Journal of Musculoskeletal and Neuronal Interactions JMNI

Original Article

Correlation of muscle and bone parameters, daily function and participation in women with generalized joint hypermobility: a descriptive evaluation

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Abstract

Objectives: Generalized joint hypermobility (GJH) has a prevalence in women of 15% to 35%. GJH may lead to impaired movement control, frequent sprains or subluxations and pain, and can be associated with early osteoarthritis or chronic fatigue. Aim of this project was to analyse muscle strength, muscle cross-sectional area (mCSA) and daily function in women with GJH and to analyse correlations between these measurements. **Methods**: Descriptive cross-sectional study of women with GJH, defined by Beighton score ≥6/9. Assessments included muscle strength, mCSA by peripheral Quantitative Computed Tomography (pQCT), stair climbing, as well as two questionnaires. Spearman's correlations between parameters were calculated. **Results**: 51 women with a mean age of 26.5 years participated, whereof 18 (35%) had a Beighton score of 9/9 and 17 (33%) attained 8/9. Internal correlations between strength measurements were high, whereas pQCT parameters were less correlated. Strength was moderately correlated with mCSA, while correlations with stair climbing and SF-36 were not significant. **Conclusions**: This study provides insight into the muscle and bone properties of women with GJH. Only slight differences were seen compared to normative values. Correlations between various dimensions were middle or low, indicating the complex relationship between strength, muscle properties and function.

Keywords: Beighton Score, Disability, Muscle Cross-Sectional-Area, Muscle Strength, Stair Climbing

Introduction

Joint hypermobility is a condition with increased range of motion in a joint compared to the general population, taking into account gender, age and ethnicity[1]. When several joints are affected it is called Generalised Joint Hypermobility (GJH), which is diagnosed by the Beighton score, measuring fingers, thumbs, elbows, knees and spine[2]. This GJH is mainly a characteristic of a person and not a clinical diagnosis. Notably women are significantly more likely to have GJH, with reported prevalence between 15% and 35%[3-6].

GJH is associated with different clinical presentations with variations in terms of severity, duration, and localisation of symptoms. Possible short-term effects of a hypermobile joint include difficulties with movement control, frequent sprains or subluxations or painful inflammation of tendons or ligaments. In the long term or when occurring recurrently, such symptoms may lead to joint damage, early osteoarthritis, chronic pain or fibromyalgia[7-9]. Experiencing symptoms due to GJH may also result in avoidance of physical activity and thus lead to deconditioning and fear of movement, with consequent loss of work ability, social withdrawal and restrictions in leisure time activities[10,11]. Several other issues

The authors have no conflict of interest.

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Edited by: G. Lyritis
Accepted 23 August 2021

may arise in association with GJH, namely skin problems, delayed wound healing, problems with blood vessels or the heart, neurological disorders, chronic fatigue or dizziness[12,13].

Up until 2017, these general symptoms were documented by means of the Brighton criteria and, if fulfilled, a Joint Hypermobility Syndrome (JHS) was diagnosed[14]. In parallel, the Ehlers-Danlos Syndromes (EDS), a group of hereditary connective tissue disorders, included the hypermobility type (or type III), which was often discussed as if it was the same as JHS[15,16]. At an expert conference new diagnostic criteria were developed and published in 2017[8,17]. Persons with GJH and fulfilling several criteria are now diagnosed with hypermobile EDS and all those who do not meet the criteria can be diagnosed with Hypermobility Spectrum Disorder (HSD). The term GJH is still used and refers to the characteristic of being generally hypermobile. Which and how many symptoms a person must have in order to be diagnosed with HSD has not been definitively clarified[8,18].

As described, joint hypermobility primarily affects the structural level of the body. Ligaments may be more flexible, tendons more elastic, muscles may be weaker or joint proprioception may be impaired[6,19,20]. According to the International Classification of Functioning (ICF) model on disease and disability, structural changes affect several levels, such as function, activities and participation[21]. For example, a problem with the stabilisation of the knee joint may cause pain when going down stairs and thus reduce stair capacity. Over time, this might lead to an avoidance of stair climbing, which then has a negative effect on physical condition or causes a person not to visit certain places.

Several studies were published about the physiological and biomechanical characteristics of people with GJH, but little is known about its impact on various tissues and possible interactions with different body systems. One study reported reduced muscle strength in persons with GJH[6], while others found values comparable to those in healthy controls[22,23]. Changes in movement control during walking were described[24,25] as well as higher moments and loads on the joints[26]. In a comprehensive review of 2016[12], the limitations and symptoms of various forms of hypermobility were investigated. For pain, fatigue, activity limitations and depression and anxiety, it was shown that persons with GJH were less affected than those with JHS or EDS, but still showed clear and significant differences compared to healthy persons. Finally, it was recently reported that people with JHS have lower values for various bone parameters and a reduced cross-sectional area of the lower leg muscles[27].

So far, to the knowledge of the authors, no research has been published looking at correlations between muscle and bone parameters in persons with GJH. There are some other studies in this area, in which the majority have studied athletes or healthy individuals. In general, fairly low correlations were found between muscle strength and cross-sectional area. As early as 1983 Maughan et al.[28] published a correlation of 0.51 for women for isometric maximum strength and muscle area measured by computer tomography for the knee extensors. In 2003 Gür et al.[29] found correlations of between 0.68 and 0.78 for the quadriceps and the cross-sectional area in women with knee osteoarthritis. In a brief review, Jones et al. in 2008[30] also pointed out that the correlation between force and muscle cross section is complex and that, in most studies, not very high correlations were found. Thus, a mean correlation in the range of 0.5 was also expected for persons with GJH for the relationship between thigh strength and muscle cross-sectional area.

