Sport and physical activity in patients with hereditary multiple exostoses

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Summary

***Background*. The purpose of this observational clinical study was to assess the type of sports and physical activities in patients with hereditary multiple exostoses (HME).**
***Methods*. The data of 170 patients with HME, older than 12 years, were evaluated and recorded. Sport and physical activities were evaluated with the University of California at Los Angeles (UCLA) Activity score and the Tegner Activity scale. The association of gender, number of exostoses, and physical activities were evaluated and correlated.**
***Results*. Mean number of exostoses in our patient group (mean age 31.34 years old) resulted 39.49 ± 34.33. Mean Tegner score resulted 3.77 ± 2.78, while mean UCLA was 5.44 ± 2.61. Comparing the clinical outcomes of the male group (MG), composed of 56 patients with the female group (FG), consisting of 114 patients, we found a significant difference between Tegner, UCLA and age ($p < 0.05$), with no significant differences for number of exostoses ($p > 0.05$). In our cohort we reported a significant negative correlation between number of exostoses and Tegner score (R= -0.233, p-value= 0.002) and between UCLA score and number of exostoses (R= -0.285, p-value < 0.001).**
***Conclusions*. HME impacts negatively on physical and sports activity of patients: in particular, the increase in the number of exostoses reduces the activity. Male patients are also more active then female as regards sports activity.**

KEY WORDS: hereditary multiple exostoses; rare disease; sports medicine; physical activity; bone tumors; osteochondromas.

Introduction

Hereditary multiple exostoses (HME) is a rare disease, with an estimated incidence of 1:50,000, characterized by development of multiple osteochondramas, benign bone tumors, caused by mutations in genes *EXT1* and *EXT2* (1, 2). These two genes play a key role as regards the production of the exostosin-1 and exostosin-2, two proteins crucial in processing of the heparan sulfate, a protein that seems to be related to the development of exostoses (3-5). Based on the gene affected by the mutation, the pathology is defined as type 1 (EXT1) or type 2 (EXT2). The difference between the two types concerns the incidence (EXT1 account for 55 to 75% of all cases of hereditary multiple osteochondromas) and the severity, in fact, patients with type 1 report more serious symptoms. In addition to type 1 and type 2, there are 15% of patients who have no genetic mutation (6, 7). The number and location of the exostoses varies enormously within the affected people; osteochondromas are not present at birth, but develop at around the age of 12 years, mainly affecting long or flat bones altering in many cases normal bone growth with dysmetry and malformations (8-10). Bowing of the forearm or ankle and abnormal development of the hip can lead to difficulty walking and general discomfort, resulting in pain, limited range of joint movement, and pressure on nerves, blood vessels and the spinal cord, with a significant decrease in quality of life (9, 11-15). Osteochondromas are typically benign, but literature reports a lifetime risk of malignant transformation 1 in 20 to 1 in 200 (16). Several articles have been reported in the literature dealing with surgical techniques in treating the deformities caused by the exostoses, reports of abnormal development and life quality studies, but there is no study that evaluates the sports activities of these patients. The purpose of this observational clinical study was to assess the type of sports and physical activities in patients with HME.

Materials and methods

A chart of clinical and radiographic records was performed. HME were diagnosed on the basis of clinical and radiographic evaluation. The inclusion criteria for this study included

Table 1 - Demographic and clinical parameters score for patients included in the study described by mean ± SD (standard deviation) and range.

	Mean	Standard Deviation	Range
Age	31.34	16.19	12-76
Number of exostoses	39.49	34.33	3-200
Tegner score	3.77	2.78	0-10
UCLA scale	5.44	2.61	1-10

Table 2 - T Student test for unpaired data, for comparison parameters between male group and female group.

	Male (56)	Female (114)	p-value
Age	27.66 ± 15.85	33.14 ±16.12	0.037*
Number of exostoses	38.3 ± 36.39	40.1 ± 33.43	0.763
Tegner score	4.63 ± 2.74	3.35± 2.73	0.005*
UCLA scale	6.07± 2.75	5.13±2.51	0.034*

MG=male group; FG=female group
**statistical significant difference (p<0.05)*

patients older than or equal to 12 years, as well as clinical and radiological diagnosis of 2 or more exostoses. Exclusion criteria were: patients younger than 12 years old, additional surgical procedures in addition to the removal of the exostoses, such as hip, knee, shoulder or other joint replacement, limb lengthening or arthrodesis, haemophilia, rheumatoid arthritis, severe metabolic disorders, ongoing chemotherapy, radiation treatment or immunosuppression, and pregnancy or lactation. This observational study was conducted on the basis of the STROBE statement guidelines (17).

