± 2,31	-0,6 ± 3,01	0,552
ADD/ABD	FFC	8,4 ± 4,01	4,9 ± 5,85	**0,022***	7,4 ± 4,14	4,0 ± 7,49	0,067
	FMC	9,3 ± 3,77	6,0 ± 5,82	**0,026***	8,3 ± 4,21	4,6 ± 7,59	0,053
	FFF	10,6 ± 4,06	7,4 ± 5,99	**0,035***	9,8 ± 4,33	6,0 ± 7,15	**0,038***
	HO	10,1 ± 4,24	6,8 ± 5,85	**0,034***	9,9 ± 4,13	5,9 ± 7,48	**0,035***
	LFC	7,0 ± 4,21	4,0 ± 5,91	0,056	6,4 ± 4,22	3,0 ± 7,45	0,064

EDS-HT, Ehler-Danlos Syndrome Hypermobility Type; PF/DF, Plantar Flexion/Dorsal Flexion; INV/EV, Inversion/Eversion; ADD/ABD, Adduction/Abduction; FFC, First Foot Contact; FMC, First Metatarsal Contact; FFF, Fore Foot Flat; HO, Heel Off; LFC, Last Foot Contact. All numbers are expressed as degrees.

2.1.3. Lateral Forefoot vs Midfoot

At the right and left lateral parts of the Lisfranc joint, significantly more dorsal flexion was shown in EDS-HT during the whole stance phase, except at FFF and HO for the right foot (see Figure 9, Figure 10 and Table 7).

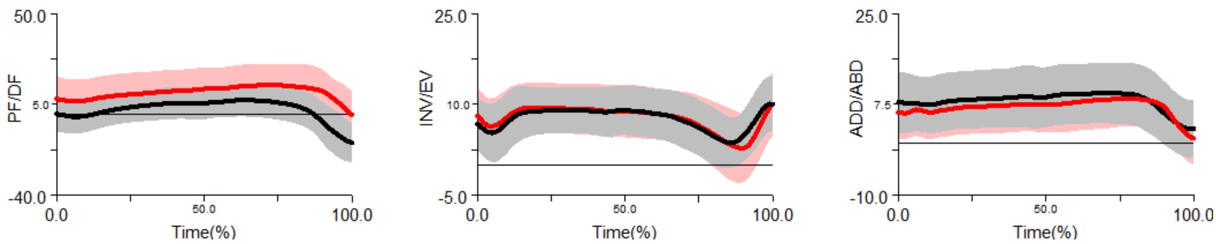


Figure 9: Lateral Forefoot vs Midfoot during stance phase (left). - EDS-HT - Control

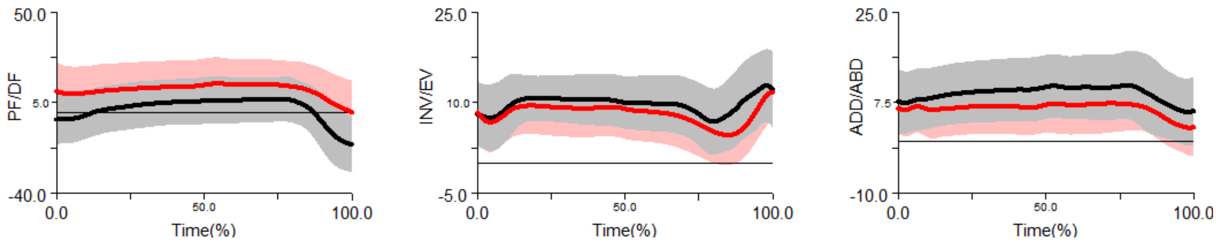


Figure 10: Lateral Forefoot vs Midfoot during stance phase (right). - EDS-HT - Control

Table 7: Kinematic data of Lateral Forefoot vs Midfoot. Values are expressed as mean ± SD.

