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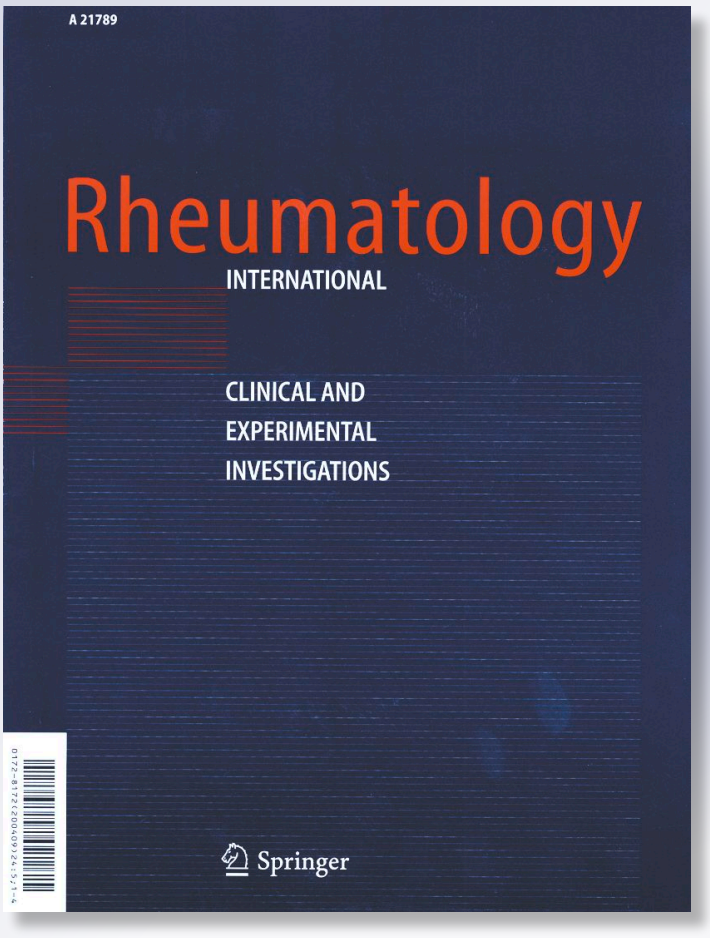

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SHORT COMMUNICATION

Evaluation of lower limb disability in joint hypermobility syndrome

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Abstract The aim of this study is to evaluate degree and possible major determinants of lower limb disability in joint hypermobility syndrome. Forty patients with joint hypermobility syndrome were studied. Lower limb function was evaluated with the lower limb functional scale (LEFS). Intensity of pain was estimated by the numeric rating scale. Rough results were compared with previously published data for osteoarthritis patients. Within the studied population, comparisons were performed by age, sex, numeric rating scale and Beighton scores. In joint hypermobility syndrome, LEFS score was similar to osteoarthritis, but in the former, comparable values were observed with a ~10 year earlier onset. LEFS scores resulted significantly related to age, pain intensity and Beighton score. No correlation with sex was observed. This study demonstrated that, in joint hypermobility syndrome, disability of lower limbs is remarkable and related to the increase in pain and age and to the decrease in residual joint hypermobility. These preliminary results may be relevant for the identification of more efficient and tailored treatment programs.

Keywords Disability · Ehlers–Danlos syndrome · LEFS · Lower extremity functional scale · Pain · Treatment

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Introduction

Joint hypermobility syndrome (JHS) is a relatively common, but largely unrecognized rheumatologic condition mainly characterized by joint hypermobility (JHM) and related musculoskeletal, dysautonomic and gastrointestinal features [1]. Familial clustering and absence of a known environmental cause suggest a genetic origin for JHS. Accordingly, an international group of experts suggested that JHS and Ehlers–Danlos syndrome hypermobility type (EDS-HT) represent the same condition with extreme clinical variability [2]. Considered "benign" for a long time, JHS/EDS-HT is now recognized as a severely disabling condition with chronic pain and fatigue being possible major determinants for such a severe deterioration of quality of life [3, 4]. Furthermore, lack of knee proprioception and lower limb dysfunction are well-known features of JHS/EDS-HT [5, 6], and it is reasonable that both may contribute to the loss of autonomy in the affected individuals. Nevertheless, no study has been performed to date aimed at quantitatively investigating disability in JHS/EDS-HT.

