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# Quality of life in patients with multifocal motor neuropathy from Serbia

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ABSTRACT

*Introduction and aim:* Multifocal motor neuropathy (MMN) is a rare, chronic disorder with potentially severe and progressive disability, which may affect patients' quality of life (QoL). Since there is still small number of studies that predominantly investigated QoL in patients with MMN, we sought to analyze QoL in these patients.

*Materials and methods:* Our study comprised 17 patients diagnosed with MMN at the same clinic. Following scales were used: SF-36 questionnaire, INCAT disability scale, Krupp's Fatigue Severity scale, and Beck Depression Inventory.

*Results:* Physical domains of QoL were slightly more affected than mental ones, but with no statistical significance (64.8 ± 22.3 vs. 70.0 ± 19.5, $p > 0.05$). Total SF-36 score was 69.2 ± 19.9. INCAT arm disability score at testing was found to correlate with the total SF-36 score (rho = −0.603, $p < 0.05$). INCAT arm disability score at diagnosis (rho = −0.57, $p < 0.05$) and at testing (rho = −0.48, $p = 0.05$) correlated with physical composite score (PCS). Disease duration (rho = −0.51, $p < 0.05$) and INCAT arm disability score at testing (rho = −0.60, $p = 0.01$) were associated with mental composite score (MCS).

*Conclusion:* QoL in patients with MMN was reduced, especially in physical domains. Although arm disability was the most significant parameter which affected QoL of MMN patients in both physical and mental aspects, longer disease duration should not be underestimated as a psychological burden for these patients.

## 1. Introduction

Multifocal motor neuropathy (MMN) is an autoimmune disease which is characterized by slowly progressive, asymmetric and predominantly distal limb weakness where the upper limbs are more affected [1,2]. It is a rare, chronic disorder with potentially severe and progressive disability that may affect patients' quality of life (QoL). Most of the previous literature was focused on different therapy response in MMN patients and their influence on QoL [3–7]. It was demonstrated that patients' QoL was mostly improved after immunoglobulin therapy, and that treatment maintenance is beneficial for patients [3–7]. There is still an insufficient number of studies with the main goal of investigating factors associated with QoL in patients with MMN.

Our aim was to analyze QoL in patients with MMN using the SF-36 generic questionnaire, as well as to analyze the influence of different sociodemographic and clinical parameters on patients' QoL.

## 2. Materials and methods

In a fifteen-year period (from 2003 to 2017) nineteen patients were diagnosed with MMN at the Neurology Clinic, Clinical Center of Serbia. Among these patients, two were excluded since one died due to the acute myocardial infarction and the other one had Parkinson's disease as a significant comorbidity. A final number of 17 patients was included in this research and all of them fulfilled the EFNS/PNS criteria for MMN diagnosis - nine of them were retrospectively reevaluated in order to see if they fulfill the criteria since they had been diagnosed before EFNS/PNS criteria were published in 2010 [8]. All patients were cross-sectionally tested during their regular neurology check-ups in 2017, including sociodemographic data, disability, depression, fatigue, and QoL. Patients' characteristics at the time of diagnosis and course of the disease were obtained retrospectively from electronic medical records. The study was approved by the Ethical Board of the Neurology Clinic, Clinical Center of Serbia and all patients gave informed consent to participate in this study.

Following sociodemographic and clinical data were assessed: gender, age, education, employment status, disease duration,

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therapeutic approaches and treatment response. Degree of functional disability was established using the INCAT disability score (*Inflammatory Neuropathy Cause and Treatment score*) at diagnosis and at testing [9]. Beck's Depression Inventory (BDI) was used to establish the level of depressiveness – score range is 0–63 and ≥ 11 points represented significant depression [10]. Krupp's Fatigue Severity Scale (FSS) was also applied [11]. Score ranges between 6 and 63, and ≥ 36 points indicated presence of significant fatigue.

Serbian version of the SF-36 questionnaire was used as a generic measure of QoL in all patients [12]. It combines eight general 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). Physical composite score (PCS), mental composite score (MCS), and the total SF-36 score are three main scores to summarize these eight concepts. All scores range from 0 to 100, where higher scores represent better QoL.

Normality of data was tested by the Kolmogorov-Smirnov test. For group comparisons, $\chi^2$ test, Mann-Whitney *U* test and Student *t*-test were used, as appropriate. Correlations were assessed using Spearman's rho. For all statistical tests, significant testing was two-sided, with alpha set at 0.05 for statistical significance and 0.01 for high statistical significance.