		Left			Right		
		EDS-HT	**Control**	***P***	**EDS-HT**	**Control**	***P***
PF/DF	FFC	8,4 ± 11,48	-0,5 ± 9,35	**0.006***	10,5 ± 14,59	-2,1 ± 10,83	**0,002***
	FMC	7,3 ± 10,89	-1,7 ± 8,66	**0,004***	9,4 ± 13,50	-1,3 ± 10,73	**0,006***
	FFF	11,8 ± 10,93	5,0 ± 8,19	**0,021***	12,7 ± 13,29	6,0 ± 10,20	0,070
	HO	14,5 ± 10,96	6,7 ± 8,35	**0,009***	14,1 ± 12,52	7,3 ± 10,18	0,058
	LFC	0,5 ± 11,56	-14,1 ± 10,14	**<0,001***	0,0 ± 15,92	-14,8 ± 13,67	**0,002***
INV/EV	FFC	8,1 ± 4,74	6,7 ± 4,42	0,306	8,2 ± 5,04	7,6 ± 5,22	0,698
	FMC	7,0 ± 4,86	6,0 ± 5,14	0,493	7,4 ± 4,86	7,7 ± 5,28	0,861
	FFF	9,4 ± 4,31	8,8 ± 4,02	0,650	8,9 ± 4,96	10,1 ± 3,80	0,398
	HO	8,5 ± 4,20	8,1 ± 4,37	0,754	8,1 ± 5,17	9,3 ± 4,05	0,427
	LFC	9,9 ± 5,30	10,1 ± 4,62	0,883	11,7 ± 4,84	11,2 ± 5,42	0,780
ADD/ABD	FFC	6,1 ± 5,30	8,4 ± 5,48	0,160	6,4 ± 5,19	7,5 ± 6,20	0,522
	FMC	6,4 ± 5,55	8,3 ± 4,56	0,223	6,6 ± 5,47	7,8 ± 6,00	0,472
	FFF	7,4 ± 5,66	9,4 ± 5,17	0,221	6,9 ± 5,60	9,7 ± 6,13	0,118
	HO	8,3 ± 5,85	10,2 ± 5,25	0,251	7,2 ± 5,85	10,2 ± 6,28	0,103
	LFC	1,1 ± 5,30	3,3 ± 4,76	0,147	2,7 ± 5,79	5,7 ± 6,61	0,116

EDS-HT, Ehler-Danlos Syndrome Hypermobility Type; PF/DF, Plantar Flexion/Dorsal Flexion; INV/EV, Inversion/Eversion; ADD/ABD, Adduction/Abduction; FFC, First Foot Contact; FMC, First Metatarsal Contact; FFF, Fore Foot Flat; HO, Heel Off; LFC, Last Foot Contact. All numbers are expressed as degrees.

2.1.4. Medial Forefoot vs Midfoot

The medial forefoot of patients with EDS-HT was significantly placed in a more dorsal flexed position relative to the midfoot. This phenomenon was seen during the whole stance phase for the left and at FFC and FMC for the right foot. Significantly more eversion occurred bilaterally, except at LFC for the left foot. Finally, significantly less abduction was present at FFC and LFC for the left and at LFC for the right foot (see Figure 11, Figure 12 and Table 8).

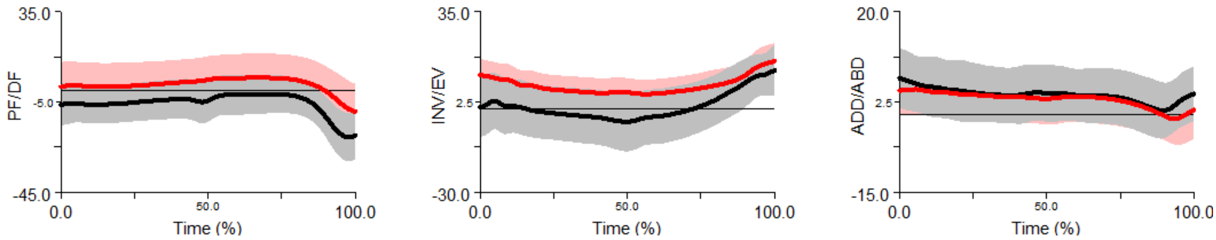


Figure 11: Medial Forefoot vs Midfoot during stance phase (left). - EDS-HT - Control

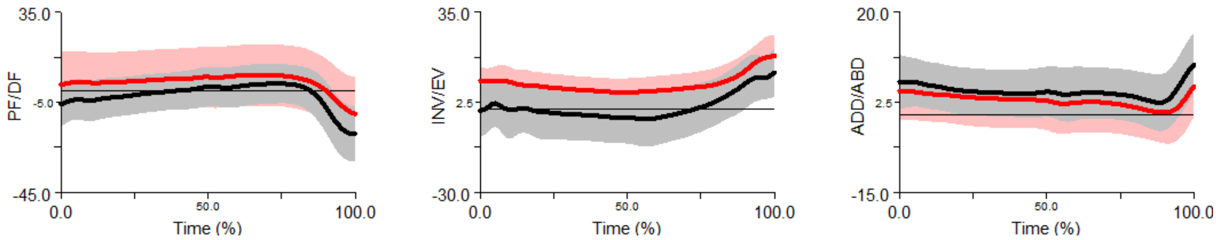


Figure 12: Medial Forefoot vs Midfoot during stance phase (right). - EDS-HT - Control

Table 8: Kinematic data of Medial Forefoot vs Midfoot. Values are expressed as mean ± SD.