The primary aim of this descriptive cross-sectional study was therefore twofold: To analyse and describe muscle strength, muscle cross-sectional area and stair climbing as a functional activity in a group of individuals with GJH and to analyse the correlations between the different parameters. In addition, in the sense of a subgroup analysis, we investigated whether there were differences in the above parameters between persons who fulfil the criteria for JHS and those who did not.

Materials and Methods

Study design

A descriptive cross-sectional analysis of various measurements in women with GJH was performed using the baseline data of a randomised controlled trial, of which the results have been presented elsewhere[31]. No external funding was received, and ethical approval was obtained by the Ethics Committee of Canton Bern, Switzerland. All participants gave written informed consent before testing.

Participants

Included in the study were women between 20 and 40 years with GJH, meaning a Beighton score of at least 6/9 points[3,32]. The BMI had to be in a range between 18-30 kg/m^2 and they had to be able to understand the German questionnaires used in the project. A formal diagnosis of GJH or JHS was not necessary.

Excluded were women who had had surgery of the lower extremities or lumbar spine in the last two years and women doing more than four hours per week of regular intense sports. Additionally, women who were pregnant or less than one year after delivery were excluded. Finally, women with a known diagnosis of a genetic disease of the connective tissue, mainly Marfan syndrome, EDS other than the hypermobility type and Osteogenesis imperfecta, were also excluded.

Inclusion and subgrouping

Participants were recruited from those in previous studies as well as from the staff of Bern University Hospital and the student body of the Bern University of Applied Science, Health Department, Switzerland. Interested participants were informed by phone and in print before the first appointment. After signing the informed consent, inclusion and exclusion criteria were checked face-to-face by one physiotherapist (CM) with more than 12 years clinical experience. For the Beighton score the test movements were: a) hyperextension of elbow

more than 10°, b) hyperextension of knee more than 10°, c) ability to touch the floor with the palms of the hands, keeping the knees fully extended, d) at least 90° dorsiflexion of 5th metacarpophalangeal joint, and e) ability to touch the inner side of the forearm with the thumb[2]. All items, except c), were tested bilaterally, resulting in a possible total score of 9 points.

Additional measurements at inclusion incorporated body weight, body height, arm span, and arm and leg length, as well as knee flexion and extension and hip internal and external rotation. Anamnestic checking of the Brighton criteria[14] was done by semi-structured interview by the same experienced physiotherapist (CM). The major Brighton criteria were: a) Beighton score of 4/9 or more (as checked and already fulfilled when included in the study) and b) arthralgia for longer than 3 months in 4 or more joints. The minor criteria included: a) arthralgia in one to three joints or back pain (>3 months), spondylosis, spondylolysis/spondylolisthesis, b) dislocation/subluxation in more than one joint, or in one joint on more than one occasion, c) soft tissue rheumatism with >3 lesions, d) Marfanoid habitus, e) abnormal skin: striae, hyperextensibility, thin skin, f) eye signs, and g) varicose veins or hernia or uterine/rectal prolapse. Participants were rated as having JHS when both major criteria or one major and two minor criteria were fulfilled. The Brighton criteria of all participants were recorded for subgrouping and to analyse differences between women with or without JHS. Note, that this study was conducted between October 2013 and November 2015 and thus the 2017 diagnostic criteria where not yet in place. Hence, throughout this article the term JHS is used for women fulfilling the Brighton criteria.

Assessments

GJH may affect an individual in several dimensions of life, like body functions, body structures, activities and participation, as defined in the International Classification of Functioning, Disability and Health (ICF)[21]. The assessments used in this study aimed to analyse the women with GJH in several dimensions of the ICF: muscle strength and muscle and bone properties as body structures; muscle activity and forces during stair climbing in terms of function and the SF-36 as general measure of activity and participation. All assessments were performed on one day, first the strength testing and stair climbing analysis, followed by the pQCT measurement and the questionnaires.

Peripheral quantitative computed tomography (pQCT)

Using a Stratec XCT 3000 scanner (Stratec Medizintechnik), the muscle and bone properties of the thigh at 33% above the knee joint and the lower leg at 33% below the knee joint were measured using standard protocols. At each site the total cross-sectional area (CSA) was calculated, as well as the respective values for muscle cross-sectional area (mCSA), bone cross-sectional area (bCSA) and fat cross-sectional area (fCSA). Additionally, muscle and bone mass (mMass and bMass) and density (mDens and bDens) were determined; all parameters as previously described[33,34]. All calculations were done with the integrated software of the device.

Muscle strength

The maximum isometric strength (MVC) and the rate of force development (RFD) were measured for the right knee extensors and flexors while sitting on a custom-built strength measurement table with a one-dimensional strain gauge (KM 1500S; Megatron) calibrated in Newton (N). The participant sat on the table with the knee and hip in 90° flexion with a sling attached above the ankle was connected to the force transducer. Study participants were then asked to pull forward respectively backwards as fast and as strong as possible and to hold the highest possible force for five seconds. After familiarization and two test trials, three measuring trials were performed at intervals of 30 s.

