Pituitary (2019) 22:373–380
https://doi.org/10.1007/s11102-019-00964-w

Assessment of static and dynamic plantar data of patients with acromegaly

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Published online: 25 April 2019

Abstract

Purpose To determine both static and dynamic plantar data of acromegalic subjects while barefoot.

Methods Seventy acromegalic patients and 48 age-, sex-, weight- and height-matched healthy controls were included. Plantar variables were measured using the footscan gait system. The data included the width and length of each foot, relative force distribution in each quadrant, mean force applied to each foot and maximum pressure while walking. Maximum pressure data were obtained from ten parts of the foot. Injury risk assessments of five different regions were performed. To analyze balance, center of pressure (CoP) measurements were performed. The patients with acromegaly were compared with the controls. Furthermore, a comparison of patients with active and controlled acromegaly was performed.

Results The foot was wider in acromegalic patients. The mean force on each foot was higher in cases of acromegaly (acromegaly: 1027 ± 180 N, control: 908 ± 180 N, p = 0.001). In the acromegalic individuals, the maximum pressure in the midfoot was higher, while the medial heel maximum pressure was lower (midfoot maximum pressure acromegaly: 11.3 ± 3.5 N/cm^2, control: 8.9 ± 3.7 N/cm^2, p = < 0.001). Injury risk was similar. CoP measurements elicited intact balance. In terms of static and dynamic plantar data, there was no difference between patients with active and controlled acromegaly.

Conclusions This is the first study to demonstrate that compared with healthy controls, patients with acromegaly experience great force on their feet while standing and high pressure in the midfoot during walking. Podiatric evaluation, custom molded orthotics and individualized rehabilitation programs for acromegalic patients may provide better force and pressure distribution throughout the foot and improve gait and skeletal symptoms.

Keywords Acromegaly · Footscan · Plantar pressure · Center of pressure

Introduction

Acromegaly is a chronic, progressive and systemic disorder caused by excess GH and IGF-1 [1]. Chronic exposure to high levels of GH and IGF-1 leads to systemic complications [2]. Despite biochemical control of the disease, some complications, such as musculoskeletal complications, continue to progress, cause debilitating symptoms and reducing quality of life [3–5].

A wide range of musculoskeletal complications accompany acromegaly [6]. Acromegalic arthropathy is the most frequent manifestation that affects both the perpendicular and appendicular skeleton. The involvement of the perpendicular skeleton may lead to deformities such as kyphosis, scoliosis and spondylolisthesis, which result in the displacement of the center of gravity towards anteroposterior or mediolateral directions. Regarding appendicular involvement, the weight-bearing joints of the lower extremity are primarily affected and eventually become deformed [7, 8]. Heel pad thickness is increased due to soft tissue growth. Muscle involvement is also quite common, and the presence of muscle hypertrophy with weakness is typical [9, 10]. Chronic bone and soft tissue enlargement may cause somatic disfigurement and gait alterations. Furthermore, the biomechanical changes observed in acromegaly alter posture and balance [11, 12]. The effects of these musculoskeletal alterations on static and dynamic plantar dynamics have not yet been studied. Hence, in this study, we aimed to measure both static and dynamic plantar variables of patients with acromegaly and analyze their balance patterns.

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Methods

Study population

The study was approved by the institutional non-interventional clinical research ethics board and performed in accordance with the ethical standards of the Helsinki Declaration and its later amendments. Informed consent was obtained from all individual participants included in the study. The study was designed as a cross-sectional case–control study. The participants included 48 healthy controls and 70 consecutive acromegalic patients without a past medical history of orthosis or prosthesis use; orthopedic surgery; neurological (including peripheral neuropathy), visual or vestibular disorders; and locomotor dysfunction. Patients who used medications that could alter balance were excluded. The clinical and demographic characteristics of patients were collected by medical chart review.

Assessment of serum GH and IGF-1 levels

All serum samples were collected in the early morning after a 12-h fasting period. Serum GH concentrations were analyzed by chemiluminescence (DPC; Immulite®, USA) with a limit of detection of 0.01 µg/L.

