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CORRELATION ANALYSIS OF T2-WEIGHTED IMAGES AND MEDICAL RESEARCH COUNCIL SCALE IN CORTICOSTEROID-NAIVE PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY

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Because of the necessity of objective instrumental methods for assessing the state of skeletal musculature in patients with Duchenne muscular dystrophy, the aim of our work was to evaluate the correlation between manual methods of assessment of the muscle strength and the results of magnetic resonance imaging (MRI) of the skeletal muscles of lower limbs. We have examined 15 corticosteroid-naive patients with Duchenne muscular dystrophy. Patients were divided into 2 groups: ambulant patients (average age 8.1 years) and non-ambulant patients (mean age 12.7 years). Muscle strength of lower extremities of all patients has been evaluated by Medical Research Council scale and MRI of skeletal muscles of the pelvic girdle, thighs and lower legs has been performed. The following results have been obtained: ambulant patients have been characterized by a high correlation of MRC scale and MRI of the lower extremities in the evaluation of the pelvic girdle and thighs muscles and the total score (pelvic girdle, thighs and lower legs) and salient correlation in the evaluation of the lower legs muscles. Non-ambulant patients have been characterized by moderate correlation in the evaluation of pelvic girdle and thighs muscles, as well as the total score of lower limbs. There was no correlation between MRC and MRI results in the muscles of the lower legs. Magnetic resonance tomography is able to reliably estimate the degree of fatty infiltration in Duchenne muscular dystrophy and is the method of choice in the diagnosis and evaluation of the severity of this disease.

Keywords: Duchenne muscular dystrophy; DMD; MRI; magnetic resonance imaging; Medical Research Council; MRC.

КОРРЕЛЯЦИОННЫЙ АНАЛИЗ T2-ВЗВЕШЕННЫХ ИЗОБРАЖЕНИЙ И ШКАЛЫ MEDICAL RESEARCH COUNCIL У ПАЦИЕНТОВ С МЫШЕЧНОЙ ДИСТРОФИЕЙ ДЮШЕННА, НЕ ПОЛУЧАВШИХ ГЛЮКОКОРТИКОСТЕРОИДНУЮ ТЕРАПИЮ

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В связи с существующей необходимостью выбора объективных инструментальных методов оценки состояния скелетной мускулатуры у больных с мышечной дистрофией Дюшенна целью нашей работы являлась оценка корреляционных связей между мануальными методами оценки силы мышц и результатами магнитно-резонансной томографии (МРТ) скелетной мускулатуры нижних конечностей. Обследовано 15 пациентов с мышечной дистрофией Дюшенна, не получавших глюкокортикостероидную терапию. Пациенты были разделены на две группы: способные (средний возраст — 8,1 года) и неспособные (средний возраст — 12,7 года) самостоятельно передвигаться. Всем пациентам была оценена сила мышц нижних конечностей по шкале Medical Research Council (MRC) и проведена МРТ скелетных мышц тазового пояса, бедер и голеней. Были получены следующие результаты: пациенты, способные передвигаться, характеризовались высокой степенью корреляции данных шкалы MRC и результатов МРТ нижних конечностей при оценке

мышц тазового пояса и бёдер и общего количества баллов (тазового пояса, бедер и голеней) и корреляцией средней степени при оценке мышц голеней. У пациентов, неспособных к передвижению, отмечалась лишь слабая взаимосвязь при оценке мышц тазового пояса и бедер, а также общего количества баллов нижних конечностей. Не было выявлено корреляции между MRC и результатами МРТ в мышцах голеней. Таким образом, МРТ позволяет достоверно оценить степень жировой инфильтрации при мышечной дистрофии Дюшенна и является методом выбора в диагностике и оценке тяжести данного заболевания.

Ключевые слова: мышечная дистрофия Дюшенна (МДД); магнитно-резонансная томография (МРТ); Medical Research Council (MRC).

Duchene muscular dystrophy (DMD) is a severe, progressive, X-linked disease characterized by muscle weakness and atrophy. Its incidence rate is 3.3 per 10,000 newborn boys [5]. The disease is caused by mutations and loss of function in the dystrophin gene (*DMD*) located on the X chromosome (Ch.21) [9].

DMD symptoms are most often seen at 3–5 years of age. The main clinical symptoms include slow progression of disease, a primary lesion of the muscles of the pelvic girdle and thighs, fatigue, an altered myopathic waddling gait, frequent falls, difficulty in climbing stairs, and difficulty in attempting to get up off the floor [18].

