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ORIGINAL ARTICLE

Prospective study of quality of life in patients with myotonic dystrophy type 2

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Summary

Introduction/aim: Although myotonic dystrophy type 2 (DM2) is generally milder than DM1, quality of life (QoL) seems to be similarly impaired in these two disorders. There are no studies that assessed QoL during DM2. Our aim was to assess QoL and disease outcome in patients with DM2 after a five-year follow-up period.

Material and Methods: Study originally comprised 49 DM2 patients at baseline. During the five-year period, seven patients died, eight were lost to follow-up, one patient moved, and one refused testing. The Short Form (36) Health Survey (SF-36) and Individualized Neuromuscular Quality of Life (INQoL) questionnaires were administered in 30 patients at baseline and at follow-up (47% males, 54±10 years old).

Results: Patients who were retested had better Role Physical (RP) and General Health (GH) scores of the SF-36 and better weakness score of the INQoL compared to non-retested ($p>0.05$). After the five-year follow-up, none of the SF-36 and INQoL scores differed compared to baseline ($p>0.05$).

Conclusion: QoL did not change in DM2 patients during a five-year period, as measured by both SF-36 and INQoL.

Key words: myotonic dystrophy type 2; quality of life; SF-36; INQoL; prospective study

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THE INTRODUCTION

Myotonic dystrophy type 2 (DM2) is an autosomal dominant inherited multisystem disease (1). Main characteristics of DM2 are proximal muscle weakness, variable myotonia, cataracts, cardiac disorders, endocrinological and metabolic disorders (diabetes mellitus type 2 and hyperlipidaemia), gastrointestinal symptoms and signs (constipation, diarrhoea) and the central nervous system manifestations.

DM2 is generally similar to myotonic dystrophy type 1 (DM1), but both muscular and non-muscular disease symptoms are less pronounced in DM2. Muscle weakness and affection of other tissues is known to be associated with poor quality of life (QoL) in patients with DM1 (2–6). Although DM2 is clinically milder than DM1, two studies that assessed QoL in DM2 showed that it was similarly affected in both diseases (7, 8). In addition, Tieleman and colleagues found a deterioration in QoL in 32 DM2 patients compared to general Dutch population (7). No prospective QoL study in patients with DM2 has been conducted so far. Also, there have not been much data on the natural history of DM2.

The aim of this study was to prospectively analyze QoL and disease outcome in patients with DM2 after a five-year follow-up period.

THE MATERIALS AND METHODS

All patients gave informed consent to participate in the study and the study was approved by the Ethical Board of the Neurology Clinic, University Clinical Centre of Serbia and the study was performed in compliance with the Declaration of Helsinki. In all patients, DM2 diagnosis was based on the clinical presentation and electromyography findings and further confirmed by genetic analysis using the repeat-primed polymerase chain reaction (RT-PCR) (9). Patients were initially consecutively tested between June 2013 and June 2015 during their regular Outpatient or Inpatient examination at the Neurology Clinic, University Clinical Centre of Serbia. They were invited and retested from September to December 2019.

Sociodemographic data and clinical data were obtained from the Serbian DM registry and patients themselves. Muscle strength was assessed according to the Medical Research Council (MRC) 0-5-point scale (0 = no movement, 5 = normal strength) by two raters. The following muscles were examined bilaterally: shoulder abductors and adductors, elbow flexors and extensors, thumb opponents, finger abductors and adductors, hip flexors, extensors, abductors and adductors, knee flexors and extensors, ankle plantar and dorsal flexors. Overall severity of motor impairment was analyzed as previously described (10). We added strength of the weakest muscle of the proximal/distal muscle groups of the upper limbs/lower limbs with maximum score being 20, where lower scores mean greater muscle impairment.

All patients completed the Serbian version of *The Short Form (36) Health Survey* (SF-36) questionnaire, as a measure of health-related QoL (11). This is a generic instrument that measures eight health concepts: physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE) and mental health (MH). Two main scores summarize these scales: physical composite score (PCS) and mental composite score (MCS), as well as total SF-36 score. All these scores fall within a 0-100 scale, with higher scores reflecting better QoL.

Patients also completed the *Individualized Neuromuscular Quality of Life questionnaire* (INQoL) version 1 (12). INQoL consists of 45 questions within 10 sections. Four sections measure the impact of common muscle disease symptoms (weakness, myotonia, pain and fatigue). Five sections measure the influence of the muscle disease on particular areas of life (activities, independence, social relationships, emotions and body image). The last section is related to the disease treatment, and it was not used in our study since it is not included in the total INQoL score. Total INQoL score is calculated from five sections assessing the influence of the muscle disease on particular areas of life (12). The final score for each of the nine sections and the total INQoL score are presented as a percentage of the maximum detrimental impact with a higher percentage indicating greater symptom impact or worse QoL.