The Lower Extremity Functional Scale (LEFS) is a questionnaire recently validated as an efficient and responsive outcome measure to evaluate disability of the lower limbs [7]. In particular, LEFS resulted more reliable and valid than the Western Ontario and McMaster Universities Osteoarthritis index for evaluating disability in symptomatic osteoarthritis (OA) patients [8]. LEFS was successfully applied for determining improvement in lower limb function in patients who underwent anterior knee ligament reconstruction [9] and after a specific rehabilitation program in patients with patellofemoral pain syndrome [10]. Therefore, this questionnaire is a potentially useful tool for quantifying functional impairment in patients with

other chronic rheumatologic disorders, such as JHS/EDS-HT.

Here, we studied lower limb dysfunction in 40 JHS/EDS-HT patients by using LEFS. Degree of disability resulted remarkable and mainly determined by age, intensity of pain and Beighton score. These preliminary results may help in identifying more tailored and efficient treatments for JHS/EDS-HT.

Patients and methods

Patient selection

All patients were directly evaluated in a multidisciplinary outpatient clinic dedicated to JHM. Subjects were selected on the basis of a clinically confirmed diagnosis of EDS-HT/JHS. Then, all selected patients were recontacted and those available reevaluated at follow-up.

Physically, JHM was mainly assessed using the Beighton score [11]. Though not included in these criteria, additional tests were performed in order to evaluate hypermobility of the spine, temporomandibular joint, hips, ankles and interphalangeal joints. Specific questions were also asked for investigating a history of JHM which was not more appreciable at the time of examination [12]. Skin texture was assessed by a qualitative, experience-based approach. Particular attention was posed on additional skin features, such as atrophic/hemosiderotic scars, molluscoid pseudotumors and subcutaneous spheroids, indicative for other EDS variants, mainly the classic type. Diagnosis was established based on both the Villefranche and Brighton criteria [13, 14], and patients were considered affected if meeting at least one of the two sets of diagnostic criteria. Additional extra-articular features were also investigated and registered accordingly.

Outcome tools

In order to evaluate the grade of disability for the lower limbs, we administered to all patients the LEFS, which consists in a 20-item functional status questionnaire applicable to a wide spectrum of patients with lower extremity conditions of musculoskeletal origin [15]. These items investigate the degree of difficulty in performing different physical activities. Each item has five response options (0, extreme difficulty or unable to perform activity, to 4, no difficulty). The scores for all items are then used to calculate a scale score ranging from 0 (low functional level) to 80 (high functional level). Pain severity in the last week was assessed using the 11-point numeric rating scale (NRS), a validated tool used to semiquantitatively measure pain (0 means no pain, 10 means the most severe pain) [16].

Statistical analysis

For LEFS, which is a scale for disability, comparison with a healthy population, assumed to have the highest value in all items (i.e., a final score of 80), is not reasonable. Therefore, we decided to compare data with another population affected by a more common condition mainly affecting the lower limbs (i.e., OA). To evaluate differences between EDS subjects and patients with OA (data published in Binkley et al. [15]), we used the Mann–Whitney U test. Within our patients' population, correlations between LEFS and Beighton score, LEFS and age, LEFS and NRS score, NRS score and Beighton score, NRS score and age, Beighton score and age were expressed by the Spearman ranking-order-correlation coefficients. If P value ≤ 0.05, statistical significance was accepted. All analyses were performed using the SPSS 15.0 software for Windows.

Results

Main clinical features of the patients' cohort are itemized in Table 1. Comparison of LEFS scores between the JHS/EDS-HT patients (mean score 39.6 ± 15.9; $N = 40$) and the OA group (mean score 34 ± 16; $N = 104$) by Binkley et al. (1999) shows that the degree of disability in our patients' cohort was not statistically different from the reference group ($P = 0.06$). The mean age at diagnosis in our patients' group (33.3 ± 15.9 years) is significantly different from the reference group (44 ± 16.2 years; $P < 0.001$). This means that a comparable degree of disability was observed in JHS/EDS-HT patients, approximately 10 years before than in individuals with OA. Within our population, no differences were observed between sexes for the LEFS score (females $= 38.6 \pm 15.6$, males $= 46.7 \pm 17.4$; P value $= 0.33$). Conversely, statistically significant results were obtained by comparing patients with persistent JHM with those who lost it [Beighton score > 5 ($N = 15$) $= 48.13 \pm 14.25$, Beighton score ≤ 5 ($N = 25$) $= 34.24 \pm 14.45$; P value $= 0.005$]. In other words, patients with a Beighton score > 5 seem to feel better and show better lower limb function than those with a lower score. Correlations between LEFS, Beighton and NRS scores, and age, are shown in Fig. 1. Inverse correlations were observed between age and Beighton score [$r(S) = -0.360$; $P = 0.023$], age and LEFS score [$r(S) = -0.321$; $P = 0.043$], NRS score and LEFS score [$r(S) = -0.495$; $P = 0.001$], while direct correlation was reported between Beighton score and LEFS score [$r(S) = -0.3$; $P = 0.05$]. No correlation was demonstrated between NRS score and Beighton score, and NRS score and age.