Serum IGF-1 levels were measured using an IRMA assay (Beckman Coulter®, USA). The analytical and functional sensitivity of the assay were 4.55 ng/mL and 9.26 ng/mL, respectively. The intra-assay variation was 5.6%, while the interassay variation was 8.3%. The IGF-1 index was calculated by dividing the serum IGF-1 value by the age and sex-specific upper limit of the reference range for IGF-1. The patients who had an IGF-1 index < 1 and a spot GH value < 1 µg/L or a suppressible GH were categorized as having controlled acromegaly [1].

Assessment of static and dynamic barefoot plantar variables

Static and dynamic plantar variables were measured using the footscan gait system with the individuals standing or walking on a special platform (RSscan International®, Belgium). The plate had 8192 sensors (arranged in a 128 × 64 matrix) and 975 × 325 mm^2 active surface area. The sensors had the ability to measure plantar pressure with a range of 1–127 N/cm^2. The data acquisition frequency was 200 Hz and the resolution was 10 bits. Dynamic barefoot plantar pressures were measured with individuals walking at their preferred walking speed. The measurements were repeated until a validated trial were recorded. A trial was considered validated if the participants made clear pedobarograph contact with good consistency.

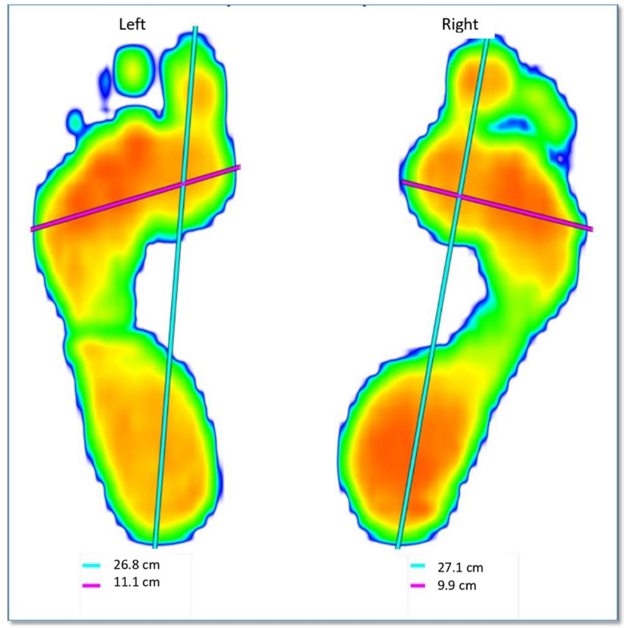

Fig. 1 Dimensions of each foot according to the footprint. The pink line indicates the width of the foot, and the blue line indicates the length of the foot

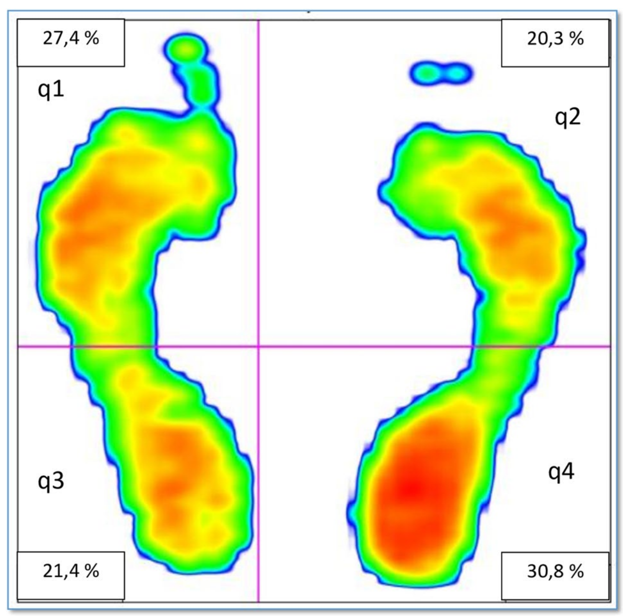

Fig. 2 Spread of the percentages of total force across the quadrants. q1—left foot anterior, q2—right foot anterior, q3—left foot posterior, q4—right foot posterior

