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Relationships between clinical data and quantitative EMG findings in facioscapulohumeral muscular dystrophy

Dystrofia twarzowo-łopatkowo-ramieniowa – korelacje elektrofizjologiczno-kliniczne

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Abstract

Background and purpose: In recently published reports, electrophysiological findings were analysed, in some facioscapulohumeral muscular dystrophy (FSHD) cases without genetic disease confirmation. In several reports, some electrophysiological findings were described, not specific for myopathy. The aim of study was to analyse electrophysiological findings in a genetically homogeneous FSHD group to find possible relationships between electromyography (EMG) abnormalities and clinical symptoms.
Material and methods: 37 patients with genetically proven FSHD (23 men and 14 women) aged 7-58 years (mean 28.8 years) were studied. Electromyographic examinations were done according to a uniform scheme for FSHD. Quantitative EMG examination was performed in vastus lateralis, tibialis anterior, deltoid and biceps brachii muscles.
Results: There was no correlation between clinical features and electrophysiological findings. EMG confirmed myopathic changes in all patients with most advanced changes in tibialis anterior and deltoid muscles. Some of these changes were unspecific for myopathy and the degree of their intensity differed in particular muscles. The most advanced changes were observed in the tibialis anterior and deltoid muscles. The usefulness of the size index for myopathic processes assessment was confirmed. Analysis of so-called outliers

Streszczenie

Wstęp i cel pracy: W dotychczas publikowanych doniesieniach analizowano zjawiska elektrofizjologiczne u chorych z dystrofią twarzowo-łopatkowo-ramieniową (*facioscapulohumeral muscular dystrophy* – FSHD), niekiedy bez genetycznego potwierdzenia rozpoznania. W niektórych badaniach wykazano obecność nieswoistych dla miopatii zmian elektrofizjologicznych. W pracy podjęto próbę oceny zmian elektromiograficznych (EMG) w genetycznie homogennej grupie chorych na FSHD. Przeanalizowano zmiany elektrofizjologiczne i wyłoniono ewentualne korelacje elektrofizjologiczno-kliniczne w FSHD.
Materiał i metody: Materiał stanowiła grupa 37 pacjentów z genetycznie potwierdzonym rozpoznaniem FSHD (23 mężczyzn i 14 kobiet) w wieku 7–58 lat (średnia wieku: 28,8 roku). Badania EMG przeprowadzono wg jednolitego schematu. Wykonywano ilościowe badanie EMG mięśni: obszernego bocznego uda i piszczelowego przedniego, naramiennego, dwugłowego ramienia.
Wyniki: Nie wykazano korelacji pomiędzy stopniem nasilenia objawów klinicznych a parametrami EMG. Badania pozwoliły na potwierdzenie miopatycznego charakteru zmian. Zmiany były nieswoiste, a stopień ich nasilenia różny w poszczególnych mięśniach. Największe zmiany obserwowano w mięśniu piszczelowym przednim i naramiennym.

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for motor unit activity potential parameters did not show any new data for evaluation of the myopathic process. Myopathic changes in our material were not as advanced as those described in classical dystrophies. Histopathological examinations of skeletal muscle were normal in about 1/3 of patients.

Conclusions: We established that myopathic changes are clearly present in FSHD, with different degrees of intensity, most pronounced in tibialis anterior and deltoid muscles. There was no correlation between electrophysiological findings and clinical features. The size index provided the highest motor unit potential diagnostic sensitivity in FSHD.

Key words: myopathy, facioscapulohumeral muscular dystrophy, electromyography, motor unit potential, size index.

Potwierdzono przydatność wskaźnika wielkości w ocenie procesu miogennego, analiza tzw. *outliers* dla parametrów potencjałów jednostki ruchowej nie wniosła nowych danych. Zmiany miopatyczne w analizowanym materiale nie były tak zaawansowane jak te w klasycznych dystrofiach. Badanie histopatologiczne mięśnia szkieletowego w ok. 1/3 przypadków było prawidłowe.

Wnioski: W FSHD badania elektrofizjologiczne potwierdzają miopatyczne uszkodzenie mięśni, o różnym stopniu nasilenia w poszczególnych mięśniach. W największym stopniu zmiany obecne są w mięśniu piszczelowym przednim i naramiennym. Parametry elektromiograficzne nie wykazują korelacji ze stopniem zaawansowania objawów klinicznych. W opracowaniu autorów największą diagnostyczną czułość dla zmian miopatycznych wykazywał wskaźnik wielkości potencjałów czynnościowych jednostek ruchowych.