Table 1 Main clinical features of the patients' cohort

Characteristic	Frequency	%
Sex (females/males)	36/4	90/10
Age at evaluation (years)	33.3 ± 12.9	–
Positive family history	19/39	48.7
Congenital contortionism	35/40	87.5
Motor delay/clumsiness	7/40	17.5
Residual joint hypermobility (Beighton ≥ 4)	30/39	76.9
Recurrent (≥3) joint dislocations	30/40	75
Recurrent (≥3) soft tissue lesions	17/40	42.5
Chronic back pain	31/40	77.5
Chronic arthralgias	34/40	85
Chronic myalgias	35/40	87.5
Chronic fatigue	35/40	87.5
Recurrent headaches	30/40	75
Unrefreshing sleep	30/40	75
Impaired memory/concentration	23/40	57.5
Velvety/smooth skin	30/40	75
Hyperextensible skin	10/40	25
Easy bruising	28/40	70
Eyelid ptosis	16/40	40
Varicose veins/hemorrhoids	6/40	15
Hernias	1/40	2.5
Uterine/vescical/rectal prolapse	4/40	10

Discussion

This work tried to examine the degree of lower limb disability in a group of 40 patients with JHS/EDS-HT. Our study first demonstrated that in JHS/EDS-HT, the extent of lower limb dysfunction is remarkable and comparable with a population of patients with OA [15]. By comparing the mean age at examination, patients with JHS/EDS-HT are 10 year younger than those with OA. Theoretically, this could be partly explained by the early evidence of an increased rate of precocious OA in JHS/EDS-HT patients [17]. However, recent advance and anedoctal, experience-based reports strongly suggest that, in JHS/EDS-HT, disability of lower limbs is likely related to a wide range of features, extending to specific functional anomalies involving hips, knees, ankles and feet, which are not directly related to precocious OA [18–20]. Moreover, further studies demonstrated that JHM *per se* may indeed represent a protective factor contributing in preventing OA [21]. These contrasting evidences are probably related to the actual lack of knowledge as to why some individuals with generalized JHM develop symptoms (and then become JHS patients) while others do not (thus remaining asymptomatic hypermobile subjects) [1].

Our preliminary results may be relevant also in terms of public health. In fact, although accurate data on the prevalence of JHS/EDS-HT are still lacking, it has been estimated that it may affect 0.75–2% of the general population [22]. Assuming comparable direct and indirect costs for OA and JHS patients with similar LEFS scores [23], a more clear picture of the potential impact of JHS on healthcare may emerge. In fact, patients with JHS/EDS-HT probably display needs similar to OA but at an early age, with dramatic consequences in terms of predictable costs and requested rehabilitative interventions.

This study also tried to identify major determinants for lower limb dysfunction in JHS/EDS-HT. In this attempt, possible statistically significant correlations with sex, age, intensity of perceived pain (NRS score) and degree of residual JHM (Beighton score) were investigated. The most striking correlation was that between intensity of pain and LEFS score. This finding corroborates once more the relevant role that pain has on functional impairment and the impact that more efficient and tailored pain-relief treatments could have in terms of quality of life in JHS/EDS-HT [4, 24]. LEFS score was also significantly related with age and Beighton score. More particularly, the degree of disability increases with age and decreases with the Beighton score. Both variables are interrelated, as a statistically significant relation was identified between age and Beighton score. This evidence strongly supports the hypothesis of a peculiar natural history in JHS/EDS-HT, in which musculoskeletal symptoms worsen with age and are often linked to progressive joint stiffness, paradoxically observed in elderly patients [25]. In spite of the common misconception that treatment of JHM patients should be based on reduction in joint range, our work indicates that a higher degree of JHM is a good indicator for high functionality of the lower limbs. Therefore, rehabilitative programs for JHS/EDS-HT patients should be focused on maintaining the full range of motion of the hypermobile joints and simultaneously aimed at improving some defective functions, such as muscle tone and proprioception [26].

