Original scientific article / Izvirni znanstveni članek

Clinical features in adult multiple sclerosis patients: a cross-sectional study

Klinične značilnosti odraslih pacientov z multiplo sklerozo: presečna raziskava

*Matej Koprivnik[1, *], Tanja Hojs Fabjan[2, 3]*

Key words: multiple sclerosis; quality of life; neurological disability; functional ability

Ključne besede: multipla skleroza; kakovost življenja; nevrološka prizadetost; funkcionalne sposobnosti

[1] University Medical Centre Maribor, Institute for Physical and Rehabilitation Medicine, Ljubljanska ulica 5, 2000 Maribor, Slovenia

[2] University Medical Centre Maribor, Department of Neurologic Diseases, Ljubljanska ulica 5, 2000 Maribor, Slovenia

[3] University of Maribor, Faculty of Medicine, Taborska ulica 8, 2000 Maribor, Slovenia

[*] *Corresponding author / Korespondenčni avtor*: fiziokop@gmail.com

The article is based on a master's thesis written by Matej Koprivnik entitled *A comparison of functional test, quality of life, fatigue and neurological disability on EDSS in patients with multiple sclerosis* (2016).

ABSTRACT

Introduction: The purpose of the study was to identify possible correlations between the quality of life, neurological disability, and functional ability in patients with multiple sclerosis.

Methods: 258 patients with multiple sclerosis were included in the cross-sectional study. They were assessed with the Expanded Disability Status Scale (EDSS), the Berg Balance Scale (BBS), the Timed 25-Foot Walk Test (T25-FW), the 9-Hole Peg Test (9HPT), the Paced Auditory Serial Addition Test (PASAT-3) and the EQ visual analogue scale (EQ-VAS). Inferential statistics were used.

Results: A positive correlation between the EQ-VAS and the BBS ($r = 0.43$, $p < 0.01$) and the PASAT-3 ($r = 0.19$, $p < 0.01$), and a negative correlation between the EQ-VAS and the T25FW ($r = –0.42$, $p < 0.01$) and the 9-HPT ($r = –0.40$, $p < 0.01$) were shown. A negative correlation was also observed between the EDSS and the BBS ($r = –0.77$, $p < 0.05$) as well as the EDSS and the PASAT-3 ($r = –0.25$, $p < 0.01$), and a positive correlation between the EDSS and the 9 HPT ($r = 0.67$, $p < 0.01$) and the T25-FW ($r = 0.80$, $p < 0.01$).

Discussion and conclusion: Associations between the variables indicate the need for complex, personalized and rational monitoring of patients with multiple sclerosis.

IZVLEČEK

Uvod: Namen raziskave je bil ugotoviti morebitne povezave med kakovostjo življenja, nevrološko prizadetostjo in funkcionalnimi zmožnostmi pri pacientih z multiplo sklerozo.

Metode: V presečno raziskavo je bilo vključenih 258 pacientov z multiplo sklerozo. Ocenjeni so bili s pomočjo Expanded Disability Status Scale (EDSS), Berg Balance Scale (BBS), Timed 25-Foot Walk Test (T25-FW), 9-Hole Peg Test (9HPT), Paced Auditory Serial Addition Test (PASAT-3) in lestvice EQ Visual Analogue Scale (EQ-VAS). Uporabljena je bila inferenčna statistika.

Rezultati: Pokazala se je pozitivna povezava med oceno EQ-VAS ter BBS ($r = 0{,}43$, $p < 0{,}01$) in PASAT-3 ($r = 0{,}19$, $p < 0{,}01$) in negativna povezava med EQ-VAS ter T25FW ($r = –0{,}42$, $p < 0{,}01$) in 9-HPT ($r = –0{,}40$, $p < 0{,}01$). Negativne korelacije smo zaznali tudi med oceno EDSS in BBS ($r = –0{,}77$, $p < 0{,}05$) ter PASAT-3 ($r = –0{,}25$, $p < 0{,}01$), pozitivne povezave pa med EDSS in 9 HPT ($r = 0{,}67$, $p < 0{,}01$) ter T25-FW ($r = 0{,}80$, $p < 0{,}01$).