		Left			**Right**		
		EDS-HT	**Control**	***P***	**EDS-HT**	**Control**	***P***
PF/DF	FFC	2,5 ± 11,00	-6,9 ± 9,83	**0,004***	2,8 ± 14,95	-7,0 ± 10,24	**0,015***
	FMC	2,9 ± 10,47	-6,6 ± 9,01	**0,002***	3,7 ± 14,07	-5,1 ± 9,47	**0,018***
	FFF	4,1 ± 10,12	-4,4 ± 9,26	**0,005***	5,3 ± 13,79	-1,1 ± 8,47	0,070
	HO	6,3 ± 10,76	-2,3 ± 9,17	**0,006***	7,1 ± 13,85	1,3 ± 9,48	0,113
	LFC	-7,8 ± 11,93	-20,4 ± 10,92	**0,001***	-11,0 ± 17,23	-20,2 ± 12,87	0,054
INV/EV	FFC	12,3 ± 6,20	0,0 ± 11,02	**<0,001***	10,3 ± 4,98	-0,2 ± 9,67	**<0,001***
	FMC	10,6 ± 6,11	0,3 ± 10,38	**<0,001***	10,2 ± 5,68	1,1 ± 10,25	**0,001***
	FFF	5,8 ± 5,39	-3,6 ± 10,32	**<0,001***	6,4 ± 4,96	-1,8 ± 9,42	**0,001***
	HO	5,8 ± 5,24	-3,0 ± 10,31	**0,001***	6,7 ± 5,46	-2,0 ± 9,38	**0,001***
	LFC	17,0 ± 6,42	13,2 ± 8,95	0,106	19,0 ± 7,68	13,7 ± 8,77	**0,039***
ADD/ABD	FFC	4,6 ± 5,06	7,7 ± 5,25	**0,048***	4,8 ± 5,69	6,3 ± 5,16	0,352
	FMC	4,7 ± 5,03	6,3 ± 4,68	0,267	4,3 ± 5,55	5,9 ± 4,65	0,301
	FFF	3,5 ± 5,13	4,5 ± 4,37	0,505	3,3 ± 5,80	4,1 ± 4,53	0,618
	HO	3,4 ± 5,34	4,4 ± 4,41	0,495	2,7 ± 6,00	4,0 ± 4,91	0,445
	LFC	0,9 ± 5,90	4,9 ± 4,40	**0,014***	5,6 ± 5,98	9,6 ± 6,12	**0,029***

EDS-HT, Ehler-Danlos Syndrome Hypermobility Type; PF/DF, Plantar Flexion/Dorsal Flexion; INV/EV, Inversion/Eversion; ADD/ABD, Adduction/Abduction; FFC, First Foot Contact; FMC, First Metatarsal Contact; FFF, Fore Foot Flat; HO, Heel Off; LFC, Last Foot Contact. All numbers are expressed as degrees.

2.1.5. *Hallux vs Medial Forefoot*

A significantly less dorsal flexed position at HO was present at the left first metatarsophalangeal joint of patients with EDS-HT. However, significantly more dorsal flexion was shown in the right foot at LFC. Further, there was a more inverted position at FFF for the left and at the greatest part of the stance phase for the right foot. Significantly less adduction happened at FFC and FMC for the left and at FFC, FMC, FFF and HO for the right hallux (see Figure 13, Figure 14 and Table 9).