Glucocorticosteroid therapy slows the progression of muscle weakness, while retaining the ability to move independently for a longer time [17]. Nevertheless, this type of therapy has numerous side effects and leads to a deterioration in the patients' quality of life [3].

For DMD, changes in a number of biochemical (e.g., increasing levels of creatine phosphokinase, lactate dehydrogenase, ALT, and AST) and genetic markers are typical [2].

A manual five-point assessment of skeletal muscle strength according to the Medical Research Council of Great Britain (MRC) scale is a method widely used to examine patients with neurological pathology, including neuromuscular diseases [4]. Clinical methods to assess the functional state of the muscular system are subjective to a great extent; the final results of these studies depend on the age, the presence of behavioral and cognitive disorders, adherence and motivation of the subject to complete the survey, and other factors [1], as well as on the experience and subjective opinion of the examiner [15].

In this regard, there is a need for objective instrumental methods to assess the state of the muscular system in patients with neuromuscular diseases, including DMD. One of the most effective and safe evaluation methods is magnetic resonance imaging (MRI) [6]. This method of evaluating skeletal muscles has a high sensitivity to tissues, can provide the most reliable estimate of the degree of replacement of skeletal muscles with fat and fibrous tissue, and can identify the inflammatory component accompanying these changes [14].

Our work herein aimed to compare the data of multiparameter MRI results with MRC results in corticosteroid-naive DMD children.

MATERIALS AND METHODS

The study was conducted at the St. Petersburg State Pediatric Medical University. In this study, 15 boys aged 5.11–16.1 years (mean age 9.9 years) with genetically confirmed DMD were examined.

All patients were divided into two groups based on functional capabilities. Group 1 (with a preserved ability for independent movement) consisted of 9 patients aged 5.11–11.5 years (mean age 8.1 years). Group 2 (without the ability of independent movement) consisted of 6 patients aged 11.4–16.1 years (mean age 12.7 years).

The strength of the skeletal muscles was evaluated manually using the MRC scale. In the proximal parts of the lower limbs, the strength of extension, flexion, abduction, and adduction in the hip joint, as well as the strength of flexion and extension in the knee joint, was evaluated manually. In the distal parts of the lower limbs, the strength of flexion and extension of the foot and toes was evaluated.

The total strength of the pelvic and hip muscles and lower legs was calculated, and the total scores for the lower limbs (the pelvic girdle, hip, and lower leg muscles) were also calculated. The MRC index was calculated by the formula [16]

$$\text{MRC (\%)} = \frac{\text{Total score of the muscles under study} \cdot 100}{\text{number of muscles under study} \cdot 5}$$

All patients underwent MRI of the skeletal muscle. The study was performed on a Philips Ingenia 1.5T magnetic resonance tomograph using an external wearable coil and the T2 protocol (TE = 40 ms, TR = 3,500 ms, flip angle = 90°, slice thickness = 10 mm, slice gap = 15 mm). The data obtained were evaluated by the semi-quantitative four-point Mercuri scale [12]. Further, the total scores for the pelvic girdle, hip, and lower leg muscles, as well as the total scores of all the studied muscles of the lower limbs, were calculated.

The muscles of the pelvic girdle (*mm. gluteus maximus, medius, minimus*), thighs (*m. adductor*

longus, m. adductor brevis, m. adductor magnus, m. quadriceps, m. biceps femoris, m. semitendinosus, and m. semimembranosus), and lower legs (*m. gastrocnemius, m. soleus, m. peroneus, m. tibialis anterior, m. tibialis posterior, m. extensor digitorum longus, and m. flexor digitorum longus*) were evaluated during the study.

For the total scores on the Mercuri scale and the MRC index for the pelvic girdle, hip, and lower leg muscles, and the total scores for the lower limbs, the mean values were calculated, and the correlation analysis was performed using the Spearman method, with an assessment of the correlation force on the Chedoke scale. The statistical analysis was performed using Microsoft Excel 2007.

RESULTS

Manual assessment of muscle strength on the MRC scale

In Group 1, the greatest preservation of the strength of muscles flexing the leg at the knee joint was observed (mean score 4.9). There was almost complete preservation of the lower leg extensor muscles (mean score 4.8). In the hip adductors, the mean score was 3.3. The lowest muscle strength was observed with extension (mean score 2.7) and flexion (mean score 3.1) in the hip joint, as well as with hip abduction (mean score 3.0).

Patients in Group 2 showed the greatest strength when flexing the leg at the knee joint (mean score 3.7). In the remaining muscle groups of the pelvic girdle and thighs, there was a decrease in muscle strength, namely, when the leg was extended at the knee joint, the mean score was 1.5, and with hip adduction and flexing at the hip joint, the mean score was 0.3. This group did not display hip abduction and extension at the hip joint (mean score 0.0). The results are provided in Figure 1.