The MVC was calculated as the maximal force in Newton and the RFD as the slope of the force curve between 20% and 80% of MVC in Newton/second and the highest value of three trials was used. Beside the values for knee extensors and knee flexors the sum of both MVC's was calculated, as well as the ratio of MVC/mCSA for extensors and flexors and the sum MVC.

Electromyography (EMG)

The muscle activity of vastus medialis (VM) and vastus lateralis (VL) and semitendinosus (ST) and biceps femoris (BF) of the right leg was measured using surface EMG. Electrode placement and measurement procedure were defined according to the recommendations of SENIAM[35]. After marking the electrode positions and skin preparation two pre-gelled AgCl-electrodes (Ambu Blue Sensor N, Ambu A/S) of 5 mm diameter were placed in parallel 2 cm apart. Additionally, a reference electrode was placed laterally over the femoral condyle. Skin impedance for each pair of electrodes had to be below 5 kΩ. All electrodes were connected by cable via pre-amplifiers (baseline noise <1uV RMS, input impedance >100MΩ, common mode rejection ratio >100dB, input range of +/- 10mV, base gain of 500, 10-500Hz bandpass filter) to a small telemetry box (TeleMyo 2400T G2, Noraxon) on the participant's back. From there the signals were transmitted to the receiver (TeleMyo 2400R G2, Noraxon) and recorded at a sampling rate of 1000 Hz using a 12-bit analog-digital converter (Meilhaus ME-2600i, SisNova Engineering) and the software package "ads" (version 1.12, uk-labs).

Stair climbing

To measure ground reaction forces (GRF) and EMG during stair climbing a custom-built wooden six-step stair was used (riser height 17.9 cm, tread 29 cm, inclination 30.4°, according to Stacoff et al.[36]), with a handrail on both sides and a platform of 1m length to allow comfortable turning. GRF were measured using two force plates (Type 9286BA, Kistler) that were embedded in the 3rd and 4th step of the stair and supported by an independent steel frame. The force signals

were transmitted via a custom-built amplifier (uk-labs) to the recording computer. To determine the second foot contact of the stride, which was not measured with a force plate, a tri-axial accelerometer (Model 317A, Noraxon) was attached to the right malleolus and connected to the EMG telemetry system described above. All signals were then recorded in sync and registered in the software package "ads" (version 1.12, uk-labs). The participants had to climb up and down the stair barefoot ten times at a comfortable self-selected speed without using the handrail.

Data Processing of EMG and GRF

All data was processed using a custom-made MATLAB toolbox (The MathWorks) in accordance with previously described algorithms[37]. All measurements were visually inspected and six trials selected for analysis of stair ascent and descent in accordance with existing recommendations[38]. The EMG of the MVC measurements was used for normalization, calculated by RMS over 500 ms and using the highest value out of three trials. Dynamic EMG data was baseline corrected, full rectified and normalized to the corresponding 100% MVC value and linear envelopes built by lowpass-filtering (second-order Butterworth, cutoff 20 Hz)[39]. Peak muscle activation during stance was calculated from the linear envelope.

The vertical force-time curves were lowpass filtered (second-order Butterworth, cutoff 30 Hz), normalized to body mass and parameterized according to the previously described method[36]. Foot contact and foot off were defined as the time points when the vertical force exceeded or fell below 3% of the subject's body mass, respectively. Foot contact at the end of the stride was determined by visual analysis of the raw accelerometer signal. The maximum force-peak during weight acceptance (Fmax) was calculated as well as the respective time after foot contact (t to Fmax), the slope of the force curve during the loading phase (loading rate, LR), and the contact time. For all parameters, the mean value from six trials for each subject and condition was calculated.

Medical Outcomes Study Short Form 36-Item (SF-36)

The SF-36 is a widely used multi-item generic health survey intended to measure "general health", which is available in German. The psychometric properties are good and well documented, and there exist normative values for many patient groups, including some in the field of rheumatology[40]. The questionnaire is self-administered and takes about 10 minutes to complete. The SF-36 scores were calculated according to the standard method described[40], resulting in scores between 0-100 for eight dimensions, with higher values indicating better health-related quality of life. Additionally, the physical and psychological sum scores were calculated.

Hypermobility Questionnaire (HM-Q)

Since at the time of the measurements no specific assessment for joint hyper mobility and related disabilities was available, a own face-validated questionnaire was used to record the pain and restrictions in daily life experienced by the participants. The questionnaire consisted of 28 items, of which 16 targeted pain in different body regions, and 12 asked about disability in daily activities like bending, stair climbing, sitting for more than one hour or carrying loads. A sum score was calculated and scaled between 20 and 100 with lower values indicating better health. The activities in the questionnaire were chosen based on the most frequently mentioned problem situations identified in a previous cross-sectional study[41].

Statistical analysis

For all parameters descriptive statistics are presented with mean and standard deviation or median and interquartile range, for the whole group and for the subgroups, respectively. For group comparison the mean differences are reported as absolute values and in percent and the 95% confidence interval (CI) is given. Differences between groups were tested for significance with Mann-Whitney U test since normal distribution, as checked with the Levene-test, was not given for most parameters. Significance level was set at $p \leq 0.05$, despite multiple testing, because of the exploratory nature of this analysis. Additionally, based on the resulting effect sizes between the subgroups, sample size considerations for future studies were done with calculations using G*Power Version 3.1.9.6[42].