The plantar pressure data included the width and length of each foot according to footprint size, as shown in Fig. 1; the relative force distribution in each quadrant, as shown in Fig. 2 (q1—left foot anterior, q2—right foot anterior, q3—left foot posterior, q4—right foot posterior); the mean force

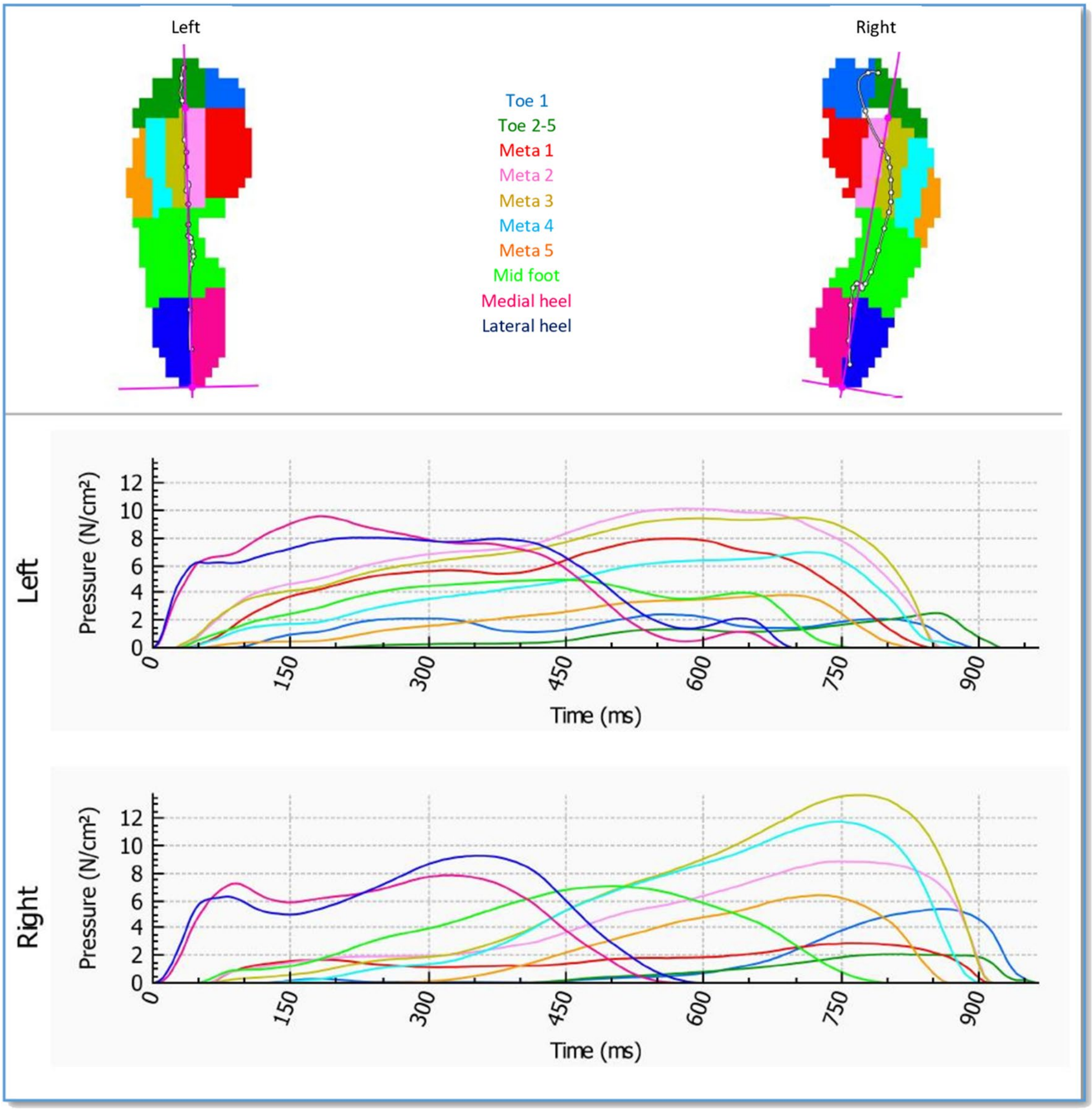

Fig. 3 Pressure per zone graphic. Each colored line indicates pressure changes during walking in a specific part of the foot. Light blue: toe 1, the hallux; dark green: toes 2–5, the second to fifth toes; red: meta 1, the first metatarsal head; pink: meta 2, the second metatarsal head; light brown: meta 3, the third metatarsal head; turquoise: meta 4, the fourth metatarsal head; orange: meta 5, the fifth metatarsal head; light green: midfoot; purple: medial heel, the medial portion of the heel; and dark blue: lateral heel, the lateral portion of the heel

applied to each foot; and the maximum pressure while walking. Maximum pressure data were obtained from ten parts of the foot (toe 1, the hallux; toes 2–5, the second to fifth toes; meta 1, the first metatarsal head; meta 2, the second metatarsal head; meta 3, the third metatarsal head; meta 4, the fourth metatarsal head; meta 5, the fifth metatarsal head; midfoot; medial heel, the medial portion of the heel; and lateral heel, the lateral portion of the heel) (Fig. 3). To describe the risk of overuse injuries such as medial-tibial stress syndrome, stress fractures, anterior knee pain, achilles tendinopathy, plantar fasciitis and to provide advice towards optimal orthoses based on individual dynamic plantar pressure measurements, injury risk assessment was carried out by grading (no risk, low risk, moderate risk, high risk) for five different regions of each foot (medial and lateral forefoot, medial midfoot, medial and lateral hindfoot) (Fig. 4). The footscan risk analysis was validated in a prospective study that aimed to identify the ability of footscan to predict the injury risk [13]. Furthermore, in another study, the effectiveness of the modular insoles which were manufactured based on the footscan injury risk analysis was proven [14]. To analyze balance, center of pressure (CoP) measurements were performed with each participant in an eyes open-feet apart state.