All patients completed the following evaluations:

- Tegner Activity Level Scale (18)
- University of California, Los Angeles (UCLA) activity scale (19)

Tegner activity level scale is a graduated list of activities of daily living, recreation, and competitive sports. The patient is asked to select the level of participation that best describes their current level of activity and that before injury. The score varies from 0 to 10. A score of 0 represents sick leave or disability pension because of knee problems, whereas a score of 10 corresponds to participation in national and international elite competitive sports >6 score can only be achieved if the person participates in recreational or competitive sport. The UCLA scale is a simple scale ranging from 1 to 10. The patient indicates her or his most appropriate activity level, with 1 defined as "no physical activity, dependent on others" and 10 defined as "regular participation in impact sports".

Moreover, sex, age and number of exostoses, for each patient were recorded. However, the location and the size of the exostoses were not assessed. The association with gender, number of exostoses and physical activities was then evaluated. All patients were provided informed consent and completed necessary paperwork for participation in the study. In the case of a minor, informed consent was signed by both parents. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Statistical analysis

Statistical analysis was conducted using a statistical software (SPSS version 17, SPSS Inc., Chicago, IL, USA). The statistical tests performed included Student's T test for paired and unpaired data. Furthermore, we evaluated significant correlation with Pearson's linear correlation coefficient R, where the correspondent p values were computed with the T Student test, under null hypothesis of Pearson's linear correlation coefficient R = 0. We considered significant all statistical tests with p-value < 0.05.

Results

Of 220 patients screened for eligibility, 170 satisfied the inclusion criteria and were enrolled in the study; 67.05% (114) of the patients were females and 32.95% (56) males, with a mean age of 31.34 years (SD ± 16.19; range 12-76). Mean number of exostoses in our patient group resulted 39.49 ± 34.33. Mean Tegner score resulted 3.77 ± 2.78 while mean UCLA was 5.44 ± 2.61. Results are summarized in Table 1.

Gender

We compared the clinical outcomes of the male group (MG), composed of 56 patients with a mean age of 27.66 ± 15.85 years with the female group (FG), consisting of 114 patients with a mean age of 33.14 ± 16.12. Results are reported in Table 2.

We found a significant difference between males and females as regards Tegner score, UCLA score and age (p<0.05), with no significant differences for number of exostoses (p > 0.05) (Figures 1, 2).

Table 3 - T Student test for unpaired data, for comparison parameters between EX- and EX+.

	EX - (78)	EX + (92)	p-value
Gender	46 F - 32M	68 F - 24 M	
Age	28.21 ± 15.13	33.98 ± 16.67	0.02*
Number of exostoses	16.53 ± 6.63	58.95 ± 36.29	<0.0001*
Tegner Score	4.63 ± 2.63	3.04 ± 2.72	<0.0001*
UCLA Scale	6.36 ± 2.55	4.66 ± 2.43	<0.0001*

EX-= patients with less than 30 exostoses; EX+=patients with 30 or more exostoses
**statistical significant difference (p<0.05)*

Number of exostoses

We considered 78 patients with a mean age of 28.21 years (58.97% females and 41.03%), represented by all patients with fewer than 30 exostoses (EX-) and 92 patients with a mean age of 33.98 years (73.91% females and 26.09% male) represented by all patients with a higher number of exostoses (EX+) or equal to 30, and verified the differences of all parameters. Results are reported in Table 3.

We found a significant difference between EX – and EX + as regards Tegner, UCLA, age and number of exostoses ($p < 0.05$) (Figures 3, 4).

Correlations

We found a significant negative correlation between number of exostoses and Tegner score (R=-0.233, p-value=0.002) and a significant negative correlation between UCLA score and number of exostoses (R= -0.285, p-value < 0.001).

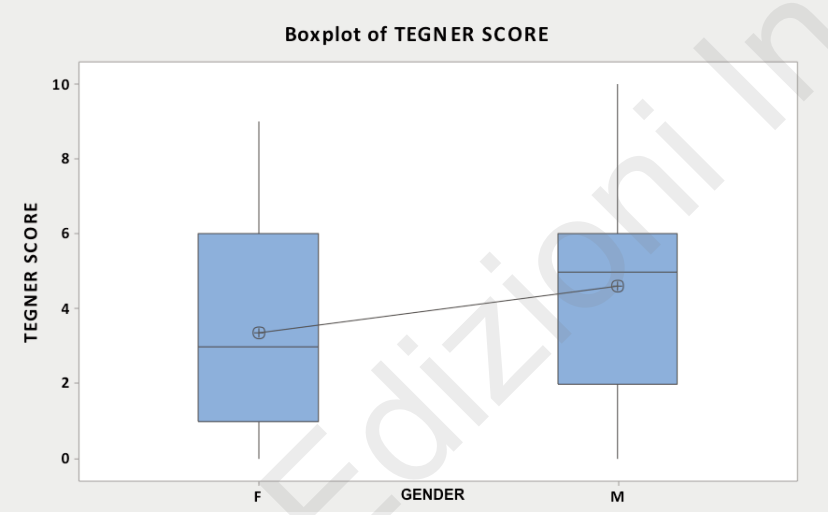

Figure 1 - The Boxplot shows the difference between male group and female group as regards Tegner Score.