The manual assessment of the strength of the lower leg muscles in Group 1 patients revealed weakness of the extensor muscles of the foot and toes (mean score 4.8). In the remaining muscles, there were no abnormalities (mean score 5.0).

In patients unable to move, the greatest muscle strength was noted in the flexor muscles of the toes (mean score 3.8). In the synergistic muscles, on flexing

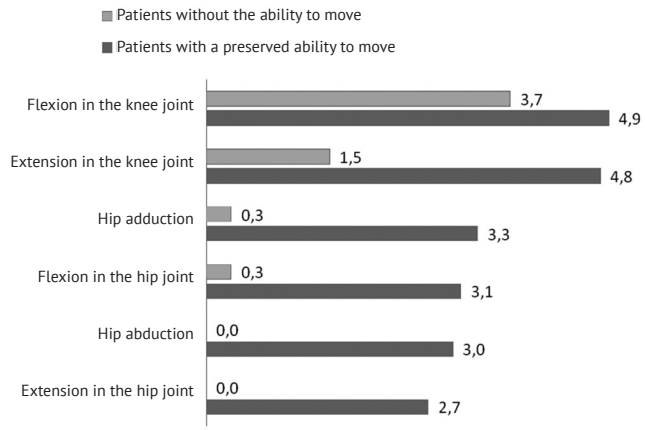

Fig. 1. The results of the MRC score of the pelvic and hip muscles (mean score)

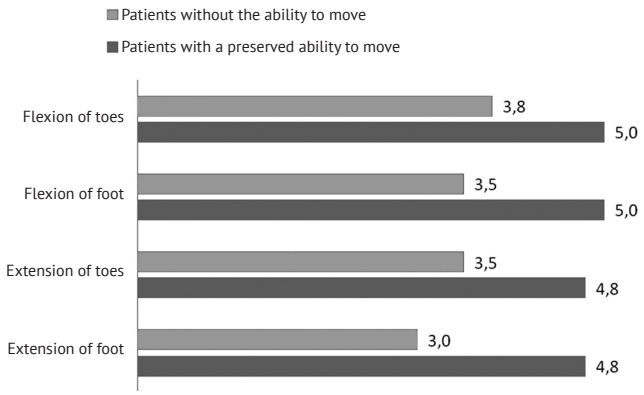

Fig. 2. The results of the MRC score of the lower leg muscles (mean score)

the foot, the mean was 3.5. When assessing the strength of extension of the toes, the mean score was also 3.5. The lowest muscle strength was observed in the extensor muscles of the foot (mean score 3.0). The results are provided in Figure 2.

The mean values of the MRC scale index for Group 1 was 77.8% for the pelvic girdle and hip muscles, 98.7% for the lower leg muscles, and 85.9% for the total score for the lower limbs. For Group 2, the mean value of strength of the pelvic girdle and hip muscles was 20%, that of the lower legs was 65.5%, and the total score for the lower limbs was 45.4% (Figure 3).

Magnetic resonance imaging

In the analysis of skeletal muscles using the Mercuri scale in Group 1 patients, the highest degree of fatty degeneration in the pelvic and femoral regions was detected in *m. adductor magnus* (mean score 3.6), as well as in *mm. gluteus maximus*, *medius*, and *minimus* (mean score 3.1). The smallest changes were observed in *m. gracilis* (mean score 1.0), *mm. adductores longus* and *brevis* (mean score 1.2), *m. semitendinosus* (mean score 1.6), and *m. sartorius* (mean score 1.6). The remaining muscles were characterized by the following degrees of fat infiltration (mean score): 2.4 for *m. vastus medialis*; 2.3 for *mm. semimembranosus* and *vastus lateralis*; 2.2 for *m. biceps femoris*; and 2.1 for *mm. rectus femoris* and *vastus intermedius*.

The largest lesions of *mm. gluteus maximus*, *medius*, and *minimus* (mean score 4.0), as well as *mm. adductor magnus* and *biceps femoris* (mean score 3.8), were observed in Group 2. The relative preservation of *m. gracilis* (mean score 1.6), *m. semitendinosus* (mean score 2.5), and *m. sartorius* (mean score 2.6) was noted. In the pelvic girdle and hip muscles, the following changes were observed (mean score): 3.7 for *m. semimembranosus*; 3.5 for *m. vastus medialis* and *mm. adductor brevis*; 3.3 for *adductor longus*, *mm. vastus intermedius*, and *rectus femoris*; and 3.2 for *m. vastus lateralis*. The results are shown in Figure 4.