In a first step the self-correlations of the parameters of each measurement were calculated using the Spearman rank test and the correlation matrix plotted. Parameters with high internal correlation, indicated by Spearman's $\rho \geq 0.8$, were discarded and then the correlations between measurements were calculated for selected parameters. Correlations were flagged as highly significant at $p \leq 0.005$ and as significant when $p \leq 0.05$. All statistics were calculated using the software JAMOVI (The JAMOVI project, Version 1.1.9.0).

Results

Participants

A total of 51 women with a mean age of 26.5 (sd 4.5) years participated in this study (Table 1). According to the Brighton criteria 22 of them were classified as having JHS, whereas 29 did not fulfill the Brighton criteria and were labelled as GJH. No differences between these groups were found in terms of age, weight and height, nor for mobility of the knee and hip or the Beighton score. Note that 18 women (35%) had a Beighton score of 9/9, 17 (33%); attained 8/9 points and the rest had 6 or 7 points on the 9-point scale.

Descriptive comparison between JHS and GJH

Regarding strength measurements (Table 2) the values for persons with JHS were often lower than those for persons with GJH, however only the MVC of the knee flexors showed a significant difference between these two

Table 1. Descriptive characteristics of participants as mean±standard deviation (sd).

	All (n=51) mean±sd	GJH (n=29) mean±sd	JHS (n=22) mean sd	Mann-Whitney-U p
Age (years)	26.5±4.5	26.4±4.1	26.7±5.0	0.962
Height (m)	1.68±0.06	1.68±0.06	1.68±.05	0.917
Weight (kg)	62.6±10.1	62.3±10.4	62.9±10.0	0.864
BMI (kg/m²)	22.1±2.8	22.1±2.8	22.1±2.9	1.000
Right knee flexion (°)	152±6	153±6	152±6	0.613
Right knee extension (°)	12±2	13±2	12±2	0.379
Left knee flexion (°)	152±7	151±7	152±7	0.350
Left knee extension (°)	12±3	12±3	12±2	0.690
Right hip internal rotation (°)	49±10	49±12	50±9	0.924
Right hip external rotation (°)	44±9	46±9	42±8	0.210
Left hip internal rotation (°)	47±10	47±12	47±8	0.893
Left hip external rotation (°)	44±9	43±9	44±9	0.572
Beighton score 6	6 (12)	4 (13)	2 (9)	χ^2
n (%) 7	10 (20)	5 (17)	5 (23)	p = 0.848
8	17 (33)	10 (35)	7 (32)	
9	18 (35)	10(35)	8 (36)	

GJH = Generalized Joint Hypermobility, JHS = Joint Hypermobility Syndrome.

Table 2. Descriptive comparison of muscle strength measurements as mean±standard deviation (sd).

		All (n=51) mean±sd	GJH (n=29) mean±sd	JHS (n=22) mean±sd	Mann-Whitney-U p	Mean diff.	Mean diff. %	95% CI	
								Lower	Upper
MVC knee extensors	N	358±100	365±99	347±103	0.340	-18	-5.0	-76	39
RFD knee extensors	N/s	1564±858	1637±890	1469±823	0.515	-168	-10.3	-568	322
MVC knee flexors	N	185±75	205±68	159±79	**0.029**	-46	-22.3	-87	-4
RFD Knee flexors	N/s	702±723	817±888	551±389	0.411	-266	-32.6	-674	142
MVC knee sum	N	543±163	570±158	506±165	0.447	-64	-11.2	-135	27
RFD knee sum	N/s	2266±1374	2454±1541	2020±1102	0.175	-434	-17.7	-1213	344
MVC/bm knee extensors	N/bm	0.58±0.16	0.59±0.14	0.57±.018	0.291	-0.02	-4.0	-0.11	0.07
RFD/bm knee extensors	N/s/bm	2.38±1.26	2.43±1.22	2.32±1.34	0.704	-0.12	-4.8	-0.84	0.61
MVC/bm knee flexors	N/bm	0.30±0.13	0.33±0.10	0.27±0.15	0.060	-0.06	-18.6	-0.13	0.01
RFD/bm Knee flexors	N/s/bm	1.07±0.87	1.16±0.95	0.95±0.75	0.390	-0.21	-18.0	-0.70	0.29
MVC ext/ mCSA thigh	N/cm²	4.46±1.08	4.55±1.03	4.34±1.15	0.411	-0.21	-4.6	-0.83	0.40
MVC flex/ mCSA thigh	N/cm²	2.32±0.91	2.55±0.74	2.02±1.03	**0.024**	-0.53	-21.0	-1.03	-0.04
MVC sum/ mCSA thigh	N/cm²	6.79±1.81	7.11±1.64	6.36±1.96	0.128	-0.74	-10.5	-1.76	0.27

GJH = Generalized Joint Hypermobility, JHS = Joint Hypermobility Syndrome, diff = difference, CI = Confidence Interval, MVC = Maximum Voluntary Contraction, RFD = Rate of Force Development, bm = body mass, mCSA = muscle Cross-Sectional Area. Significant differences between groups (p>O.O5) are in bold.

groups. For all parameters high standard deviations were observed, ranging between a third and half of the mean values, which also resulted in wide confidence intervals for group differences, mainly crossing the zero line. An additional significant decrease for persons with JHS was seen in the ratio of knee flexor strength to the muscle CSA of the thigh.