Słowa kluczowe: miopatia, dystrofia twarzowo-łopatkowo-ramieniowa, elektromiografia, potencjał czynnościowy jednostki ruchowej, wskaźnik wielkości.

Introduction

Facioscapulohumeral muscular dystrophy (FSHD), one of the most common muscular dystrophy variants [1], was first described in the middle of the 19th century [2]. The inheritance is autosomal dominant and the genetic defect results from deletion of D4Z4 tandem repeats at the 4q35 locus [3]. The molecular pathology is very complicated and not clearly understood [4].

Clinical features are very characteristic, and the distribution of the weakness is quite unique. Facial weakness is evident in limited movements of lips; patients are unable to whistle or inflate their cheeks. Scapular winging and characteristic appearance of the shoulder girdle, so-called triangular shoulders, is typical. Lower limb weakness affects mainly distal muscles, especially the anterior tibialis muscle, which, if evident, may suggest the neurogenic process. Contrary to other dystrophies, asymmetry and selectivity of muscle involvement are very characteristic for FSHD.

Before molecular tests became available, the diagnosis of FSHD was based on the clinical grounds, family history and electromyography (EMG) findings. At that time, FSHD diagnosis in some cases was difficult to make, due to relatively high frequency of atypical and subclinical cases, also due to intra- and interfamilial clinical variability of the disease.

The results of EMG in FSHD were generally assessed as myopathic [5,6]. In some patients, however, EMG changes atypical for myopathy were described. Changes atypical for myopathy included increased amplitude of single motor unit potentials (MUPs) and spontaneous activity at rest [7]. One of the causes of atypical electrophysiological findings recorded in FSHD could be the presence of inflammatory changes seen in a muscle specimen [8-11]. Munsat even suggested the existence of an FSHD inflammatory variant and showed the presence of fibrillations at rest, which he interpreted as a neurogenic sign [12]. It is now known that fibrillations and positive sharp waves may be recorded not only in neurogenic but also in myopathic processes, especially in the acute stages of myositis and in quickly progressive muscular dystrophy [13,14]. There are no current data available on the frequency of so-called inflammatory changes in FSHD muscles in patients with the diagnosis confirmed by molecular tests.

The aim of the study was electrophysiological characterisation of FSHD, especially in the view of recent reports. We intended to assess the relationship between clinical and electrophysiological findings and discuss appropriate selection of particular muscle and MUP parameters to be tested. We also planned to assess the electrophysiological changes in subclinical cases of FSHD.

Material and methods

We performed quantitative EMG in 37 patients (23 men and 14 women) aged 7-58 years (mean: 28.8 years) with the diagnosis of FSHD confirmed by molecular tests. The group was genetically homogeneous (Table 1). The clinical status was assessed according to the FSHD grading scale (Table 2, Fig. 1). Nine cases were of early onset according to Brouwer's criteria [15]. These were associated with a rather quick and unfavourable course. Three patients presented with subtle or subclinical symptoms. The remaining 25 cases had a typical FSHD phenotype (Tables 1 and 3).

The Medical Research Council (MRC) scale (grades 0-5) was used to assess muscle strength. Mean results of muscle strength assessment in different FSHD types are presented in Table 4 and Fig. 2.

Electrophysiological tests comprised a conduction study of motor and sensory nerves (median, peroneal and sural) and quantitative concentric needle electromyographic (CNEMG) examination of 4 muscles (biceps brachii – BB, deltoid – DD, vastus lateralis – VL, tibialis anterior – TA). Electromyographic recordings were done on one side; in case of asymmetric muscle involvement, the examination was performed in the more clinically affected muscle.

Quantitative EMG was performed in a standard way using concentric needle electrodes (type DCN 37, Medtronic) and Keypoint, Medtronic Functional Diagnostics EMG system; MUPs were registered using multi-MUAP software. Only muscles with at least 20 different MUP samples were included for further analysis. During voluntary movement, MUP parameters (duration, amplitude, size index and number of polyphasic potentials) were analysed.

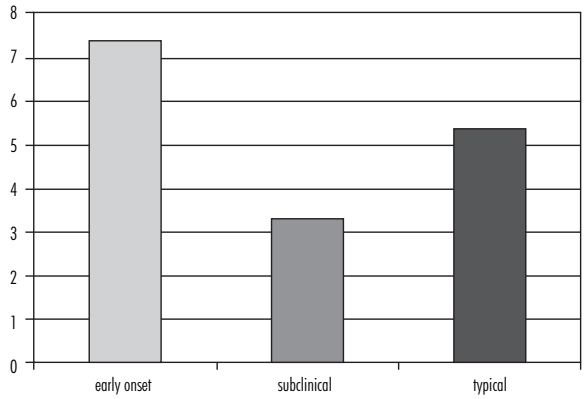
Activity at rest, amplitude and density of electrical activity at maximal effort were evaluated visually and quantitatively directly from the screen of the monitor.