Normality of data was assessed by the Kolmogorov-Smirnov test. Student t-test for paired samples was used to compare the results at baseline and at follow-up. The significance of all tests was two-sided, with $p<0.05$ for statistical significance and $p<0.01$ for high statistical significance.

THE RESULTS

At baseline, 49 patients were enrolled. During a five-year follow-up period, seven patients died, eight patients were lost to follow-up, one patient moved, and one refused testing. Two patients developed other serious diseases (epilepsy and laryngeal carcinoma) and were not retested because of the potential influence of these diseases on their QoL. Thus, 30 (61.2%) patients were retested at follow-up.

Retested patients compared to the non-retested were more commonly females and younger at baseline **(Table 1)**.

Patients who were retested had better RP and GH scores of the SF-36 and better weakness score of the INQoL compared to the non-retested ($p>0.05$) **(Table 2)**.

There were no differences in either SF-36 or in INQoL scores between baseline and follow-up testing **(Table 3)**.

Table 1. Baseline clinical features of DM2 patients

Features	Retested patients	Non-retested patients
N	30	19
Gender (% males) *	20.0	47.4
Age at testing (years, mean±SD)*	48.8±10.5	55.6±10.0
Education (years, mean±SD)	11.6±3.3	11.4±3.4
Age at onset (years, mean±SD)	36.0±8.7	35.6±13.0
Disease duration (years, mean±SD)	12.7±11.0	19.9±16.4
MRC score (mean±SD)	17.6±2.0	16.5±2.3

SD – standard deviation, MRC – Medical Research Council; * $p<0.05$

Table 2. Baseline quality of life scores in DM2 patients

QoL score	Retested patients	Non-retested patients
N	30	19
PF	53.5±30.2	43.2±23.6
RP *	53.8±44.5	23.5±33.6
BP	58.0±31.4	56.2±26.6
GH *	55.0±23.8	40.1±21.2
VT	50.8±24.4	39.1±28.5
SF	72.6±25.7	60.3±35.7
RE	60.3±46.2	47.1±42.6
MH	65.4±19.0	57.6±27.5
PCS	54.2±27.4	40.4±21.7
MCS	60.8±22.5	48.8±26.5
SF-36 total score	58.7±24.5	45.9±24.2
Weakness *	48.1±35.6	71.7±21.3
Myotonia	35.1±32.7	42.8±34.9
Pain	37.4±34.0	40.1±36.2
Fatigue	48.8±34.4	56.2±31.2
Activities	41.4±28.8	57.6±30.5
Independence	30.2±27.9	39.3±34.0
Social relations	19.3±21.5	19.6±23.2
Emotions	26.2±25.9	35.2±24.2
Body image	28.0±28.8	42.4±30.0
INQoL total score	35.6±25.0	45.7±22.5

physical functioning - PF, role physical - RP, bodily pain - BP, general health - GH, vitality - VT, social functioning - SF, role emotional – RE, mental health - MH, physical composite score - PCS, mental composite score - MCS; * $p<0.05$

Table 3. Quality of life scores at baseline and follow-up in DM2 patients (N=30)

QoL scores	First testing	Retest
PF	53.5±30.2	59.6±29.7
RP	53.8±44.5	60.6±49.1
BP	58.0±31.4	59.1±35.1
GH	55.0±23.8	51.5±24.2
VT	50.8±24.4	47.3±24.9
SF	72.6±25.7	74.5±31.3
RE	60.3±46.2	78.2±41.0
MH	65.4±19.0	67.2±21.5
PCS	54.2±27.4	55.6±27.3
MCS	60.8±22.5	63.7±24.1
SF-36 total score	58.7±24.5	62.2±26.5
Weakness	48.1±35.6	56.5±32.9
Myotonia	35.1±32.7	36.5±32.6
Pain	37.4±34.0	37.7±36.1
Fatigue	48.8±34.4	42.8±38.0
Activities	41.4±28.8	37.6±27.3
Independence	30.2±27.9	30.1±33.8
Social relations	19.3±21.5	12.0±18.8
Emotions	26.2±25.9	23.4±24.0
Body image	28.0±28.8	32.2±32.1
INQoL total score	35.6±25.0	33.7±25.0

physical functioning - PF, role physical - RP, bodily pain - BP, general health - GH, vitality - VT, social functioning - SF, role emotional – RE, mental health - MH, physical composite score - PCS, mental composite score - MCS

DISCUSSION

Understanding natural history of a certain disease has a great significance, not only for providing information about prognosis to patients, but also for designing possible clinical trials. These studies are lacking in patients with DM2. In order to fill in this gap, we prospectively monitored QoL in DM2 patients.