For the tissue properties of thigh and shank, as measured by pQCT (Table 3), no significant differences were found, as indicated additionally by the 95% confidence intervals of the

Table 3. Descriptive comparison of tissue properties as measured by pQCT as mean±standard deviation (sd).

		All (n=51) mean±sd	GJH (n=29) mean±sd	JHS (n=22) mean±sd	Mann-Whitney-U	Mean diff.	Mean diff. %	95% CI	
								Lower	Upper
Parameters for thigh									
Total CSA	cm^2	150.9±28.4	151.8±29.7	149.8±27.2	0.903	-1.9	-1.3	-18.2	14.4
mCSA	cm^2	79.9±10.9	80.0±11.3	80.0±10.7	0.903	0.04	0.1	-6.2	6.3
Bone CSA	cm^2	6.0±0.8	6.0±0.8	6.1±0.8	0.419	0.1	1.7	-0.4	0.6
Fat CSA	cm^2	63.4±23.1	64.2±24.2	62.2±22.0	0.932	-2.1	-3.2	-15.3	11.2
mCSA/bm	mm^2/bm	13.1±1.8	13.1±1.9	13.1±1.8	0.827	-0.0	-0.2	-1.1	1.0
Muscle mass	mg	645±92	647±95	644±91	0.977	-3	-0.5	-56	50
Bone mass	mg	400±44	401±43	400±47	0.676	-1	-0.3	-26	24
mDensity	mg/cm^3	80.6±1.7	80.8±1.8	80.4±1.6	0.962	-0.5	-0.6	-1.4	0.5
Bone density	mg/cm^3	673±70	679±68	665±75	0.515	-14	-2.1	-54	26
Parameters for shank									
Total CSA	cm^2	102.3±16.7	102.6±16.4	101.7±17.4	0.658	-0.9	-0.9	-10.5	8.7
Muscle CSA	cm^2	69.7±10.6	69.0±9.5	70.5±12.1	0.770	1.4	2.1	-4.7	7.5
Bone CSA	cm^2	5.7±0.7	5.7±0.7	5.7±0.7	0.655	-3	-0.5	-0.4	0.4
Fat CSA	cm^2	25.6±10.1	26.6±11.6	24.3±7.9	0.917	-2.3	-8.6	-8.1	3.5
MCSA/bm	mm^2/bm	11.4±1.6	11.3±1.7	11.4±1.6	0.962	0.1	1.2	-0.8	1.1
Muscle mass	mg	564±86	560±77	568±98	0.917	8	1.4	-41	57
Bone mass	mg	458±53	459±55	456±51	0.962	-3	-0.7	-33	27
mDensity	mg/cm^3	81.0±1.6	81.2±1.7	80.7±1.4	0.517	-0.5	-0.6	-1.4	0.4
Bone density	mg/cm^3	808±54	808±46	808±64	0.970	-0	0.1	-30	31

pQCT = Peripheral Quantitative Computer Tomgraphy, GJH = Generalized Joint Hypermobility, JHS = Joint Hypermobility Syndrome, diff = difference, CI = Confidence Interval, CSA = Cross-sectional area, mCSA = muscle cross-sectional area, mDensity = Muscle density, bm = body mass.

Table 4. Descriptive comparison of stair climbing as a functional activity. Parameters of ground reaction force and electromyography as mean±standard deviation (sd).

		All (n=51) mean±sd	GJH (n=29) mean±sd	JHS (n=22) mean±sd	Mann-Whitney-U p	Mean diff.	Mean diff. %	95% CI	
								Lower	Upper
t to Fmax up	ms	0.203±0.030	0.209±0.031	0.196±0.029	0.117	-0.013	-6.2	-0.030	0.004
Fmax/bm up	%bm	109.0±6.3	108.0±5.6	110.0±7.1	0.332	2.1	1.9	-1.5	5.6
Loading rate up	%bm/s	118.0±42.2	114.0±46.8	123.0±35.7	0.189	8.9	7.8	-15.2	33.0
Contact time up	ms	0.750±0.088	0.774±0.084	0.719±0.084	**0.015**	-0.056	-7.2	-0.103	-0.008
t to Fmax down	ms	0.164±0.022	0.163±0.023	0.166±0.020	0.304	0.003	2.1	-0.009	0.016
Fmax/bm down	%bm	141.0±13.2	143.0±12.8	138.0±13.4	0.140	-5.0	-3.5	-12.4	2.5
Loading rate down	%bm/s	162.0±46.6	162.0±44.4	161.0±50.4	0.947	-0.9	-0.6	-27.7	25.8
Contact time down	ms	0.717±0.094	0.741±0.088	0.685±0.095	**0.032**	-0.056	-7.6	-0.108	-0.004
Biceps femoris max up	%MVC	13.6±14.8	9.1±5.4	18.9±20.0	**0.026**	9.7	106.5	1.5	17.9
Semitendinosus max up	%MVC	15.8±13.8	13.1±9.2	19.0±17.6	0.355	5.9	45.4	-1.9	13.8
Vastus lateralis max up	%MVC	40.2±21.7	35.0±17.0	47.2±25.5	0.074	12.3	35.0	-0.1	24.5
Vastus medialis max up	%MVC	40.5±26.1	37.3±28.3	45.0±22.6	0.099	7.7	20.6	-7.3	22.7
Biceps femoris max down	%MVC	7.4±8.8	5.9±4.2	9.3±12.1	0.576	3.4	58.1	-1.7	8.5
Semitendinosus max down	%MVC	9.5±10.7	8.3±9.1	11.1±12.4	0.912	2.8	34.2	-3.4	9.0
Vastus lateralis max down	%MVC	22.6±14.0	21.3±15.8	24.5±11.3	0.095	3.2	15.2	-4.9	11.3
Vastus medialis max down	%MVC	22.9±14.0	21.1±15.3	25.2±11.8	0.087	4.1	19.3	-4.0	12.1