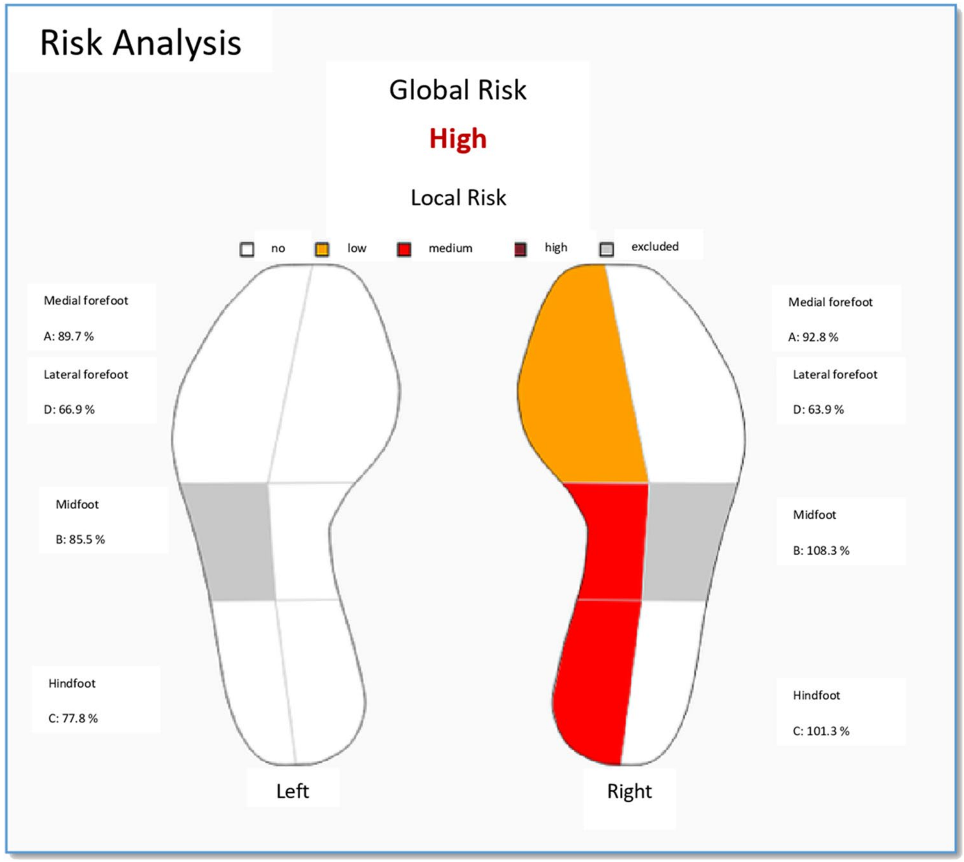

Fig. 4 Injury risk analysis. The risk analysis gives the global and local risk (lateral and medial forefoot, medial midfoot, lateral and medial hindfoot) for the feet in the dynamic measurement according to impulse measurements. The lateral midfoot risk was not calculated and is grayed out

Statistical analysis

Statistical analyses were performed using SPSS software version 21.0. The variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk's test) to determine whether they were normally distributed. Descriptive analyses are presented using means and standard deviations, median and interquartile range (IQR) or frequencies, where appropriate. The Chi square or Fisher's exact test, Mann–Whitney U test and Student's *t* test were used to compare groups. A value of $p < 0.05$ was considered significant. First, the right and left foot measurements were compared, and no significant difference was found. Hence, the final analyses were made using left foot measurements.

Results

There were no significant differences between the acromegalic patients (28 M/42 F, age: 48.1 ± 11.9) and the healthy controls (28 M/20 F, age: 45.0 ± 10.1) in terms of age, sex, height and weight. The median (IQR) disease duration of the acromegalic patients was 4.5 (2–10.5) years. While the median (IQR) GH level was 1.53 (0.52–3.34) μg/L, the median (IQR) serum IGF-1 level and IGF-1 index were 240 (156–393) ng/mL and 0.82 (0.53–1.50), respectively (Table 1).

The demographic and clinical characteristics of acromegalic individuals were further compared between the patients with active acromegaly and those with controlled acromegaly. The disease was active in 30 patients (43%). There was no significant difference between the subgroups of acromegaly patients in terms of age, sex, body height and weight. The median (IQR) disease duration of the subjects with controlled acromegaly was longer; active acromegaly 2.5 (2–7.5) years, controlled acromegaly 8 (2.5–12.5) years, $p = 0.035$. The median (IQR) GH levels were higher in the active acromegaly group; 3.47 (1.50–6.06) μg/L in the active group, 0.96 (0.25–1.73) μg/L in the controlled group, $p < 0.001$. While the median (IQR) IGF-1 level and IGF-1 index of the patients with controlled acromegaly were 167.5 (132–212) ng/mL and 0.58 (0.47–0.73), respectively, the median (IQR) serum IGF-1 level and IGF-1 index of the patients with active acromegaly were 442 (330–706) ng/mL and 1.62 (1.26–2.13), respectively; p values were < 0.001 for both (Table 1).

The acromegaly patients had a greater foot width than the control patients, but the groups did not differ in foot length (foot width acromegaly 10.7 ± 0.9 cm, control 10.3 ± 0.9 cm, $p = 0.033$). Both the acromegaly patients and the healthy controls had a high load on the posterior regions,

Table 1 Demographic and clinical characteristics of the patients with acromegaly and healthy controls