Table 1. Clinical characteristics and heterogeneity in studied patients with facioscapulohumeral muscular dystrophy (FSHD)

	Familial cases (*n* = 25)	Sporadic cases (*n* = 12)	Total (*n* = 37)
Sex			
Female	10	4	14
Male	15	8	23
Age [years], mean (range)	32.4 (13-58)	22.5 (7-47)	28.3 (7-58)
FSHD variants			
Early onset variant	4	5	9
Subclinical variant	4	0	4
Typical variant	17	7	24

Table 2. Grading system for facioscapulohumeral dystrophy (modified from scale by Ricci and Padberg)

0	no signs of muscle weakness
1	facial weakness only
2	mild scapular weakness, no limitations of abduction or elevation, often asymptomatic
3	moderate scapular weakness arm abduction above 60°, usually symptomatic
4	severe scapular weakness arm abduction above 60°, no lower limb involvement abdominal muscles might be weak
5	foot-extensor weakness; no pelvic girdle weakness
6	mild pelvic girdle weakness stands up without support
7	moderate pelvic girdle and proximal leg weakness stands up with support of one arm
8	severe pelvic girdle and proximal leg weakness stands up with support of both arms, cannot walk stairs walks unaided, uses wheelchair for some outdoor activities
9	walks a few steps, needs wheelchair outdoors, uses wheelchair indoors
10	completely wheelchair dependent



Phenotype assessment in FSHD patients [7]. Patients with early onset of the disease presented with higher mean grading. Subclinical cases had the lowest grading.

Fig. 1. Mean grading in different types of facioscapulohumeral dystrophy (FSHD)

Table 3. Clinical and electrophysiological features of patients with facioscapulohumeral dystrophy (FSHD)

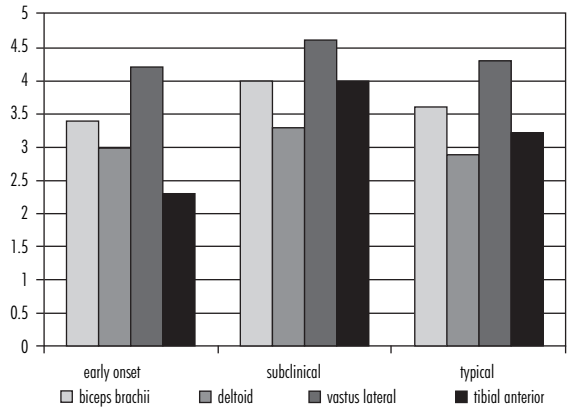
Patient	Gender	Age at examination	FSHD 4q23 deletion	Family history	Disease duration	Grading*	Clinical phenotype	EMG results
1	F	15	14	sporadic	15	6	early onset	myopathy
2	M	22	24	sporadic	6	7	typical	myopathy
3	M	16	20	familial		3	typical	myopathy
4	F	14	20	familial		7	typical	myopathy
5	M	32	20	familial	19	7	typical	myopathy
6	F	58	20	familial	–	2	subclinical	myopathy
7	M	15	10	familial		7	early onset	myopathy
8	F	56	27	familial	20	6	typical	myopathy
9	F	20	27	familial		6	typical	myopathy
10	F	52	24	familial		7	typical	myopathy
11	M	47	15	sporadic	7	7	typical	myopathy
12	M	23	24	sporadic		5	typical	myopathy
13	F	13	10	sporadic		10	early onset	myopathy
14	M	13	19	familial		7	early onset	myopathy
15	M	54	22	familial	12	7	typical	myopathy
16	M	14	10	sporadic		3	typical	myopathy
17	M	20	19	familial		5	typical	myopathy
18	M	16	16	sporadic	2	3	typical	myopathy
19	F	10	15	familial	15	7	early onset	myopathy
20	M	38	15	familial	29	10	early onset	myopathy
21	M	51	20	familial	33	6	typical	myopathy
22	M	13	11	sporadic	10	7	early onset	myopathy
23	M	38	17	familial	24	6	typical	myopathy
24	M	33	22	familial	3	5	subclinical	myopathy
25	M	19	27	familial		2	typical	myopathy
26	M	46	15	familial	28	5	typical	myopathy
27	M	24	11	familial		8	typical	myopathy
28	F	14	17	familial		3	typical	myopathy
29	F	30	24	familial	20	?	typical	myopathy
30	F	7	10	sporadic		7	early onset	myopathy
31	F	12	16	familial		6	typical	myopathy
32	F	43	22	sporadic	15	6	typical	myopathy
33	M	44	20	sporadic		6	typical	myopathy
34	M	37	26	familial		3	subclinical	myopathy
35	F	20	22	familial	–	2	subclinical	size index only
36	M	14	10	sporadic		6	early onset	myopathy
37	M	55	24	familial	40	7	typical	myopathy with some unspecific changes