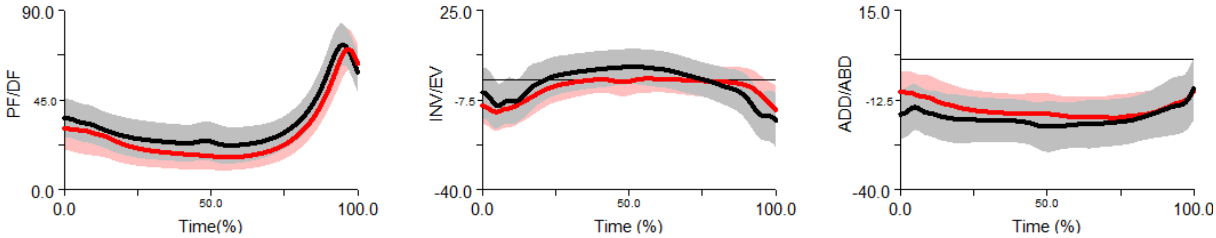


Figure 13: Hallux vs Medial Forefoot during stance phase (left). - EDS-HT - Control

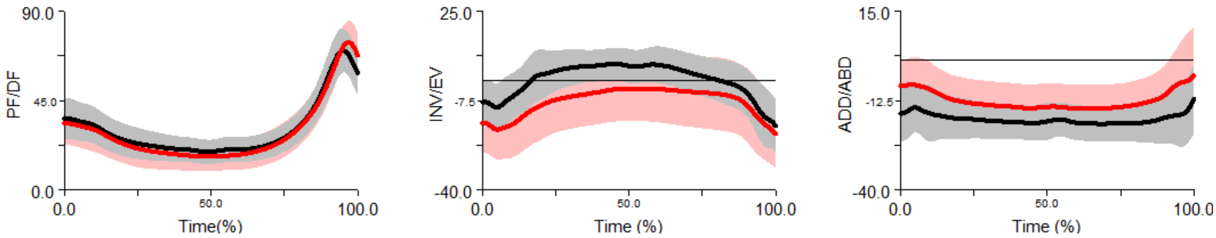


Figure 14: Hallux vs Medial Forefoot during stance phase (right). - EDS-HT - Control

Table 9: Kinematic data of Hallux vs Medial Forefoot. Values are expressed as mean ± SD.

		Left			Right		
		EDS-HT	**Control**	***P***	**EDS-HT**	**Control**	***P***
PF/DF	FFC	31,3 ± 10,62	36,5 ± 10,46	0,104	33,1 ± 11,10	38,4 ± 10,29	0,100
	FMC	29,8 ± 11,99	33,6 ± 9,90	0,254	30,9 ± 11,25	35,6 ± 9,47	0,140
	FFF	18,6 ± 7,99	23,5 ± 9,22	0,063	17,7 ± 8,08	21,8 ± 6,33	0,067
	HO	17,7 ± 6,68	23,1 ± 9,00	**0,024***	18,3 ± 7,75	21,8 ± 6,57	0,110
	LFC	62,8 ± 9,50	59,8 ± 9,68	0,300	67,9 ± 11,41	60,5 ± 10,17	**0,028***
INV/EV	FFC	-9,7 ± 6,12	-5,4 ± 8,64	0,056	-15,7 ± 10,76	-8,2 ± 7,83	**0,012***
	FMC	-10,8 ± 6,52	-8,4 ± 6,87	0,232	-17,1 ± 11,34	-8,8 ± 9,04	**0,009***
	FFF	-0,5 ± 4,35	3,3 ± 5,72	**0,016***	-4,5 ± 11,50	5,0 ± 5,49	**0,001***
	HO	0,1 ± 4,66	2,8 ± 6,15	0,100	-3,4 ± 12,29	4,8 ± 6,72	**0,008***
	LFC	-11,2 ± 8,09	-15,7 ± 9,50	0,095	-19,4 ± 12,23	-16,8 ± 9,51	0,435
ADD/ABD	FFC	-9,1 ± 6,08	-17,2 ± 7,62	**<0,001***	-8,0 ± 8,36	-15,8 ± 9,05	**0,004***
	FMC	-10,7 ± 6,67	-16,3 ± 7,06	**0,008***	-8,5 ± 8,89	-14,7 ± 8,68	**0,021***
	FFF	-15,9 ± 6,02	-19,0 ± 6,55	0,100	-14,5 ± 7,53	-18,6 ± 4,96	**0,037***
	HO	-17,0 ± 6,23	-20,1 ± 7,26	0,130	-15,0 ± 7,56	-19,2 ± 5,16	**0,035***
	LFC	-8,9 ± 7,98	-9,1 ± 9,39	0,919	-5,0 ± 14,96	-10,7 ± 10,69	0,150

EDS-HT, Ehler-Danlos Syndrome Hypermobility Type; PF/DF, Plantar Flexion/Dorsal Flexion; INV/EV, Inversion/Eversion; ADD/ABD, Adduction/Abduction; FFC, First Foot Contact; FMC, First Metatarsal Contact; FFF, Fore Foot Flat; HO, Heel Off; LFC, Last Foot Contact. All numbers are expressed as degrees.