	Acromegaly n: 70	Healthy controls n: 48	p-value	Active acromegaly n: 30	Controlled acromegaly n: 40	p-value
Age (years)[a]	48.1 ± 11.9	45.0 ± 10.6	0.13	47.2 ± 10.6	49.0 ± 12.9	0.62
Sex M/F n (%)	28/42 (40/60)	28/20 (58/42)	0.08	12/18 (40/60)	16/24 (40/60)	1.00
Height (cm)[a]	164.8 ± 10.7	168.0 ± 11.3	0.12	165.9 ± 10.8	164.1 ± 10.7	0.49
Weight (kg)[a]	79.6 ± 11.4	78.2 ± 13.4	0.57	79.5 ± 11.2	79.6 ± 11.7	0.97
Disease duration (years)[b]	4.5 (2–10.5)	na		2.5 (2–7.5)	8 (2.5–12.5)	0.035
GH (μg/L)[b]	1.53 (0.52–3.34)	na		3.47 (1.50–6.06)	0.96 (0.25–1.73)	< 0.001
IGF-1 (ng/mL)[b]	240 (156-393)	na		442 (330–706)	167.5 (132–212)	< 0.001
IGF-1 index[b]	0.82 (0.5–1.5)	na		1.62 (1.26–2.13)	0.58 (0.47–0.73)	< 0.001

na not applicable

[a]Mean ± SD

[b]Median (IQR)

Table 2 The results of the static analyses

	Acromegaly n: 70 Mean ± SD	Healthy controls n: 48 Mean ± SD	p-value	Active acromegaly n: 30 Mean ± SD	Controlled acromegaly n: 40 Mean ± SD	p-value
Foot width (cm)	10.7 ± 0.9	10.3 ± 0.9	0.033	10.7 ± 0.8	10.7 ± 1.0	0.83
Foot length (cm)	26.8 ± 2.1	27.1 ± 1.8	0.44	27.1 ± 2.0	26.5 ± 2.1	0.23
Left foot anterior, q1 (%)	24.0 ± 5.4	23.1 ± 4.0	0.33	24.4 ± 4.5	23.7 ± 6.0	0.57
Right foot anterior, q2 (%)	22.8 ± 5.0	24.4 ± 4.3	0.07	22.5 ± 4.3	23.0 ± 5.5	0.72
Left foot posterior, q3 (%)	27.1 ± 6.0	25.0 ± 5.0	0.06	26.6 ± 5.3	27.4 ± 6.6	0.56
Right foot posterior, q4 (%)	26.2 ± 4.8	27.2 ± 4.6	0.26	26.5 ± 4.3	28.0 ± 5.2	0.65
Total anterior, q1 + q2 (%)	46.8 ± 7.9	47.6 ± 6.3	0.54	46.9 ± 7.1	46.7 ± 8.6	0.89
Total posterior, q3 + q4 (%)	53.2 ± 7.9	52.3 ± 6.4	0.44	53.1 ± 7.1	53.4 ± 8.6	0.87
Mean force for each foot (N)	1027 ± 180	908 ± 180	0.001	1041 ± 168	1016 ± 190	0.56

but no differences were noted between the groups in terms of relative force distribution. The mean force applied to the foot was greater in the acromegaly patients (acromegaly 1027 ± 180 N, control 908 ± 180 N, $p = 0.001$) (Table 2). There were no significant differences between the patients with active and controlled acromegaly in terms of static footscan parameters (Table 2).

Compared to the healthy controls, the acromegaly patients' midfoot maximum pressure during walking was higher (11.3 ± 3.5 N/cm^2 vs. 8.9 ± 3.7 N/cm^2, $p < 0.001$), and their medial heel maximum pressure was lower (18.5 ± 4.3 N/cm^2 vs. 20.2 ± 3.4 N/cm^2, $p = 0.017$) (Table 3). However, the dynamic plantar pressure values were similar for the patients with active and controlled acromegaly. Injury risk assessment revealed no difference between acromegalic individuals and healthy controls (Table 4). Injury risk was also similar for the subjects with active and controlled acromegaly. CoP results indicated no distinction between the groups for both cohorts (acromegaly vs. healthy controls and active acromegaly vs. controlled acromegaly) (Table 5).

Discussion

In this study, we investigated both the static and dynamic barefoot plantar pressure data of acromegalic subjects. Our study is the first to assess plantar pressure dynamics in patients with acromegaly. We demonstrated that plantar pressure dynamics change in acromegaly.