When assessing the muscles of the lower legs in Group 1, the greatest changes were noted in *mm. peroneus* (mean score 2.2), as well as in *gastrocnemius* and *soleus* (mean score 1.7), and the relative preservation of *m. tibialis anterior* revealed a mean score of 0.6. In the remaining muscles of the lower leg, no pathological changes were detected.

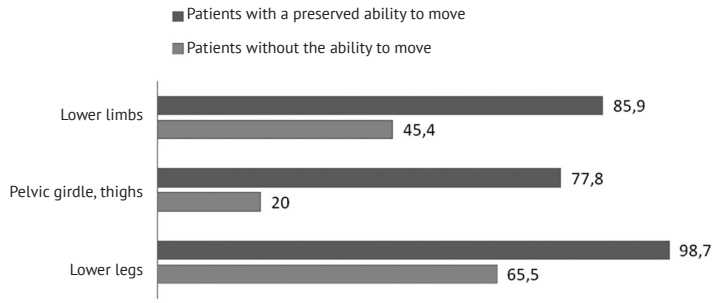

Fig. 3. Average values of the *MRC* index (%)

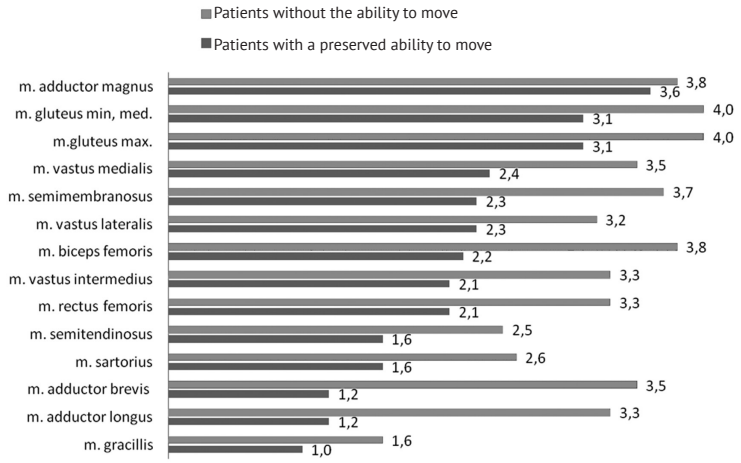

Fig. 4. Results of the evaluation of the pelvic and hip muscles on the Mercuri scale (mean score)

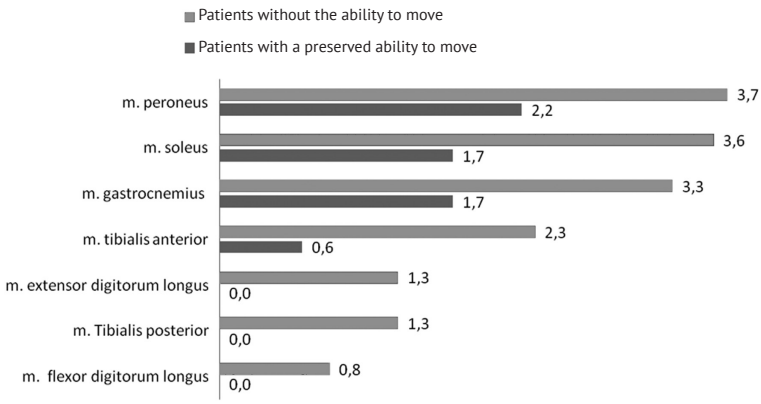

Fig. 5. Results of the evaluation of lower leg muscles according to the Mercuri scale (mean score)

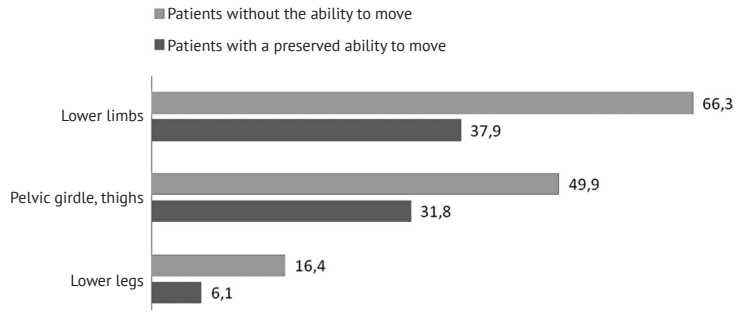

Fig. 6. Average values of the total score on the Mercuri scale

Group 2 was characterized by the greatest lesions found in *mm. peroneus* (mean score 3.7), *soleus* (mean score 3.6), and *gastrocnemius* (mean score 3.3). In the remaining lower leg muscles, the following changes were observed (mean score): 2.3 for *m. tibialis anterior*; 1.3 for *m. extensor digitorum long* and *tibialis posterior*; and 0.8 for *m. flexor digitorum long*. Details are shown in Figure 5.