EMG – electromyography, M – male, F – female
**Grading – clinical phenotype according to FSHD scale (see Table 2)*

Table 4. Muscle strength in 136 examined muscles of patients with FSHD

Examined muscles	Biceps brachii muscle (*n* = 35)	Deltoid muscle (*n* = 34)	Vastus lateralis muscle (*n* = 37)	Tibialis anterior muscle (*n* = 30)
Mean strength (MRC grade)	3.6	3.2	4.2	3.3
% of muscle with preserved full strength (MRC scale grade 5)	29.4	14.7	50.0	26.7

MRC – Medical Research Council scale (0-5)



VL muscle strength is well preserved in all clinical FSHD types; it is between 4.5 and 4.1 MRC grade.
The second best preserved muscle is BB.

Fig. 2. Mean strength (MRC grade) of muscles in different types of facioscapulohumeral dystrophy (FSHD)

In the majority of familial cases, EMG examination was performed in the one affected only. In four families electromyography was done in two affected persons from the same family.

Muscle biopsies were done in 28 cases (10 VL and 18 BB muscles), on the side which was not affected by EMG examination.

Statistical methods used for data analysis were as follows: for interval variables – simple descriptive statistics, such as means, standard deviations (SD), medians and ranges.

The Shapiro-Wilk W-statistic was used to test for normality, and Spearman coefficients were used as a measure of the relationship between variables. *P*-value < 0.05 was used to reject the 'null' hypothesis [16]. Calculations were performed using SAS System [17].

Results

Obtained results were compared with the normal values adopted by the Neurophysiological Unit of the Neurological Department, Medical University of Warsaw.

Conduction velocities, distal latencies and amplitudes of evoked potentials in motor ad sensory fibres were within normal limits.

The CNEMG tests revealed myopathic changes in all examined patients and in 130 out of 136 muscles.

In the minority of cases, fibrillations and/or positive sharp waves (13.5%) and pseudomyotonic discharges (2.7%) were recorded. No spontaneous activity was observed in DD muscles.

The pattern of electrical activity was proportional to the effort (normal) in 60.5% of examined muscles. A pathological interference pattern was recorded in less than 40% of examined muscles. A decreased (lower than 1 mV) amplitude at maximal effort was found in less than 50% of muscles – most frequently in TA and DD muscles (Table 5).

Pathological interference pattern (50% of cases) with decreased (< 1.0 mV) maximal effort amplitude (64% of muscles) correlated with decreased TA muscle strength (grade 3.2 in MRC).

Maximal effort amplitude higher than 5.0 mV, without decrease in density, was recorded in 8.8% of all examined muscles, most frequently in DD and VL (Table 5).

In individual muscles, different degrees of single MUP abnormalities were recorded, most frequently in TA and DD muscles (Tables 6 and 7). Short duration of potentials and decreased size index in more than 50% of DD and TA muscles were noted.

In only 14% of FSHD cases, decreased duration and SI values in all four examined muscles were recorded (Table 8). This finding confirms selective muscle involvement.

In 17.7% of DD muscles, mean MUP amplitude was decreased, and in 11.8% of DD and 11% of VL it was increased. There was no mean MUP duration or SI above 2 SD of control (normal value) in any of the examined muscles.