2.2. Kinetics

Patients with EDS-HT showed significant differences in the horizontal ground reaction force components. At FMC and FFF, significantly higher ground reaction forces in posterior direction were generated at the left and right foot. A significantly lower ground reaction force in forward direction was registered at HO for the left foot. However, at LFC, the ground reaction force in anterior direction was significantly higher at both feet (see Figure 15, Figure 16 and Table 10).

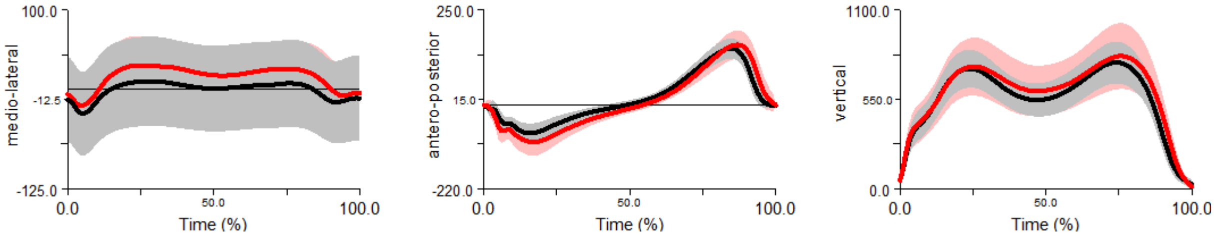


Figure 15: Ground reaction forces during stance phase (left). - EDS-HT - Control

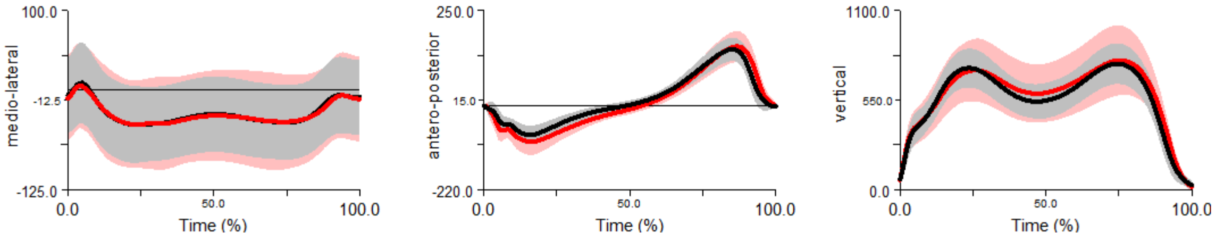


Figure 16: Ground reaction forces during stance phase (right). - EDS-HT - Control

Table 10: Kinetic data (ground reaction forces). Values are expressed as mean ± SD.

		Left			Right		
		EDS-HT	**Control**	***P***	**EDS-HT**	**Control**	***P***
Med-Lat	FFC	-12,3 ± 53,48	-12,0 ± 53,50	0,985	-9,7 ± 52,72	-9,7 ± 55,23	0,999
	FMC	-19,4 ± 55,30	-22,5 ± 53,07	0,848	-4,1 ± 53,66	-5,5 ± 57,55	0,934
	FFF	19,8 ± 49,79	7,5 ± 54,75	0,430	-38,7 ± 54,94	-40,3 ± 53,88	0,921
	HO	16,4 ± 49,34	6,2 ± 54,35	0,506	-36,5 ± 59,56	-40,7 ± 54,50	0,807
	LFC	-10,8 ± 53,22	-10,6 ± 53,42	0,986	-10,8 ± 52,46	-11,8 ± 54,38	0,950
AP	FFC	-1,6 ± 4,23	-2,1 ± 3,37	0,653	-2,0 ± 3,69	-2,0 ± 3,33	0,968
	FMC	-66,6 ± 27,71	-48,9 ± 15,85	**0,011***	-64,1 ± 21,61	-49,3 ± 16,92	**0,015***
	FFF	-35,1 ± 15,70	-16,8 ± 10,39	**<0,001***	-32,9 ± 11,99	-17,1 ± 11,96	**<0,001***
	HO	30,8 ± 11,89	42,5 ± 12,46	**0,002***	32,6 ± 14,91	40,9 ± 14,85	0,070
	LFC	1,9 ± 3,07	-0,3 ± 2,62	**0,011***	2,4 ± 3,13	-0,9 ± 3,00	**0,001***
Vertical	FFC	55,5 ± 35,20	56,4 ± 29,52	0,921	60,3 ± 38,13	65,4 ± 31,85	0,629
	FMC	429,5 ± 126,88	418,7 ± 91,63	0,742	429,6 ± 114,04	424,6 ± 85,02	0,867
	FFF	646,5 ± 193,86	591,6 ± 109,12	0,243	640,0 ± 191,97	594,5 ± 114,59	0,343
	HO	710,3 ± 196,59	687,0 ± 129,10	0,637	713,6 ± 207,20	685,7 ± 125,14	0,589
	LFC	18,4 ± 32,43	26,3 ± 29,89	0,397	17,9 ± 31,34	29,5 ± 30,12	0,212