The mean values of the total score on the Mercuri scale for Group 1 were 31.8 points for the pelvic girdle and hip muscles, 6.1 points for the shin muscles, and 37.9 points for the lower limbs (pelvic girdle, thighs, and lower legs). For Group 2 patients, the mean values were 49.9 points for the pelvic girdle and hip muscles, 16.4 points for the thighs, and 66.3 points for the total of the lower limbs (Figure 6).

The relationship between manual assessment and visualization of skeletal muscles

In Group 1, a high correlation was revealed between the MRC index and the total score on the Mercuri scale in the pelvic girdle and hip muscles ($r = -0.7$) and also in the total score for the lower extremities ($r = -0.8$). For the lower legs, the average correlation force between the scales ($r = -0.5$) was established.

For Group 2, there was a weak correlation force when evaluating pelvic and hip muscles as well as the total score ($r = -0.4$). There was no correlation between the MRC index and the total score on the Mercuri scale in the lower leg muscles ($r = -0.1$).

DISCUSSION

The data obtained were confirmed by Kim et al. [8], who quantitatively assessed the skeletal muscles of the pelvic girdle and thighs in children with DMD using the T2 mapping protocol, where the highest degree of fat substitution was detected in *m. gluteus maximus*.

In the works of K. Polavarapu, M. Manjunath, V. Preethish-Kumar et al. [13], children aged 4–15 years were examined (7.8 ± 2.8 years). Based on the visualization results of the skeletal muscles of the pelvic girdle and thighs with further evaluation by the Mercuri scale, severe fatty degeneration of *mm. gluteus medius* and *minimus* was established, as well as that of *m. adductor magnus*, which was in line with the results of our study. The greatest preservation of *mm. sartorius, gracilis*, and *semimembranosus* was observed, while, according to our study, the lowest degree of hip muscle damage was noted in *mm. sartorius*, *gracilis*, and *semitendinosus*.

In the work of K. Polavarapu, M. Manjunath, V. Preethish-Kumar et al., there was a strong inverse correlation between the results of the MRC scale and the MRI data of skeletal muscles, which coincides with our results obtained during the examination of Group 1 patients. However, in our work, a correlation was not observed in Group 2 patients regarding the lower leg muscles ($r = -0.1$), and the pelvic girdle and hip muscles, as well as the total score for the lower limbs, was characterized only by an average correlation force ($r = -0.4$). This can probably be explained by difficulties in manually assessing the muscle strength in older patients due to progressive contractures of the knee joints [7].

The visualization data on the preservation of hip muscles were inconsistent with the work of G.C. Liu, Y.J. Jong et al. [10]. The MRI results indicated the relative preservation of *m. gracilis*, *sartorius*, *semitendinosus,* and s*emimembranosus*. Nevertheless, according to the Mercuri scale, the mean change of *m. semimembranosus* in our work was estimated as 3.7 points in Group 2, which corresponded to severe fatty infiltration. In Group 1 patients, the lesion patterns were characterized by a relative preservation of only *mm. sartorius*, *gracilis*, and *semitendinosus*.

The results of our semi-quantitative assessment of the lower leg muscles corresponded to the study of Torriani, Townsend et al. [11]. When applying the T1w mode, the highest degree of fat substitution was observed in *mm. gastrocnemius*, *soleus*, and *peroneus*, while *m. tibialis posterior*, *tibialis anterior*, *extensor digitorum*, and *flexor digitorum* were characterized by a smaller degree of lesions or relative preservation.

CONCLUSIONS

Comparing the MRI data with the MRC scale enabled us to identify the strong inverse correlation in Group 1 patients when assessing the total number of skeletal muscles of the lower limbs and a separate evaluation of the pelvic and hip muscles. The degree of fatty degeneration and the strength of muscles of the lower legs were characterized by an inverse correlation of average strength.

In Group 2 patients, an inverse correlation of weak strength was revealed when evaluating the pelvic and hip muscles, as well as the total score for the lower limbs. There was no significant correlation in the muscles of the lower legs.

MRI allowed us to reliably determine the extent of fatty infiltration in DMD and is a method of choice in diagnosing and evaluating disease severity.

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