Table 5. Electrophysiological results: amplitude of interference pattern

Muscles	Interference pattern amplitude [mV]; range	Muscles with max. effort amplitude higher than 5 mV, % (*n*)	Muscles with max. effort amplitude lower than 1 mV, % (*n*)	Muscles with pathological interference pattern in max. effort, % (*n*)
Biceps brachii ($n = 35$)	0.1-7.0	8.57 (3)	54.34 (19)	32.35
Vastus lateralis ($n = 37$)	0.1-9.0	11.44 (4)	39.39 (13)	22.86
Deltoid ($n = 34$)	0.2-8.0	12.50 (4)	35.45 (11)	51.52
Tibialis anterior ($n = 30$)	0.1-5.5	3.33 (1)	64.27 (18)	50.00
Total ($n = 136$)	0.12-7.4	8.8 (12)	44.8 (61)	39.50

Table 6. Mean values of chosen motor unit action potential (MUP) parameters in examined muscles of FSHD patients and controls

Muscle	Subjects	Amplitude of MUP (mV)*	Duration of MUP (ms)*	Size index*
Biceps brachii	FSHD	389 ± 152 (91-988)	7.33 ± 1.16 (4.55-10.3)	0.034 ± 0.4 (−1.01-1.19)
	Controls	436 ± 115 (206-666)	9.9 ± 1.4 (7.1-12.7)	0.65 ± 0.33 (−0.01-1.31)
Deltoid	FSHD	496 ± 205 (233-1228)	7.55 ± 1.37 (3.1-9.5)	0.28 ± 0.41 (−0.89-1.45)
	Controls	550 ± 110 (330-770)	10.4 ± 1.3 (7.8-13.0)	0.85 ± 0.31 (−0.23-1.47)
Vastus lateralis	FSHD	710 ± 354 (223-1960)	8.74 ± 1.92 (6.0-14.2)	0.63 ± 0.58 (−0.5-1.74)
	Controls	687 ± 239 (209-1165)	11.7 ± 1.9 (7.9-15.5)	1.24 ± 0.39 (−0.46-2.02)
Tibialis anterior	FSHD	561 ± 226 (160-1395)	7.79 ± 1.62 (4.3-11.2)	0.298 ± 0.50 (−0.95-1.02)
	Controls	666 ± 254 (158-1174)	11.4 ± 1.2 (9.0-13.8)	1.17 ± 0.30 (−0.57-1.77)

**Data are presented as means ± standard deviations (range)*
FSHD – facioscapulohumeral dystrophy

Table 7. The percentage of facioscapulohumeral dystrophy patients with abnormal values (> 2 standard deviations [SD]) of mean motor unit action potential (MUP) parameters in examined muscles

Muscle	Mean MUP amplitude		Mean MUP duration		Mean MUP size index	
	> 2 SD below	> 2 SD above	> 2 SD below	> 2 SD above	> 2 SD below	> 2 SD above
Biceps brachii ($n = 35$)	5.7%	2.9%	42.9%	0%	34.3%	0%
Deltoid ($n = 34$)	17.7%	11.8%	55.8%	0%	50%	0%
Vastus lateralis ($n = 37$)	0%	10.8%	37.8%	0%	40.5%	0%
Tibialis anterior ($n = 29$)	0%	3.5%	72.4%	0%	68.9%	0%

Table 8. Number and percentage of muscles with at least 3 outlier values of individual MUP amplitude, duration or size index

Muscle	MUP amplitude below lower limit	MUP amplitude above upper limit	MUP duration below lower limit	MUP duration above upper limit	MUP size index below lower limit	MUP size index above upper limit
Biceps brachii ($n = 35$)	19 (54%)	2 (5.7%)	2 (5.7%)	0	2 (5.7%)	0
Deltoid ($n = 34$)	6 (17%)	1 (3%)	2 (6%)	0	1 (3%)	0
Vastus lateralis ($n = 37$)	7 (19%)	3 (8%)	0	0	0	0
Tibialis anterior ($n = 29$)	11 (38%)	2 (7%)	4 (14%)	0	2 (6.6%)	0

Table 9. Percentage of diminished mean motor unit action potential values obtained in the same patient with facioscapulohumeral dystrophy

Number of muscles	Duration *n* (%)	Amplitude *n* (%)	Size index *n* (%)
4 muscles	4 (14.29%)	–	4 (14.81%)
3 muscles	7 (25%)	–	3 (11.11%)
2 muscles	4 (14.29%)	–	20 (40.74%)
1 muscle	8 (28.57%)	5 (17.86%)	4 (14.81%)

In all four examined muscles, MUP duration and size index were decreased only in about 14% of cases, which shows and confirms the selectivity of muscle involvement.

In 19 BB muscles (54%) and in 11 TA (38%) muscles, the amplitude of outliers was below the lower limit, whereas in 2 (7%) TA muscles the amplitude of outliers was above the upper limit (Tables 8 and 9).

Generally, there was no correlation between the degree of EMG changes, the age of FSHD patients and clinical phenotype (early onset, subclinical and typical).