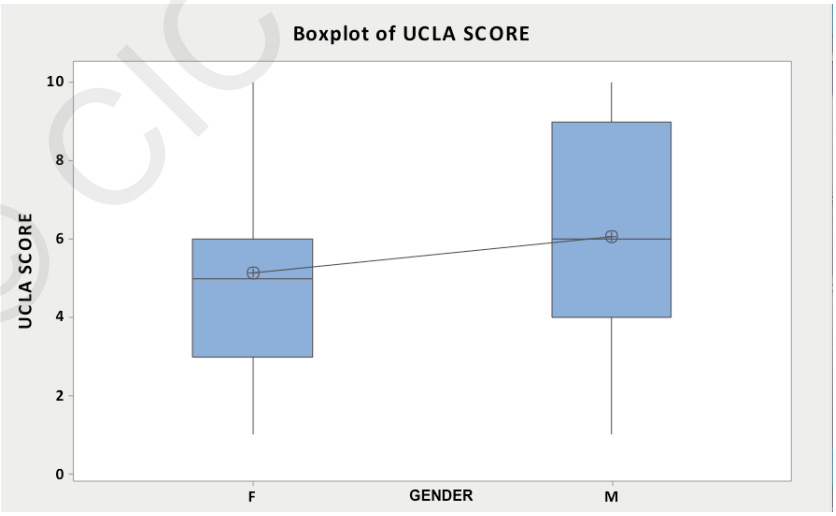

Figure 2 - The Boxplot shows the difference between male group and female group as regards UCLA Activity Scale.

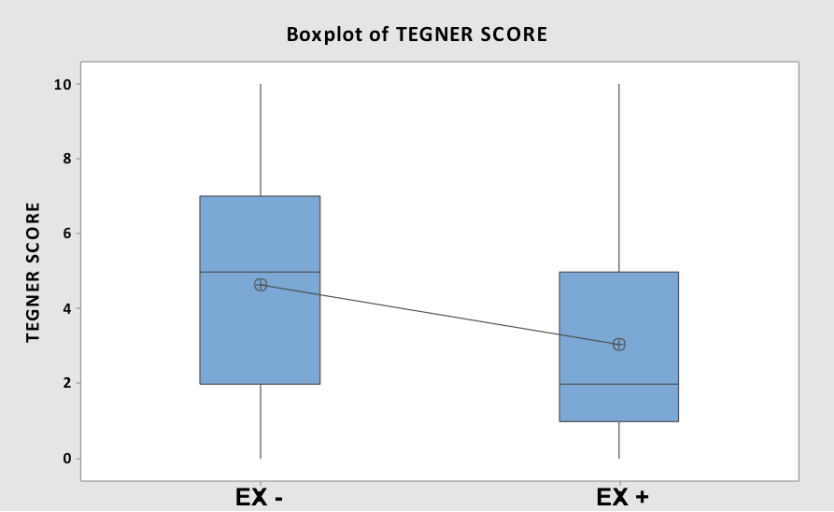

Figure 3 - The Boxplot shows the difference between EX- and EX+ as regards Tegner Score.