## 3. Results

Main sociodemographic, clinical and laboratory features of investigated patients at the moment of diagnosis and at testing are presented in Table 1. Male to female ratio was 2.4:1, and mean age at onset of the disease was 38.3 ± 12.4 (minimum 23, maximum 63) years.

According to the INCAT disability scale at diagnosis, 41% of our patients had symptoms and signs which prevented one or two functions of the arms and in 23% of patients independent walking was impaired but possible (Fig. 1). All of our patients were treated with IVIg (loading dose of 2.4 g/kg during five days, followed by 0.4 g/kg monthly) for mean period of five years (from 1 to 173 months). In majority of patients slight improvement was observed after loading dose, while disability was stable with booster doses afterward. Mean total treatment duration was 5.5 (one to 15) years. Therapy was discontinued at some point in nine (53%) of our patients, while in five of them therapy needed to be reintroduced after six months to two years due to the disease worsening. Later, therapy was discontinued in four of these five patient with not further worsening. Corticosteroids were administered in 23% of MMN patients before adequate diagnosis was made, but with no effect. Cyclophosphamide was tried in 23% and cyclosporine in 29% of patients in addition to IVIg, but without any beneficial effects. At the moment of testing, mean disease duration was 6.1 ± 3.8 years (from 6 months to 14 years). On average, INCAT arm and leg disability scores did not differ at diagnosis and at testing. Looking individually, 23% of patients had improvement of at least one point on INCAT arm disability score, 18% had worsening of at least one point, and 59% did not change. Regarding INCAT leg disability score, 6% improved and 94% did not change.

Fatigue and depression were present in 18% each (mean FSS 21.0 ± 14.7, mean BDI 4.6 ± 8.5). Around 36% of our patients were unemployed/retired due to the disease.

Results on SF-36 questionnaire are shown in Table 2.

Total SF-36 score was 69.2 ± 19.9. Physical domains were somewhat more affected than the mental ones, but statistical significance was not reached (PCS = 64.8 ± 22.3 vs. MCS = 70.0 ± 19.5, $p > 0.05$). GH and RP domains had the worst scores, while RE and BP were domains with the best scores. Following MMN features were not in correlation with PCS, MCS or total SF-36 score: age, gender, diagnostic delay, INCAT leg disability score at diagnosis and at testing, fatigue and depression. Only INCAT arm disability score at testing (rho = −0.603, $p < 0.05$) correlated with the total SF-36 score. INCAT arm disability score at diagnosis (rho = −0.57, $p < 0.05$) and INCAT arm disability score at testing (rho = −0.48, $p = 0.05$) were associated with PCS. Disease duration (rho = −0.51, $p < 0.05$) and INCAT arm disability score at testing (rho = −0.60, $p = 0.01$) correlated with MCS.

**Table 1**
Sociodemographic, clinical and laboratory features of MMN patients (n = 17).

| Feature | At diagnosis | At testing |
|---|---|---|
| Male (n (%)) | 12 (71%) | – |
| Age at onset of the disease (years, mean ± SD) | 38 ± 12 | – |
| Diagnostic delay (months, mean ± SE) | 19 ± 16 | – |
| First clinically affected nerve (n (%)) | | – |
| Radial nerve | 11 (65%) | |
| Ulnar nerve | 3 (18%) | |
| Median nerve | 1 (6%) | |
| Peroneal nerve | 1 (6%) | |
| Unknown | 1 (6%) | |
| Conduction blocks (n (%))[a] | | – |
| Radial nerve - lower arm | 1 (7%) | |
| - upper arm | 3 (21%) | |
| Ulnar nerve - lower arm | 5 (36%) | |
| - upper arm | 4 (29%) | |
| Median nerve - lower arm | 6 (43%) | |
| - upper arm | 3 (21%) | |
| Peroneal nerve - upper leg | 1 (7%) | |
| Tibial nerve - lower leg | 2 (14%) | |
| None | 1 (7%) | |
| Number of nerves with conduction blocks | 2.1 ± 0.7 | |
| INCAT disability score – arms (mean ± SD) | 2.5 ± 1.1 | 2.7 ± 1.2 |
| (median, range) | 3 (1–5) | 2 (1–5) |
| INCAT disability score – legs (mean ± SD) | 0.8 ± 1.3 | 0.6 ± 1.3 |
| (median, range) | 0 (0–5) | 0 (0–5) |
| INCAT disability score – total (mean ± SD) | 3.3 ± 2.0 | 3.4 ± 2.2 |
| (median, range) | 3 (1–10) | 3 (1–10) |
| Cramps (n (%)) | | |
| Arms | 1 (6%) | 1 (6%) |
| Legs | 1 (6%) | 1 (6%) |
| Fasciculations (n (%)) | | |
| Arms | 2 (12%) | 2 (12%) |
| Leg | 1 (6%) | 1 (6%) |
| Pain (n (%)) | | |
| Arms | 0 (0%) | 1 (6%) |
| Legs | 1(6%) | 0 (0%) |
| Back | 3 (18%) | 1 (6%) |
| Paresthesias (n (%)) | | |
| Arms | 9 (53%) | 5 (29%) |
| Legs | 1 (6%)(6%) | 1 (6%) |
| Muscle reflexes in weak limbs – arms (n (%)) | | |
| Decreased | 15 (88%) | 15 (88%) |
| Normal | 1 (6%) | 1 (6%) |
| Brisk | 1 (6%) | 1 (6%) |
| Muscle reflexes in weak limbs – legs (n (%)) | | |
| Decreased | 10 (59%) | 13 (76%) |
| Normal | 4 (23%) | 2 (12%) |
| Brisk | 3 (18%) | 2 (12%) |
| CSF proteins (g/L, mean ± SD) | 0.4 ± 0.5 | – |
| Elevated (> 0.45g/L) (n (%)) | 5 (29%) | |
| CSF leucocytes (n/L) | | |
| Elevated (> 5/L) (n (%)) | 0 (0%) | – |