In two out of three patients with subclinical FSHD phenotype, EMG showed typical myopathic changes. In one subclinical case (no. 35, Table 3) only SI was decreased and the other MUP parameters remained within normal limits.

There were no pathological changes in nine (31%) out of 28 muscle biopsy specimens (BB, VL). In the remaining cases, the degree/intensity of myopathic changes in muscle biopsy differed; mainly atrophy of fibres and decreased number of type 1 fibres were observed. In one case inflammatory-like changes were demonstrated.

There was no clear relationship between weakness in any given (VL, BB) muscle and EMG results or histopathological findings. However, EMG findings and histopathological material identified did not come from the same muscle, because the biopsy was always done on the side opposite to the EMG-tested side.

We found that decreased MUP parameters (SI, duration, single potential amplitude, mean effort amplitude) were most frequently observed in TA. The next most affected muscle was DD. A pathological interference pattern was most frequently seen in DD and TA muscles.

Discussion

It is believed that EMG studies in FSHD could provide much less information than in other dystrophies. Why EMG in such clear myopathy can be myopathic, normal, or can present with some findings unspecific for myopathy, is not known. Even in cases with clearly pure myopathic phenotype, EMG may show differently expressed myopathic features.

The study was conducted in quite a large, genetically homogeneous FSHD group; nevertheless, the occasional presence of spontaneous activity at rest, high mean MUP amplitude and high maximal effort amplitude is rather unexpected.

Several previous studies [5,6,13,18] provided data on the sensitivity of quantitative EMG in FSHD patients.

In any kind of myopathy, BB and VL muscles are routinely examined in EMG. It is known, however, that selective and asymmetric muscle involvement is characteristic for FSHD [1,7].

Electrophysiological findings in our FSHD patients showed myopathic changes in all cases. Nonetheless, the degree of abnormalities was differently expressed in particular muscles. Relatively early and marked clinical involvement of TA and DD muscles reflected clear myopathic changes. VL muscles were often spared (Tables 4 and 5, Fig. 3).

Podnar and Zidar showed that thickness (area/amplitude) was the most sensitive MUP parameter, followed by duration and finally by size index [5,19,20]. We found that SI was most informative among evaluated parameters.

Both parameters (SI and thickness) are dependent on area and amplitude. SI also evaluates potentials' thickness, but it has an advantage over area/amplitude in that it is independent of the needle's movement [21]. Therefore we considered SI to be the most objective and informative parameter.

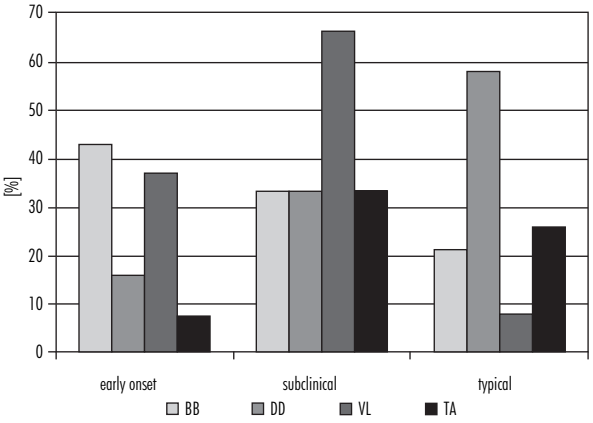
The SI parameter was first shown to be very sensitive in detecting neurogenic changes in muscle [19]. We found that SI was also a relatively sensitive parameter for evaluating myopathic changes [14]. The current study confirmed that SI is a very informative MUP parameter in FSHD. SI reduction reflects a decrease of motor unit potential area due to diminished size and number of activated muscle fibres.

The discrepancy between our and Podnar's results may be due to the number of muscles being studied. We studied four muscles: TA, VL, BB and DD. Podnar and Zidar evaluated two muscles, BB and VL, which are not markedly affected in FSHD [5]. We tested muscles on the more affected side, while in Podnar's study, right-sided muscles were examined, irrespective of muscle asymmetry involvement.

Podnar and Zidar found that outliers demonstrated higher sensitivity than mean MUP values [5]. We showed that decreased amplitude was the only outlier present in about half of BB and TA muscles.