Finally, no correlation between sex and LEFS score was identified. This could represent a bias related to paucity of affected males and/or to the fact that, in spite of a range of joint complications directly related to joint laxity, disability is one of the most common reasons of referral to physicians in JHS/EDS-HT. In other words, while the downward spiral determining symptom development and worsening in EDS-HT/JHS is facilitated in females, the consequences of these symptoms in terms of overall functional abilities are essentially the same among sexes. This also implies that the management of JHS/EDS-HT is presumably similar for both sexes. No correlation was also identified between NRS and Beighton scores. This implies that perception of pain in JHS/EDS-HT is not uniquely linked to joint damage (i.e., nociceptive or inflammatory pain). Accordingly, recent evidence suggest that JHS/EDS-HT often shows a

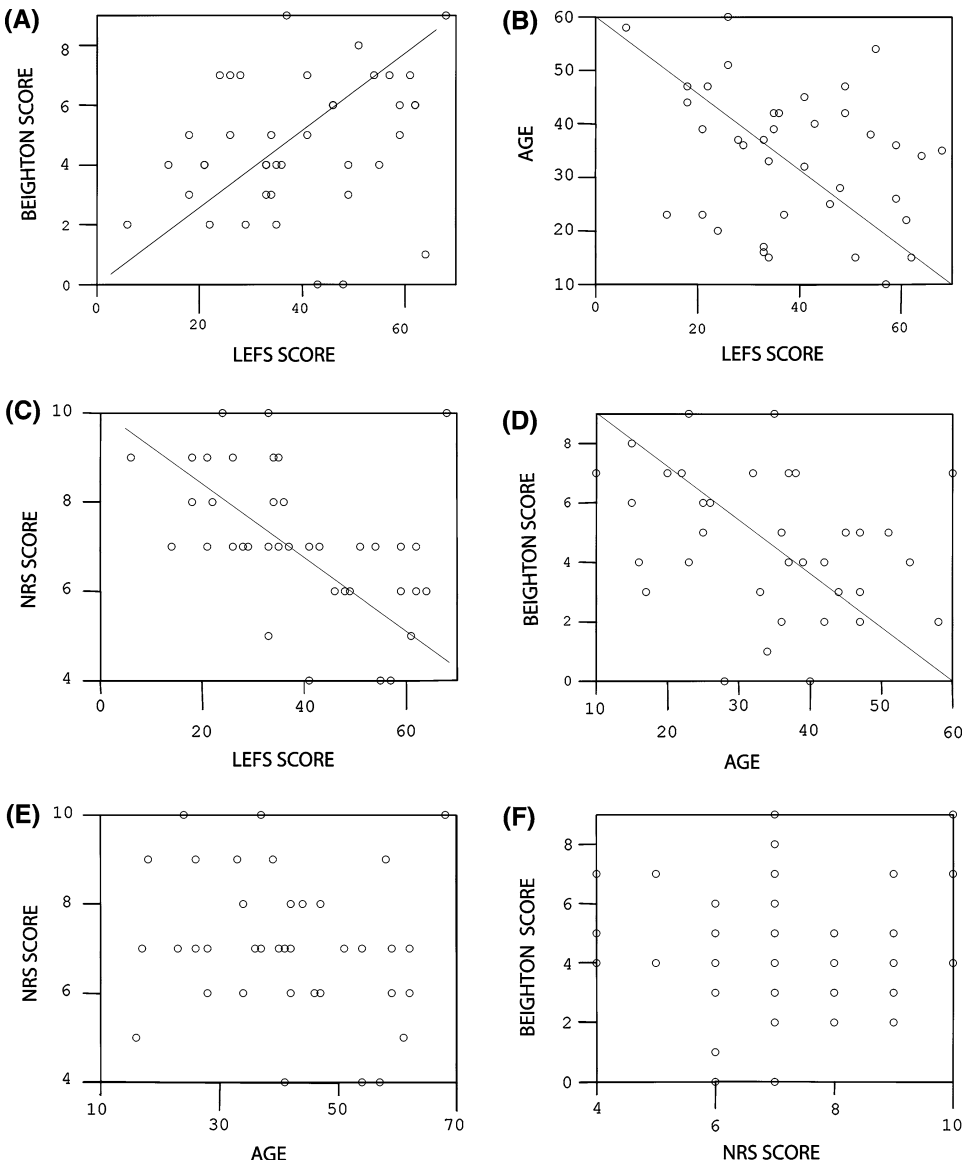

Fig. 1 Spearman ranking-order-correlation among couples of features in our patients' cohort. Direct correlation was noted between Beighton score (degree of joint hypermobility) and LEFS score (severity of disability), (**a**) while inverse correlation was observed between age at evaluation and LEFS score (**b**), NRS score (severity of perceived pain) and LEFS score (**c**), and Beighton score and age (**d**). No correlation was evident between NRS score and age (**e**), and Beighton and NRS scores (**f**)

neuropathic component [27] that may be in part related to peripheral nerve damage. However, both nociceptive/inflammatory and peripheral neuropathic pain does not explain the entire range of pain-related features, which probably reflect a more complex pathogenesis also including a functional/central component. Further studies are needed to investigate origin(s) of pain and its relation with disability in JHS/EDS-HT.

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