EDS-HT, Ehler-Danlos Syndrome Hypermobility Type; Med-Lat, Medio-Lateral; AP, Antero-Posterior; FFC, First Foot Contact; FMC, First Metatarsal Contact; FFF, Fore Foot Flat; HO, Heel Off; LFC, Last Foot Contact. All numbers are expressed as forces in Newton.

2.3. Pain intensity

Pain intensity is displayed as a VAS-score on a total of 10 in Table 11. Patients with EDS-HT reported significantly higher scores for pain intensity at the lower limb and foot in contrast with healthy controls, both before and after the three-dimensional gait analysis. The VAS-scores at the lower limb and foot in the EDS-HT group increased non-significantly after testing.

Table 11: Pain intensity. Values are expressed as mean ± SD.

Pain intensity (VAS)		EDS-HT	Control	*P*
Before testing	Lower limb	1,9 ± 2,11	0,0 ± 0,00	**< 0,001***
	Foot	3,5 ± 2,55	0,0 ± 0,00	**< 0,001***
After testing	Lower limb	3,1 ± 2,69	0,0 ± 0,21	**< 0,001***
	Foot	5,0 ± 2,86	0,1 ± 0,52	**< 0,001***
P	Lower limb	0,112	0,328	
	Foot	0,079	0,328	

EDS-HT, Ehler-Danlos Syndrome Hypermobility Type; VAS, Visual Analogue Scale.

3. Questionnaires

Patients with EDS-HT demonstrated significantly higher total and domain scores for the FFI and a significantly lower total score for the LEFS (see Table 12).

Table 12: Total and domain scores for questionnaires. Values are expressed as mean ± SD.

Questionnaire	Score	EDS-HT	Control	*P*
LEFS	Total (/80)	42,2 ± 16,06	78,1 ± 3,18	**< 0,001***
FFI	Total (/230)	89,2 ± 37,82	23,1 ± 2,47	**< 0,001***
	Pain (/90)	40,3 ± 16,61	9,0 ± 2,10	**< 0,001***
	Physical disability (/90)	37,5 ± 18,88	9,2 ± 0,65	**< 0,001***
	Activity limitation (/50)	11,4 ± 7,25	5,0 ± 0,00	**< 0,001***

EDS-HT, Ehler-Danlos Syndrome Hypermobility Type; LEFS, Lower Extremity Functional Scale; FFI, Foot Function Index.

Discussion

This study investigated differences in kinematics and kinetics of the ankle-foot complex during gait in the context of foot function and pain between EDS-HT and healthy age-matched controls. To our knowledge, this is the first quantitative study in which a multi-segmented foot model was applied to these patients.

Regarding kinematics, significant differences between patients with EDS-HT and healthy subjects were observed at the ankle and several foot segments during walking.

In the sagittal plane, significantly lower plantar flexion angles were present in patients with EDS-HT at the talocrural and the Lisfranc joint, whereas a higher plantar flexed position was observed at the Chopart's joint during stance phase. This finding seems in contrast with previous literature in which a more plantar flexed position of the feet during initial contact and at toe-off was concluded (Cimolin et al., 2011; Galli et al., 2011). However, these authors used a single segment model, based on marker positioning as described by Davis, Ounpuu, Tyburski and Gage (1991). Applying markers to the lateral malleolus and the lateral aspect of the fifth metatarsal head results in a segment which includes rearfoot, midfoot and forefoot. Consequently, by using a multi-segmented foot model, this current study can indicate the midfoot as an important reason for the plantar flexed position of the feet in patients with EDS-HT. This plantar flexion of the midfoot during the whole stance phase can possibly be linked with a weakness of the tibialis anterior muscle, due to its partial insertion into the medial cuneiform bone (Galli et al., 2011). The reduced calf muscle strength and endurance capacity could explain the more dorsal flexed position in the rearfoot during stance phase (Cimolin et al., 2011; Galli et al., 2011; Rigoldi et al., 2012). Joint hypermobility could be associated with the dorsal flexion movement at the tarsometatarsal joints during stance phase.