GJH = Generalized Joint Hypermobility, JHS = Joint Hypermobility Syndrome, diff = difference, CI = Confidence Interval, Fmax = maximum force peak during weight acceptance. Significant differences between groups (p>0.05) are in bold.

Table 5. Descriptive comparison of general health as measured by SF-36 and HM-Q, presented as median (interquartile range 25th - 75th).

	All (n=51) median (25th-75th)	GJH (n=29) median (25th-75th)	JHS (n=22) median (25th-75th)	Mann-Whitney U p
SF36 physical functioning	100 (95-100)	100 (95-100)	95 (90-100)	**0.029**
SF36 role functioning	100 (100-100)	100 (100-100)	100 (100-100)	0.555
SF36 bodily pain	84 (62-100)	100 (72-100)	73 (54.5-84)	0.053
SF36 health perception	82 (72-89.5)	85 (77-92)	77 (68.3-87)	0.240
SF36 vitality	60 (45-70)	60 (50-70)	55 (45-69.2)	0.486
SF36 social role	100 (87.5-100)	100 (87.5-100)	93.8 (75-100)	0.097
SF36 emotional role	100 (100-100)	100 (100-100)	100 (100-100)	0.830
SF36 mental health	80 (64-84)	80 (68-84)	75.5 (60-84)	0.213
SF36 physical health (sum score)	55.1 (50.9-58.2)	56.9 (52.0-58.9)	53.8 (50.4-56.6)	0.110
SF36 mental health (sums core)	52 (45.8-55.6)	52.6 (47.1-55.9)	50.1 (44.8-54.2)	0.458
HM-Q sum score	27.1 (24.3-35)	25.7 (22.1-32.9)	31.1 (26.4-37.3)	**0.032**

GJH = Generalized Joint Hypermobility, JHS = Joint Hypermobility Syndrome, SF-36 = Medical Outcomes Study Short Form 36-Item Questionnaire (scale 0-100, with higher values indicating better health, sums core with reference to US-population with 50 indicating the population mean), HM-Q = Hypermobility Questionnaire (scale 20-100, with higher values indicating more pain and disability). Significant differences between groups (p>0.05) are in bold.

mean difference, the latter being symmetrical on both sides of the zero line. Muscle mass at thigh and shank was on a comparable as was muscle density, while bone density was clearly higher for the shank.

In the parameters measured during stair climbing (Table 4) some differences between persons with JHS and GJH were seen. A significantly shorter contact time on the step indicates faster stair ascent and descent velocity for persons with JHS, while the parameters for the first force peak were comparable between groups. EMG values showed a tendency for higher muscle activation in persons with JHS, whereby only the EMG of the biceps femoris was significantly higher in persons with JHS.

Finally, no significant differences between groups were recorded on the SF-36, although notably high values were found in several domains, like role functioning, emotional role and physical functioning. The hypermobility questionnaire revealed significantly higher pain and impairments in daily life for persons with JHS compared to those with GJH, with rather low values in both groups.

Sample size considerations

Based on the two significant differences between the subgroups in maximum knee flexor strength and flexor strength to mCSA ratio for the effect size according to Cohen were calculated as d=0.52 and d=0.51, respectively, which corresponded with an achieved statistical power of 35% and 31% respectively. When calculating the necessary sample size for 80% power for a future study a minimum of 124 and 130 persons respectively, will be necessary.

Internal correlations

For strength measurements all 13 parameters were highly correlated with p-values below 0.005 and Spearman's ρ between 0.40 and 0.98.

The 18 pQCT parameters were less highly correlated with 53 (35%) comparisons being highly correlated and 16 (11%) correlated at p<0.05. Generally, the density parameters were not correlated to the CSA measurements, while the same parameters of thigh and shank were all highly correlated with Spearman's ρ between .44 and .87.

In terms of stair measurements there were no significant correlations between GRF and EMG. Of the 8 GRF parameters 17 (61%) correlations were highly significant and 3 (11%) were significant, with very variable coefficients (Spearman's ρ between 0.04 and 0.88). For the 8 parameters of the EMG all correlations were significant with only 3 (11%) being not highly significant and with rather high correlation coefficients (Spearman's ρ between 0.32 and 0.79).

In the questionnaires the face-validated hypermobility questionnaire correlated well with some dimensions of the SF-36, i.e. highly significant with a Spearman's ρ=0.68 on the pain subscale. In total 24 (44%) correlations were highly significant and 9 (16%) were significant, including the self-correlations of the various dimensions of the SF-36.