[a] Original NCS data were available for 14 patients.

## 4. Discussion

This study was conducted in order to provide additional information about QoL in patients with MMN. To date, the main focus of investigation in MMN was mostly a comparison between different therapy modalities (for instance, intravenous vs. subcutaneous immunoglobulins) [3–5]. QoL was analyzed only as a secondary outcome measure in some of these papers.

Total SF-36 score in our MMN patients was in accordance with the data from similar-size cohort published by Braine and Woodall (mean total SF-36 score 62 and 76 in IVIg and SCIg subgroups, respectively) [3]. On the other hand, total SF-36 score in MMN patients was somewhat better compared to our 106 CIDP patients (57 ± 25) [13]. Large

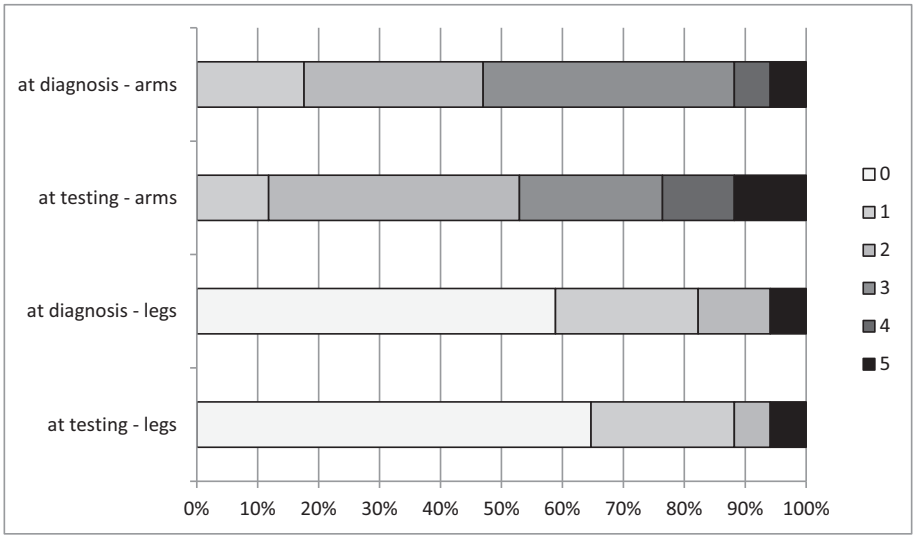


**Fig. 1.** Degree of disability according to the INCAT disability scale in MMN patients at time of diagnosis and at testing (n = 17).