In the frontal plane, inversion was found to be significantly higher at the rearfoot and hallux, whereas significantly more eversion happened at the medial forefoot for the greatest part of the stance phase in EDS-HT. From a clinical point of view, the inversion of the rearfoot comprises a conscious compensation strategy to prevent instability during stance phase and create a normal roll-off pattern at the first metatarsophalangeal joint during propulsion. Further, the everted position of the medial forefoot corresponds to the study of Pau et al. (2013) in which a stress concentration in the forefoot during dynamic conditions in patients with EDS-HT was concluded. Finally, the altered movements at the hallux and medial forefoot reflect an insufficient use of the first ray which can be explained by hypermobility of the proximal foot segments. This phenomenon is quite relevant as it affects load transmission to the whole forefoot, possibly leading to pathological conditions and mechanical breakdown of the bony structures (Roukis and Landsman, 2003; Kim et al., 2008; Christensen and Jennings, 2009; Hansen, 2009).

In the horizontal plane, patients with EDS-HT walked with significantly more abduction at the Chopart's joint. Further, the greatest portion of the stance phase was characterized by a less adducted position of the hallux. The increased abduction positions at the midfoot and the hallux can be linked with structural foot deformities such as asymptomatic pes planus and hallux valgus, frequently seen in patients with EDS-HT (Beighton and Horan, 1969; Tompkins and Bellacosa, 1997; Pau et al., 2013).

Concerning kinetics, significant differences between the patient and control group were only found for the horizontal ground reaction force components. The higher ground reactions forces in backward direction at FMC and FFF in EDS-HT correspond to the inability of decelerating movement at the ankle-foot region. Further, a reduced propulsion capacity could be suggested in these patients, as increased ground reaction forces in anterior direction were not found at HO but only at LFC. The latter statement is in agreement with the reduced peak of ankle plantar flexor moment and restricted maximum ankle power during terminal stance reported by Cimolin et al. (2011), Galli et al. (2011) and Rigoldi et al. (2012). The lower ability to generate propulsion power results in a decrease in step velocity and could be explained by the reduced calf muscle strength and the greater level of fatigue in this population (Galli et al., 2011; Rombaut et al., 2011; Celletti et al., 2012). Moreover, the increased magnitude of the horizontal ground reaction force at FMC, FFF and LFC can be linked with the BMI which had the tendency to be higher in the patient group in this study. Indeed, deceleration and acceleration peaks from the anterior-posterior components of the ground reaction force decreased as body weight unloading increased in a study of Barela et al. (2014). The fact that no significant differences were observed for the vertical ground reaction force does not confirm the results of Celletti et al. (2012) in which these patients would have a lower vertical ground reaction force due to the higher intensity of fatigue in this pathology.

The secondary purpose of this case-control study was to objectify foot function and pain. Regarding pain, a significantly higher pain distribution and pain intensity was observed in patients with EDS-HT. Joint pain revealed a similar pattern to the study of Rombaut et al. (2010) as the highest prevalence of pain was located at the knee joint, followed by the ankle joint. The fact that 73,91%, 60,87% and 69,57% of the patients with EDS-HT reported pain at respectively the shank, ankle joint and the foot region can be linked with the altered kinematics and kinetics. As expected, patients described a higher intensity of pain at the lower limb and foot region, which increased non-significantly after testing. However, this consideration is clinical relevant as mean VAS-scores at the lower limb and foot raised at least with 10% after testing. Chronic pain and central sensitization can be both considered as causes of disability in EDS-HT and its severity determines the physical fitness level (Rombaut et al., 2010; Castori et al., 2013).

To better understand this impact of foot function and pain on ADL and quality of life, FFI and LEFS questionnaires were implemented. Patients with EDS-HT demonstrated total and domain scores corresponding to more pain, foot dysfunction, greater disability and a reduced quality of life due to foot pathology. An important consideration is that clinicians need to be aware of the potential aggravation of the foot dysfunctions and altered movements in real life as the vast majority of patients reported more difficulties when taking a walk on uneven ground.