Our results showed no deterioration of QoL during a five-year follow-up period which, once again, confirms the previously known fact that DM2 is a slowly progressive disease (14, 15). On the other hand, the lack of changes in QoL measures may also indicate that used instruments are non-sensitive to detect changes in DM2. This probably means that these outcome measures are not a good choice for future clinical trials in DM2. If they cannot detect a change in QoL after five years, it is hard to believe that they would be able to do so in a shorter period of time, which is usual for clinical trials. The SF-36 is a generic questionnaire, which has to-date been widely applied in order to evaluate the QoL of patients suffering from different neurological and non-neurological chronic diseases (11, 15-17). One of the main advantages of this questionnaire is the ability of QoL analysis and comparison of different diseases. On the other hand, although widely used, this QoL measure has several limitations, including inability to capture disease-specific features of neuromuscular disorders. In order to overcome these limitations, Vincent and colleagues have created the INQoL questionnaire (12). It is a patient-reported outcome suggested to have advantages in the assessment of QoL in different neuromuscular diseases over widely used generic questionnaires (18-20). However, in our study neither SF-36 nor INQoL were able to detect a change in DM2 during a five-year follow-up period. Currently there are no QoL questionnaires specifically developed for DM2. All these facts indicate that it is necessary to

develop new, specific patient-reported outcome measures for DM2, which would have all the characteristics of modern instruments and which would be responsive.

The most significant limitation of our study is the small number of participants, although this is a pretty large cohort for such a rare disease. Another drawback of the study is the relatively small percentage (61%) of retested patients from the original cohort. In addition, retested patients were more often young and of female gender, which may indicate a selection bias. It is also possible that the patients who were retested are actually the ones who are generally better and therefore see their doctor more regularly. Anyway, our research gives important clues regarding the course and prognosis of DM2. Multicentric studies with a larger number of subjects from different cultural backgrounds are needed to definitely understand the natural course of DM2.

CONCLUSION

Quality of life in DM2 patients did not change significantly over a five-year follow-up period, which confirms a slowly progressive course of the disease and also suggests inability of currently available measures to detect changes in DM2.

Ethics approval

This research was approved by the Ethical Board of the Neurology Clinic, University Clinical Centre of Serbia.

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PROSPEKTIVNA STUDIJA KVALITETA ŽIVOTA KOD PACIJENATA SA MIOTONIČNOM DISTROFIJOM TIPA 2

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Sažetak

Uvod/cilj: Uprkos činjenici da miotonična distrofija tipa 2 (DM2) ima generalno blažu fenotipsku prezentaciju od miotonične distrofije tipa 1 (DM1), postoje pretpostavke da je kvalitet života (KŽ) obe grupe pacijenata podjednako narušen. U dosadašnjoj literaturi nema prospektivnih istraživanja, koja su procenjivala KŽ tokom progresije DM2. Cilj ove studije je bila procena KŽ i ishoda bolesti kod pacijenata sa DM nakon petogodišnjeg perioda praćenja.

Materijal i metode: Inicijalna analiza je obuhvatila 49 DM2 pacijenata. Tokom petogodišnjeg perioda praćenja, sedam pacijenata je preminulo, osam pacijenata je izgubljeno iz praćenja, jedan pacijent se preselio, a jedan je odbio ponovno testiranje. Upitnici za procenu KŽ, „Mera zdravlja kratke forme"(engl. The Short-Form (SF-36) Health Survey - SF-36) i „Individualizovani upitnik o kvalitetu života kod neuromišićnih bolesti"(engl. Individualized Neuromuscular Quality of Life (INQoL)), primenjeni su kod 30 pacijenata nakon perioda praćenja.

Rezultati: Pacijenti koji su retestirani nakon pet godina imali su bolje skorove fizičkog funkcionisanja (engl. Role Physical (RP)) i opšteg zdravlja (engl. General Health (GH)) na SF-36 upitniku i bolji INQoL skor povezan sa slabošću u poređenju sa pacijentima koji nisu retestirani nakon pet godina ($p<0,05$). Posle petogodišnjeg perioda praćenja, nijedan od SF-36 i INQoL skorova se nije razlikovao u poređenju sa skorovima uočenim tokom inicijalne analize ($p>0,05$).

Zaključak: KŽ se nije promenio kod pacijenata sa DM2 tokom petogodišnjeg perioda praćenja, mereno generičkim SF-36 i individualizovanim INQoL upitnikom.

Ključne reči: Miotonična distrofija tip 2; kvalitet života; SF-36; INQoL; prospektivna studija

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