Correlations between the dimensions

Regarding the correlations between the dimensions of selected parameters the significant values are depicted in Table 6.

The MVC parameters were moderately correlated with the muscle CSA of the thigh, whereby persons with JHS showed

Table 6. Significant Spearman's correlations between selected parameters of the various domains for all participants and both subgroups.

		MVC extensors/ bm	RFD extensors/ bm	MVC flexors/ bm	RFD flexors/ bm	mCSA thigh/ bm	Fmax up	contact time up	Fmax down	contact time down	%EMG Bic fem up	%EMG Vast lat up	%EMG Bic fem down
RFD extensors/bm	All GJH JHS	**0.57** **0.50** **0.56**											
MVC flexors/bm	All GJH JHS	**0.79** **0.76** **0.82**	**0.51** **0.54** **0.46**										
RFD flexors/bm	All GJH JHS	**0.55** 0.37 **0.70**	**0.70** **0.61** **0.71**	**0.67** **0.53** **0.79**									
mCSA thigh/bm	All GJH JHS	0.44 0.37 0.54		0.38 0.54									
Fmax up	All GJH JHS	0.29				**0.55** 0.52 0.59							
contact time up	All GJH JHS					0.36	**-0.59** **-0.58** -0.57						
Fmax down	All GJH JHS			0.31 0.55									
contact time down	All GJH JHS					-0.37 -0.43	**0.48** -0.55	**0.88** **0.85** **0.87**					
%EMG bic fem up	All GJH JHS	-0.36 -0.63	-0.31	**-0.51** **-0.64**	**-0.49** -0.60								
%EMG vast lat up	All GJH JHS	-0.33 -0.53	-0.39 -0.63	**-0.46** **-0.66**	**-0.48** -0.64						**0.46** 0.58		
%EMG bic fem down	All GJH JHS	-0.29 -0.53		**-0.49** **-0.64**	-0.44 **-0.67**						**0.78** **0.80** **0.79**	0.42 **0.69**	
%EMG vast lat down	All GJH JHS	**-0.46** -0.57	**-0.49** -0.40 -0.58	**-0.58** **-0.63**	**-0.47** -0.64						**0.57** 0.41 0.62	**0.78** **0.68** **0.83**	**0.57** 0.42 **0.70**

Bold numbers = correlation significant with p < 0.005, all others = correlation significant with p < 0.05. RFD = rate of force development, MVC = maximum voluntary contraction, bm = body mass, mCSA = muscle cross-sectional area, Fmax = peak ground reaction force. Note: Shaded areas are self-correlations in one measurement.

slightly higher values than those with GJH. Correlations of strength parameters with ground reaction forces were mainly not significant, while the EMG parameters correlated moderately negatively with the strength parameters, illustrating lower activation levels in persons with more strength. This was again more accentuated in the JHS group. The muscle CSA of the thigh correlated moderately positively with the peak force during stair up and with contact time up and moderately negatively with contact time down, but not with the EMG parameters. Finally, between the GRF

parameters and the EMG no significant correlation was found. No significant correlations were seen between the self-reported questionnaires and the various other dimensions, indicating that no direct association could be found between body structures and function, on the one hand and disability and participation on the other.

Discussion

The first aim of this descriptive analysis was to compare women with GJH and those with JHS in terms of strength, muscle and bone properties and functional activities. The parameters mainly showed no differences between groups, however, there was a tendency towards lower strength in women with JHS compared to women with GJH. This is in line with the results of To et al.[43], whereas our previous study[22] did not find significant differences between symptomatic and asymptomatic women with GJH. The evidence regarding muscle strength in persons with various forms of joint hypermobility is still conflicting[44] and a possible reason might be the variability of symptoms and disability even in persons with the same diagnosis. In our study this is illustrated by the high standard deviations of strength parameters in both groups with average amounts of 30% to 50% of the respective mean value, resulting in large 95% CI for the mean differences. In the bone and muscle parameters no differences between the subgroups were seen and all values were in the normal range[27,45]. However, comparison with other studies is difficult since only a few studies were done with young women and, furthermore, measurement methods and sites were very variable. In stair climbing women with JHS had significantly shorter (minus 7%) contact times than those with GJH, pointing to faster speeds on the stair. Within this task only the biceps femoris during stair up demonstrated higher maximal activation, indicating that the faster speeds did not generally influence the muscle activation patterns. Finally, on the SF-36, no differences were seen for high values, indicating possible ceiling effects in this study group with fairly few disabilities and mild pain. Only for bodily pain was a tendency towards greater pain (indicated by lower values) identified in the JHS group. On the Hypermobility questionnaire significantly higher values were seen in participants with JHS versus GJH, pointing towards more pain and greater disability. However, the differences were small and all values still in the lower third of the scale. Thus, from the questionnaire and the functional measurements, we conclude that our participants were mostly not severely affected and were mainly able to manage their daily life.