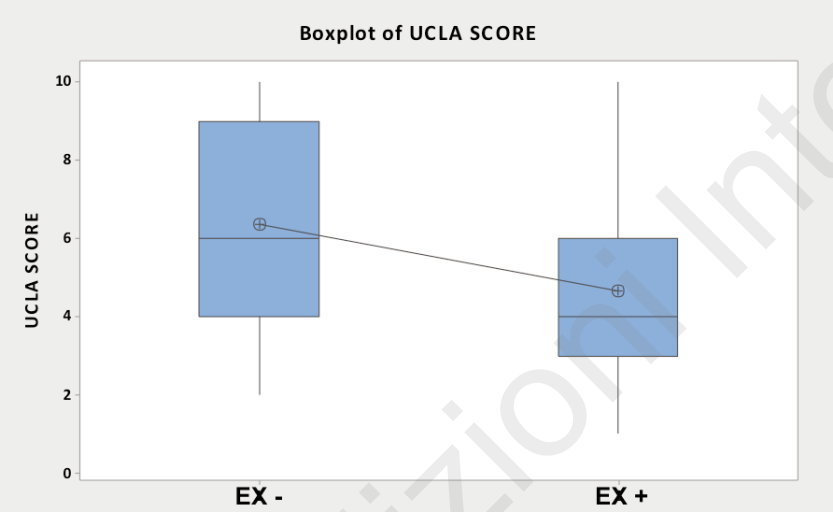

Figure 4 - The Boxplot shows the difference between EX- and EX+ as regards UCLA Activity Scale.

Discussion

The aim of this study was to assess the level of sports activity in patients with HME and to evaluate their relationship with other factors such as gender and number of exostoses. To our knowledge this is the first study to evaluate the level of sports activity in patients affected by HME; in fact, literature concentrates mainly on surgical techniques in the treatment of exostoses, and only recently have some studies on quality of life been published. In 2012 Goud, evaluating all 322 known patients with multiple hereditary exostoses in the Netherlands, demonstrated that patients with HME have lower quality of life with pain and strong limitation on daily activities, as well as on social and psychological well-being, causing significant disability (13).

In the same year Chhina assessed the quality of life among adults and children with HME and found that the adult HME population had lower scores than both the US and Canadian general population in almost all domains (11). Short-Form-6D utility scores indicate the quality of life for some individuals as near death, and for others, it is comparable or better than individuals with rheumatoid arthritis. Children with HME scored less than the US general population; particularly, lower scores were seen in bodily pain and emotional self-esteem.

Recently we found that HME impacts patient quality of life similarly to the limitations associated with osteoarthritis or diabetes (12).

In our patient cohort with a mean age of 31.34 years, with a mean number of exostoses 39.49, we found a mean Tegner score of 3.77 and a mean UCLA score of 5.44.

Comparing our results regarding sports activity with other orthopaedics conditions it is possible to observe how our cohort report similar or slightly values; in fact, a systematic recent review evaluated UCLA score in patients underwent unicompartimental knee arthroplasty showing a mean value of 7.4 (20).

A similar study reviewed retrospectively 101 patients, younger than 60 years, underwent medial unicompartimental knee arthroplasty, with a minimum follow-up of 2 years patients, using the Tegner and UCLA to assess their level of physical activity patients showed at final follow-up a mean UCLA of 6.8 and a mean Tegner score of 3.8 (21).

Instead patients with total knee arthroplasty showed a mean

Tegner score of 3.0 at 24 months after surgery, a lower value than our sample (22). It is interesting to see how, in patients with total hip replacement, the UCLA score, two years after surgery, was 8, significantly higher than the patients with HME in our study (23).
We also compared sports between different gender, highlighting how males are significantly sportier than women (UCLA 6.07 *vs* 5.13, Tegner 4.63 *vs* 3.35). This result is similar to what has been reported in the study of quality of life, indeed in that case in the male group, mental component score, physical component score and Quality of Life Enjoyment and Satisfaction Questionnaire were significantly higher than those of the female group (12).
This difference between the gender can be explained by a study of 2014 on 143 patients reporting that the anatomical distribution of exostoses varies according to genotype and gender; however, the reason for this difference is not clear and may relate to different biochemical pathways (24).
Another interesting aspect of our study was to analyze how exostoses influences sports activity; in fact, dividing the sample on the number of exostoses (<30 *vs* ≥ 30) we have seen how patients with a lower number of exostoses are significantly more active than others (Tegner 4.63 *vs* 3.04, UCLA 6.36 *vs* 4.66). This result is in contrast with the previous article, where we did not find any difference in the quality of life in patients with many or few exostoses (12).
Although there was no difference between the two groups with different number of exostoses, we reported a signficatve negative correlation between the exostoses and the values of Tegner (R=-0.233) and UCLA (R=-0.285), indicating how the activity type and level are strongly related to the number of exostoses.
The importance of physical activity to relieve pain in patients with exostoses has been reported in a recent case report that focuses on how eccentric training might decrease pain, increase range of motion, muscle strength, and functional levels in patients with HME (25).
The major limitation of the study is the lack of sub-analysis based on location and size of the exostoses.

Conclusions

We can conclude that HME impacts negatively the physical and sports activity of patients: in particular, the increase in the number of exostoses reduces the activity. Male patients are also more active then female as regards sports activity.

Patient Declaration Statement

"The Authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed".

Conflict of interest

All the Authors declare they have no conflicts of interest.

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