In our material muscle biopsy was done in 73% of cases. Only in one patient were inflammatory-like changes detected (individual no. 36). In this case, there was no spontaneous activity at rest. This particular patient (no. 36, Table 3) was a sporadic case with an early onset FSHD phenotype that clinically did not differ from other early onset patients in our material. On the other hand, in all patients with typical FSHD phenotype and with spontaneous activity at rest, muscle biopsy did not show any inflammatory changes. In our study, spontaneous activity at rest was detected in 13.5% of cases. This is the result of hyperexcitability of destroyed muscle fibre membrane.

Overall, muscle biopsy was not helpful in making the FSHD diagnosis; in about one third of cases, no pathological changes were observed. Nevertheless, muscle biopsy is important in excluding alternative diagnoses such as inflammatory, structural and metabolic myopathies.



BB – biceps brachii, DD – deltoid, VL – vastus lateral, TA – tibial anterior
Full muscle strength of VL is preserved in over 60% of subclinical FSHD, but varies considerably in early onset and typical cases.

Fig. 3. Percentage of muscles with normal strength (5 on MRC scale) in different types of facioscapulohumeral dystrophy (FSHD).

In Stubgen's study [6], a clear correlation between patient age, disease duration and EMG results (MUP amplitude, duration in triceps brachii muscles) was demonstrated. In this study, however, the group of patients was clinically homogeneous. The correlations were less obvious in TA muscle, where clinical data inversely correlated with the MUP duration.

The lack of correlation between patient's age and EMG parameters in our study was not unexpected. Our FSHD patients presented with heterogeneous phenotype (early onset, subclinical and typical); the onset of the disease in particular cases differed, and the severity and involvement of individual muscles varied considerably.

The present study confirmed high diagnostic sensitivity of multi-MUP parameters analysis, particularly MUP size index and duration. In patients with subclinical FSHD phenotype, decreased SI values without other EMG abnormalities may be the only electrophysiological sign suggesting myopathic lesion.

Marked and evident myopathic changes were noted in TA muscles relatively early; therefore EMG of these muscles should be included in the standardized electrophysiological procedure in patients with suspected FSHD.

In typical muscular dystrophy, myopathic features were previously well described [13]. The study was done before genetic testing became available; therefore the population could consist mainly of patients with Duchenne and typical Becker muscular dystrophies – the most frequent myopathies.

Myopathic changes in FSHD were not so advanced as those seen in dystrophinopathies, which were the electrophysiological model for myopathy [13]. In FSHD, BB and VL may be only mildly or not affected. Compared to dystrophinopathy, FSHD is rated as a mild and slowly progressing myopathy, with some subclinically affected muscles. This relatively mild progression is reflected by rare spontaneous activity, no signs of denervation, presence of high mean MUP amplitude and high maximal effort amplitude, the latter being a sign of regeneration.

Fibrillations and pseudomyotonic discharges were only occasionally seen in FSHD; they occurred most frequently in acute and quickly progressing myopathic processes. Activity at rest is more frequently observed in acute progressing Duchenne muscular dystrophy (DMD).

In Emery-Dreifuss muscular dystrophy (EDMD), EMG results were generally compatible with myopathy. However, high amplitude polyphasic motor unit potentials, so-called irregular MUPs (atypical for myopathy), were also observed [22]. This dystrophy is characterized by relatively slow symmetric progression, hypoplastic muscle and relatively well preserved muscle strength. High amplitude potentials reflected the process of regeneration, a sign of slowly progressing myopathy.

When discussing the results obtained by Stubgen, Podnar and ours, it should be stressed that in each study the most sensitive MUP parameter in detecting myopathic changes in FSHD is different. In Podnar's study it was thickness [5], in Stubgen's study it was MUP duration [6], in our study it was SI followed by duration. In each study, however, different muscles were analysed. Additionally, FSHD patients in the study of Stubgen were clinically relatively homogeneous [6], in the study of Podnar clinical phenotype was not presented [5], and in our study FSHD patients presented with heterogeneous phenotype.

Due to the factors discussed above, clinical heterogeneity of the disease, selectivity and asymmetry of muscle involvement in FSHD, and different inclusion criteria for each of the studies, electrophysiological results in relation to sensitivity of particular MUP parameters must be heterogenic.

Conclusions

1. We did not find any clear correlation between clinical FSHD type, age of onset and electrophysiological findings.
2. Myopathic changes were most advanced in TA and DD muscles, and correlated well with early and marked clinical involvement of these muscles. TA and DD muscles should be examined in any suspected FSHD case.
3. The most frequent abnormal MUP parameter providing the highest diagnostic sensitivity was SI, followed by MUP duration. SI may be the only abnormal parameter in subclinical muscle involvement.
4. Rare high amplitude potentials and high amplitude of maximal effort were regarded as atypical for myopathy and could result from muscle fibre regeneration.