As expected, the foot width of the acromegaly patients was greater than that of the controls. Although there was no difference in body weight between the groups, the mean vertical force applied to each foot was greater in the patients with acromegaly. In the acromegaly patients, the alteration of the center of gravity towards the anterior direction may change the amount of force on the foot compared with controls, despite similar weight. Kyphosis, an increase in heel thickness, and deformations in weight-bearing joints may all cause the center of gravity to move anteriorly [11, 15, 16].

Table 3 The results of maximum pressure measurements during walking for ten different parts of the foot

	Acromegaly n: 70 Mean ± SD	Controls n: 48 Mean ± SD	p-value	Active acromegaly n: 30 Mean ± SD	Controlled acromegaly n: 40 Mean ± SD	p-value
Maximum pressure (N/cm^2)						
Toe 1	16.0 ± 6.0	16.5 ± 7.1	0.69	16.7 ± 9.1	14.3 ± 6.0	0.35
Toes 2–5[a]	5.9 ± 3.9	5.6 ± 2.8	0.16	6.0 ± 4.2	5.3 ± 3.5	0.56
Metatarsal 1[a]	15.7 ± 6.0	15.0 ± 5.3	0.76	17.4 ± 6.1	16.1 ± 6.5	0.24
Metatarsal 2[a]	20.9 ± 6.2	20.0 ± 3.7	0.87	22.3 ± 4.4	21.2 ± 6.5	0.14
Metatarsal 3	21.6 ± 5.4	21.0 ± 4.5	0.46	21.4 ± 4.4	21.6 ± 5.6	0.83
Metatarsal 4[a]	17.9 ± 5.8	17.8 ± 5.9	0.71	17.4 ± 4.5	18.1 ± 6.4	0.78
Metatarsal 5[a]	13.5 ± 6.3	14.5 ± 6.4	0.89	13.0 ± 5.2	13.3 ± 5.3	0.79
Midfoot	11.3 ± 3.5	8.9 ± 3.7	< 0.001	10.5 ± 3.4	11.9 ± 3.5	0.11
Medial heel	18.5 ± 4.3	20.2 ± 3.4	0.017	20.2 ± 5.2	18.8 ± 4.2	0.21
Lateral heel	18.2 ± 4.3	18.9 ± 3.4	0.40	19.2 ± 4.5	18.6 ± 4.1	0.57

[a]These parameters were not normally distributed

Table 4 Injury risk assessment for five different foot regions

	Acromegaly n: 70 n (%)	Controls n: 48 n (%)	p-value
Medial forefoot			0.36
No risk	69 (98.6)	46 (95.8)	
Low risk	0 (0)	1 (2.1)	
Medium risk	1 (1.4)	1 (2.1)	
High risk	0 (0)	0 (0)	
Lateral forefoot			0.50
No risk	38 (54.3)	29 (60.4)	
Low risk	25 (35.7)	15 (31.2)	
Medium risk	5 (7.1)	4 (8.3)	
High risk	2 (2.9)	0 (0)	
Medial midfoot			0.50
No risk	63 (90.0)	45 (93.8)	
Low risk	6 (8.6)	3 (6.2)	
Medium risk	1 (1.4)	0 (0)	
High risk	0 (0)	0 (0)	
Medial hindfoot			0.20
No risk	45 (64.3)	37 (77.1)	
Low risk	20 (28.6)	10 (20.8)	
Medium risk	3 (4.3)	1 (2.1)	
High risk	2 (2.9)	0 (0)	
Lateral hindfoot			0.41
No risk	69 (98.6)	48 (100)	
Low risk	0 (0)	0 (0)	
Medium risk	1 (1.4)	0 (0)	
High risk	0 (0)	0 (0)	

Maximum pressure measurements of ten different regions of the foot revealed that acromegaly patients have a great deal of pressure on the midfoot area and less pressure on the medial heel area during walking when compared with healthy controls. Consistent with the previous finding of our study, the anterior displacement of the center of gravity may lead to these alterations. Furthermore, soft tissue enlargement in the midfoot region may also contribute to these findings.