A second endpoint of this study was analysis of the correlations of the various parameters in the different dimensions of the ICF. First, internal consistency was checked by analysing each dimension individually. A high number of high or moderate significant correlations were seen in all the measurements, indicating good internal consistency of the assessments. MVC and RFD of the same muscle were highly correlated. In the pQCT the muscle density was independent of CSA whereas during stair climbing GRF and EMG were not clearly correlated, indicating that additional factors like body position and movement control have high influence on these two parameters. The self-developed hypermobility questionnaire correlated well with the SF-36, suggesting its ability to evaluate the disabilities of persons with joint hypermobility correctly. However, since now the Bristol Impact on Hypermobility questionnaire as a validated alternative has now been as published[46], this self-developed questionnaire will no longer be used.

Finally, correlations between selected parameters of the various measurements were analysed. The correlations between MVC and muscle CSA were only moderate, which confirms that it is not only muscle area or muscle mass that determines the ability to generate strength, but also neurological and metabolic factors, as has already been described by similar correlation values for healthy persons and athletes[28,47]. Moderate and significant negative correlations between strength and muscle activation on stairs were found for those with JHS and, subsequently, for the whole group, but were lower and not significant for those with GJH. Since the women with JHS had a tendency towards lower strength and higher muscle activation, a possible explanation might be that these women were performing closer to their limit and thus using a consistently greater amount of their maximum strength. Similar mechanisms have already been described for elderly women[48] and for persons with knee osteoarthritis[29], but not for young women. Finally, the lack of significant correlations between the measurements and the questionnaires might indicate that the young participants in this study were not really impaired in their daily life. They showed some concerns regarding pain and disability but were still able to perform their daily activities and had enough capacity in terms of strength and muscle area to live a normal life.

Limitations

This descriptive study has several limitations in terms of the participants and the measurements performed. A main issue is that it was not possible to incorporate a control group without joint hypermobility. Thus, we have to rely for comparisons on the literature and partially on our previous cross-sectional study, where women with normal mobility were compared to those with joint hypermobility[22,37,41]. While the subgrouping, based on the Brighton criteria for JHS, was done after the inclusion of the participants, the two groups were not similar in size. Additionally, most of the participants in this study were not severely affected by their GJH and thus did not experience a lot of pain and disability. Consequently, the differences between those with JHS and those with GJH were not very clear. This illustrates the fact that these two entities are more part of a spectrum than two clearly distinguishable clinical pictures. In the current 2017 nosology nearly all the participants would be described as having Hypermobility Spectrum Disorder (HSD), with maybe a few fulfilling the

criteria for hypermobile EDS[8,17]. Since no systematic data on the familial history and presence of joint hypermobility in relatives was gathered, it is impossible to clearly classify the participants retrospectively.

Regarding the sample size the present study was clearly underpowered. Since this is an additional and descriptive analysis of the baseline data of a randomised controlled trial the power calculation in the present project was based on the respective intervention and the expected changes. Thus, for this comparison of subgroups at baseline the study reached a power of about 35% and for future comparisons larger groups with about 130 to 150 participants might be necessary.

Additional limitations are related to the assessments used in the study. The strength measurement was performed isometrically, which was not easy for all participants to perform since not all were used to performing maximum contractions against resistance. This might have increased the variability between participants since experienced users had more strength and were able to perform better, while inexperienced women may not have reached their absolute maximum. On the stair it was not possible to measure kinematics, which might have shown differences in movement control and could help to explain the variance in terms of GRF and EMG. In hindsight, stair climbing as an activity was perhaps insufficiently demanding to illicit differences between the groups and bring the participants to their limits. Possibly, it would have been better to use jumping or running as activities to provoke higher muscle activation and thus establish the limits in the various groups. On the other hand, it might be difficult to find enough participants with JHS who are willing to perform such demanding activities, which might trigger pain or even injury.

Further research

To our knowledge only a few studies exist that look at differences between persons with joint hypermobility in various grades. Our study adds a small piece to this knowledge, but further research is needed. On the one hand, it is important to find better parameters for the description of the impairments and disabilities that persons with various grades of joint hypermobility experience. It is important to know which measurements might distinguish between persons who are more or less affected and which parameters may also serve as prognostic factors for future developments of pain and disabilities. On the other hand, a better description of the disabilities and deficits in persons with joint hypermobility would help to improve management and to design appropriate and targeted interventions for these patients. Since no curative therapy is available for joint hypermobility the long-term management and the individual support of affected persons is crucial. Future research should provide the foundation for this and thus better equip health professionals to manage the condition and patients.

Conclusion

The aim of this project was to provide an insight into various parameters of body structures, body function, daily activities and participation of young women with joint hypermobility. Only small and non-relevant differences to healthy young women were found in terms of muscle strength, muscle and bone properties, forces and muscle activation during stair climbing and in self-reported health. The participants in our study were not severely affected, thus the assessments used may not have been sufficiently sensitive to provide a deeper insight into the phenomenon of hypermobile joints.

Authors' contributions

All authors contributed to the design and planning of this study; GL and DA were responsible for all the assessments, CM for recruitment and inclusion of participants. GL was responsible for data analysis and statistics. The writing of this manuscript was guided by GL, all authors contributed to the manuscript and have read and approved the final version. GL has the full responsibility for the conduct of the study and the integrity of the data analysis.

Acknowledgements

The authors like to thank several people for their support during the conduct of this study: Prisca Eser, PhD, and Inna Galli-Lyssak for instructions concerning the use and evaluation of the pQCT. Michaela Hähni and Sarah Mahnig for support in data analysis.

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