Considering the altered movements, kinetics, pain and foot dysfunction in patients with EDS-HT, an appropriate rehabilitation program is relevant. Optimizing ankle strategy, strengthening muscles and increasing proprioception and balance would lead to a more stable and physiological way of walking (Cimolin et al., 2011; Galli et al., 2011; Rigoldi et al., 2012). Based on the results of this study, strengthening the tibialis anterior muscle seems a key component in the rehabilitation program. Due to its anatomical position, this muscle has the ability to stabilize the midfoot and medial forefoot, which in turn could result in increased foot function, less foot pain and anomalies on a structural level. Increasing calf muscle strength and endurance could improve kinematics and kinetics. Additionally, chronic pain management, improving physical fitness level and body weight unloading including an appropriate diet are necessary for effective treatment. Customized orthoses and correct, supportive footwear can alter dysfunctional movement patterns and ground reaction forces at different ankle and foot segments.

The present results must be viewed within the limitations of the study. First, the number of participants was rather moderate, which makes it hard to generalize conclusions. Secondly, a selection bias may have introduced as only EDS-HT patients with less foot pain and dysfunction might have been interested and participated in this study. Thirdly, some results need to be interpreted with caution. The fact that patients answered the questionnaires after testing could influence subjects' perception as mean VAS-scores were increased after the measurement. A final limitation concerns step pattern variability during three-dimensional gait analysis. However, the GFM model shows reproducible within subject data and enough sensitivity to display differences between subjects with no obvious deformity (De Mits et al., 2012). In this context, a recent study of Cimolin and Galli (2014) stated that three-dimensional gait analysis can be used to obtain crucial information for the determination of the level of functional limitation due to pathology.

As regards future prospects, the kinematic and kinetic data gathered in this study can be analysed via statistical parametric mapping (SPM). This statistical method allows a comprehensive curve analysis over the entire stance phase rather than five key moments as selected in this study (De Ridder et al., 2014). Furthermore, randomized controlled trials are necessary to develop more evidence-based recommendations about rehabilitation and its different components. In this context, electromyographic studies can be a valuable additive to extract muscle activation patterns during walking. Finally, further research could investigate the influence of shoes and different insoles on gait parameters in EDS-HT. In fact, only one study investigated spatio-temporal parameters while wearing shoes (Rombaut et al., 2011).

In conclusion, patients with EDS-HT demonstrate peculiar kinematics at the ankle and foot segments in the three planes during barefoot walking. Regarding kinetics, other ground reaction force patterns are found for the horizontal components. Finally, more foot dysfunction and pain is shown in these patients. Whether this impaired foot function and pain is the cause or the consequence of the altered kinematics and kinetics during gait, needs to be confirmed in future studies.

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Abstract (layman's terms)

Het hypermobiele type van het Ehler-Danlos Syndroom is een genetische aandoening, waarbij het bindweefsel in het lichaam is aangetast. De gewrichten van hypermobiele patiënten kunnen over een grotere bewegingsuitslag bewogen worden in vergelijking met de norm. Naast dit belangrijkste kenmerk hebben deze patiënten ook tal van andere symptomen van het bewegingsstelsel zoals spier- en gewrichtspijn. Deze klachten hebben een aanzienlijke impact op het dagelijks functioneren zoals stappen. Het doel van dit driedimensionale gangonderzoek was het analyseren van het gangpatroon met focus op de enkel en voet van deze studiegroep. Door te vergelijken met gezonde personen en gebruik te maken van technische apparatuur zoals infrarood camera's, krachten- en drukplatformen werden significante verschillen gevonden in de manier van stappen. De resultaten toonden aan dat deze patiënten tijdens de gang een afwijkende positie van de enkel en voet hebben, alsook meer problemen bij het afduwen. Verder werden via vragenlijsten de verdeling en intensiteit van pijn in het onderste lidmaat en de beperkingen in het dagelijkse leven bij deze patiënten in kaart gebracht, die duidelijk verhoogd aanwezig waren in de patiëntengroep. Op basis van deze conclusies kan een revalidatieprogramma geadviseerd worden met onder meer het optimaliseren van spierkracht.

Ethical committee

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Advies voor monocentrische studie met als titel:
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