Injury risk evaluation elicited no differences among groups. Injury risk is a function of multiple relevant parameters such as applied pressure and the contact time of the particular foot region during walking (pressure × time: impulse) [17]. The putative reduction of contact time of the midfoot area may explain this result.

Earlier reports have shown that acromegaly patients have balance instability. In their work in 2014, Lopes et al. evaluated 28 subjects with acromegaly (mean age 52) via a force platform system to quantify body balance. They assessed the balance of acromegalic subjects both in eyes open-feet apart and eyes closed-feet together states and they found that the individuals with acromegaly had balance instability towards the anteroposterior and mediolateral directions in eyes open-feet apart state [11]. In 2016, the same group examined 17 elderly subjects with acromegaly (median age 67) and demonstrated that they had lateral instability both in eyes open-feet apart and eyes closed-feet together states. Moreover, individuals with acromegaly had an increased risk of falls [12]. In our study we analyzed balance of acromegalic subjects only in eyes open-feet apart state and contrary to previous studies, we found no difference among groups in terms of CoP dynamics. The absence of any difference in CoP measurements in our study indicates that the patients' balance control was not affected. Our study cohort comprised relatively younger patients (by approximately 4 years) compared to previous studies. Considering the progressive nature of acromegalic arthropathy, balance problems could become more pronounced at advanced ages. In addition,

Table 5 Displacement statistics of the center of pressure with the participant in an eyes open-feet apart position

	Acromegaly n: 70 Median (IQR)	Controls n: 48 Median (IQR)	p-value	Active acromegaly n: 30 Median (IQR)	Controlled acromegaly n: 40 Median (IQR)	p-value
CoP traveled distance (mm)	94 (65–139)	89 (72–121)	0.70	85.5 (62–133)	96.5 (72–146)	0.38
CoP ellipse area (mm^2)	7 (3–15)	8 (4–16)	0.50	7 (3–11)	8 (3.5–17.6)	0.38
Average CoP displacement on X axis (mm)	− 4 (− 7/− 1)	− 4 (− 7/− 2)	0.40	− 4.5 (− 7/− 2)	− 3 (− 7/− 1)	0.21
Average CoP displacement on Y axis (mm)	2 (0–4)	3 (0–5)	0.55	2 (1–4)	2 (0–4)	0.51

CoP Center of pressure

disease duration could be an independent determinant of balance disorders in acromegaly. The median disease duration of the patients in previous studies has not been reported, so a comparison could not be made.

The other unique feature of our study is that we compared static and dynamic plantar pressure variables with balance in individuals with active and controlled acromegaly. Our results showed that there was no difference between active and controlled acromegaly patients in terms of static, dynamic and balance parameters. Considering the progressive nature of acromegalic arthropathy (despite disease control), it can be said that rather than disease activity, exposure to high GH and IGF-1 and chronic musculoskeletal alterations are the determinants of plantar pressure changes.

There were several strengths and limitations of our study. When compared to the previous studies which were conducted to assess static and dynamic plantar pressures of acromegalic individuals, our study cohort was larger. In our study, the control group was relatively smaller. Therefore, acromegalic individuals may be oversampled. However, measuring an index foot for final analysis (left foot), made the conclusions of our study less biased. Exclusion of acromegalic individuals who had diseases that may alter static and dynamic plantar pressure measurement such as peripheral neuropathy or who had a history of any drug use that may affect postural control was another strength of the study. We did not evaluate the foot types of the participants which could be another determinant of pressure distribution.

Conclusion

The force on the foot and the barefoot plantar pressures are altered in patients with acromegaly. The contribution of these changes to musculoskeletal symptoms and quality of life remains to be established. Custom molded orthotics and individualized rehabilitation programs based on footscan analyses may provide better pressure distribution throughout the foot and improve gait and skeletal symptoms. Further studies will address these questions.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The study was approved by the institutional noninterventional clinical research ethics board with project no: GO 17/846 and was performed in accordance with the ethical standards of the Helsinki Declaration and its later amendments. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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