Disclosure

Authors report no conflict of interest.

References

1. Padberg G.W. Facioscapulohumeral disease. Thesis. University of Leiden, Leiden 1982.
2. Duchenne G.B. Recherches sur la paralysie musculaire pseudohypertrophique, ou paralysie myosclerosique. *Arch Gen Med* 1868; 179: 5-11.
3. Wijmenga C., Hewitt J.E., Sandkuijil L.A., et al. Chromosome 4q DNA rearrangements associated with facioscapulohumeral muscular dystrophy. *Nat Genet* 1992; 2: 26-30.
4. Tawil R., van der Maarel S.M. Facioscapulohumeral muscular dystrophy. *Muscle Nerve* 2006; 34: 1-15.
5. Podnar S., Zidar J. Sensitivity of motor unit potential analysis in facioscapulohumeral muscular dystrophy. *Muscle Nerve* 2006; 34: 451-456.
6. Stubgen J.P. Facioscapulohumeral muscular dystrophy. A quantitative electromyographic study. *Electromyogr Clin Neurophysiol* 2007; 47: 175-182.
7. Padberg G.W., Lunt P.W., Koch M. Facioscapulohumeral muscular dystrophy. In: Emery A.E.H. [ed.]. Diagnostic criteria for neuromuscular disorders. *Royal Society of Medicine Press*, London 1997, p. 22.
8. Bodensteiner J.B., Schochet S.S. Facioscapulohumeral muscular dystrophy: the choice of a biopsy site. *Muscle Nerve* 1986; 9: 544-547.
9. Brooke M.H., Engel W.K. The histologic diagnosis of neuromuscular diseases: review of 79 biopsies. *Arch Phys Med Rehabil* 1966; 47: 99-121.
10. Dubowitz V., Brooke M.H. Muscle biopsy: a modern approach. *Saunders*, London 1973, pp. 202-212.
11. Arahata K., Ishihara T., Fukunaga H., et al. Inflammatory response in facioscapulohumeral muscular dystrophy (FSHD): immunocytochemical and genetic analyses. *Muscle Nerve* 1995; Suppl. 2: 56-66.
12. Munsat T., Piper D., Cancilla P., et al. Inflammatory myopathy with facioscapulohumeral dystrophy. *Neurology* 1972; 22: 335-347.

13. Buchthal F., Kamieniecka Z. The diagnostic yield of quantified eletromyography and quantified muscle biopsy in neuromuscular disorders. *Muscle Nerve* 1982; 5: 265-280.
14. Rowińska-Marcińska K., Szmidt-Sałkowska E., Kopeć A., et al. Motor unit changes in inflammatory myopathy and progressive muscular dystrophy. *Electromyogr Clin Neurophysiol* 2000; 40: 431-439.
15. Brouwer O.R., Padberg G.W., Wijmenga C., et al. Facioscapulohumeral muscular dystrophy in early childhood. *Arch Neurol* 1994; 51: 387-394.
16. Armitage P., Berry G., Matthews J.N.S. Statistical methods in medical research. 4th ed. *Blackwell Science Ltd*., 2002.
17. SAS Institute Inc. SAS/STAT user's guide. Version 8. *SAS Institute Inc*., Cary 1999.
18. Fawcett P., Kennett R.P., Schofield I.S. A neurophysiological investigation of the facio-scapulo-humeral (FSH) syndrome. *J Neurol Sci* 1999; 98 (Suppl): 195.
19. Sonoo M., Stalberg E. The ability of MUP parameters to discriminate between normal and neurogenic MUPs in concentric EMG: analysis of the MUP "thickness" and the proposals of "size index". *Electroencephalogr Clin Neurophysiol* 1993; 89: 291-303.
20. Nandedkar S.D., Barkhaus P.E., Sanders D.B., et al. Analysis of amplitude and area of concentric needle EMG motor unit action potentials. *Electroencephalogr Clin Neurophysiol* 1988; 69: 561-567.
21. Zalewska E., Hausmanowa-Petrusewicz I. Effectiveness of motor unit potentials classification using various parameters and indexes. *Clin Neurophysiol* 2000; 111: 1380-1387.
22. Rowińska-Marcińska K., Szmidt-Sałkowska E., Fidziańska-Dolot A., et al. Atypical motor unit potentials in Emery-Dreifuss muscular dystrophy (EDMD). *Clin Neurophysiol* 2005; 116: 2520-2527.