**Table 2**
Quality of life measured by SF-36 questionnaire in patients with MMN (n = 17).

| SF-36 scale | Score |
|---|---|
| Physical functioning (SF) | 74.7 ± 27.5 |
| Role physical (RF) | 54.4 ± 58.1 |
| Bodily pain (BP) | 79.8 ± 26.3 |
| General health (GH) | 49.8 ± 21.7 |
| Vitality (VT) | 65.3 ± 16.5 |
| Social functioning (SF) | 70.6 ± 33.3 |
| Role emotional (RE) | 86.3 ± 33.4 |
| Mental health (MH) | 77.9 ± 16.5 |
| Physical composite score (PCS) | 64.8 ± 22.3 |
| Mental composite score (MCS) | 70.0 ± 17.3 |
| Total SF-36 score | 69.8 ± 19.5 |

variability of SF-36 scores is present in previous studies about QoL in MMN and further investigation and systematization is still needed. For instance, there is a wide discrepancy between the highest and the lowest mean PCS and MCS scores in previous studies, from PCS 39 and MCS 47 of the SIGNS registry (n = 80) to mean PCS score of 76 and MCS of 84 presented by Braine and Woodall (n = 16) [3,4,6]. The main reason for this divergence could be, not only the difference of disease duration and duration of treatment in these cohorts, but also a huge variability in clinical presentation and severity of the disease. Variable cohort size may also affect the observed differences.

In our group of MMN patients, physical domains of the SF-36 questionnaire were somewhat more impaired than the mental ones, which is similar to previous findings [3,4,6]. This is probably due to the fact that MMN is a peripheral nerve disease with no direct affection of the central nervous system. As in our research, RP (role limitations due to physical health problems) and GH (overall health as seen by patients) were the most impaired scores in majority of to-date studies [3,4,6].On the other hand, RE (role limitations due to emotional health problems) and MH (mental health) were the most preserved domains in our and previously published cohorts [3,4]. Also, patients scored well on BP (bodily pain) domain since MMN is not a painful disease [3,4]. Accordingly, only 12% of our patients reported pain at time of testing.

INCAT arm disability score correlated with the physical domains of SF-36 score in our MMN patients. In our recent research on CIDP patients worse total (arm and leg) INCAT disability score was a significant predictor of the worse SF-36 score [13]. However, in MMN cohort correlation was observed between QoL and arm disability, but not leg disability, since arms are more affected than legs in MMN. Arms disability may cause problems with every-day, work and leisure activities, thus may also have influence on mental areas of life. In line with this, worse arm INCAT score correlated with worse MCS in our MMN subjects. It is also of note that disease duration correlated with MCS. This means that longer disease duration and possibly prolonged therapy are a psychological burden for patients, besides relatively good response on therapy. Thus, recommendations when neurologists should try to stop IVIg therapy should be considered in the future guidelines. All of our patients received IVIg therapy for mean interval of five and a half years, and 23% of patients improved their total INCAT disability score for at least one point, while 18% deteriorated besides therapy. In accordance with our findings, Austrian research noted sustained improvement in 37% of patients and deterioration of response to treatment in 23% after the mean treatment duration of 7.5 years [14]. It is of note that our patients had similar level of improvement although we used approximately half the dose of IVIg compared to Austrians due to the economic issues. Previous data underlined that the decline despite IVIg treatment possibly occurs after 3–7 (mean 4.8) years of treatment [15].

Fatigue can be a significant burden in patients with different inflammatory neuropathies and may affect patients' QoL [13,16,17]. Also, depression is a common comorbid disorder in patients with different chronic diseases [18]. In our MMN cohort fatigue was present in only 18% of patients, which is less than in a previous study where fatigue was reported in up to 50% of subjects [19]. Around 18% of our MMN patients had depression, which is less common than in the research by Mahdi-Rogers and colleagues where 37% of MMN patients were moderately anxious and depressed [20]. Also, depression seems to be less frequent in Serbian MMN patients compared to Serbian CIDP patients [13,21]. Fatigue and depression were not in correlation with the total SF-36 score in our MMN patients, so we should look further for factors not comprised in this research, such as social support, coping behavior, employment-related factors etc. However, fatigue and depression still may affect many daily activities in some patients and should be adequately treated.

The main limitation of this study is a small group of MMN patients, thus larger multicentric studies are needed. Also, we used generic questionnaire to measure QoL that is probably not able to capture all issues important for MMN patients. On the other side, it allows us to compare MMN with other diseases, especially when there is still no disease specific QoL measure for MMN. IN-QoL questionnaire was developed as a QoL measure in a group of different inflammatory neuropathies including MMN. However, it showed a lack of responsiveness

in MMN [22]. Another limitation of the study is that we did not use a hand grip strength as an outcome measure.

In conclusion, QoL in patients with MMN was clearly reduced, especially in physical domains. Arm disability is the most significant factor which affects QoL of MMN patients in both physical and mental domains. Despite a relatively satisfactory therapy response, longer disease duration should not be underestimated as a psychological burden for MMN patients.

## Declarations of conflict of interest

None.

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