Diskusija in zaključek: Povezave med navedenimi spremenljivkami kažejo na potrebo po kompleksnem, personaliziranem in racionalnem spremljanju pacientov z multiplo sklerozo.

Received / Prejeto: 13. 1. 2020
Accepted / Sprejeto: 24. 5. 2020

https://doi.org/10.14528/snr.2020.54.2.3016

Introduction

Multiple sclerosis (MS) is a chronic inflammatory disorder of the central nervous system that can lead to demyelination and neurodegeneration (Ysrraelit, et al., 2018). There are several different forms of MS in which new symptoms occur through discrete attacks or slowly over time (Opara, et al., 2010). Because of the type and number of present symptoms, which vary greatly between individuals and depend on the sites of lesions in the brain or spinal cord (European Multiple Sclerosis Platform & Rehabilitation in Multiple Sclerosis, 2012), MS is categorized as a complex (Shapiro, 2011) and highly unpredictable disease (Slavkovic, et al., 2019).

Since the progression of MS is difficult to quantify, we should decide which aspects of the disease progression we want to capture. For this reason, the use of sensitive clinical outcome measures that can detect small changes in the disability that reliably reflect long-term changes in sustained disease progression is required. We should be aware that all outcome measures have their strengths and weaknesses and that the use of a single MS outcome measure may remain elusive (Goldman, et al., 2010). No single outcome measure will be applicable in all settings (Cohen, et al., 2012).

In the past, the measurement of disability, particularly walking, assessed by the Expanded Disability Status Scale (EDSS), dominated in the assessment of the functional disability of MS patients. The Multiple Sclerosis Functional Composite broadened the functional disability assessment to the areas of cognitive functions and the upper limb dexterity (Karabudak, et al., 2015). Functional disability is also assessed with various other assessment instruments; in our case, it was upgraded with the Berg Balance Scale (BBS) (Rugelj & Palma, 2013). Assessment of patient-reported outcomes in association with clinician-assessed objective disability outcomes can provide important information from patients' perspectives (Cohen, et al., 2012). The measurement of the quality of life in MS patients also has an important role for the patient and the physician, who must be able to assess the effect of disease progression and therapeutic interventions on the patient as a whole (Karabudak, et al., 2015).

Aims and objectives

MS requires a broad multidisciplinary approach. Transparent, multidimensional, rational monitoring and recording of the condition of the patient is imperative. Knowledge and consideration of the selection of the most suitable assessment instrument is needed. The aim of our study was to present the association between the assessment of individual research instruments currently in use, and thus contribute to the highlighting of the appropriate, professional and rational way of data collection and monitoring of patients with MS.

Methods

In this non-experimental observational cross-sectional study a quantitative methodological approach was used.

Description of the research instrument

Data were collected using a self-designed questionnaire on basic demographic and clinical data, EQ visual analogue scale (EQ-VAS), EDSS, BBS, Timed 25-Foot Walk (T25FW), 9–Hole Peg Test (9HPT) and Paced Auditory Serial Addition Test - three-second version (PASAT-3).

Self-designed questionnaire on basic demographic and clinical data: gender, age, duration and the phenotype of the disease and disease modifying-treatment (DMT).

EQ-VAS is the second part of a generic 3-level version of the EQ-5D (EQ-5D-3L) instrument, a quantitative measure of health outcome that reflects patients' judgement (Reese, et al., 2013; EuroQol Group, 2017). On this visual analogue scale, respondents rate their self-assessed health with 0, representing the worst imagined health, and 100, being the highest imagined health (Jones, et al., 2013).

EDSS designed by Kurtzke (1983) is the gold-standard measure of MS disease progression and commonly the standard that other outcome measures are compared with (Goldman, et al., 2010). This clinician-administered assessment scale (Meyer-Moock, et al., 2014) is based on a neurological examination of eight functional systems (Cutter, et al., 1999) of the central nervous system. It consists of an ordinal rating system (Meyer-Moock, et al., 2014) ranging from 0 (normal neurological status) to 10 (death due to MS) with increment intervals of 0.5 (Meyer-Moock, et al., 2014; Piri Çinar & Güven Yorgun, 2018) when reaching EDSS 1 (Meyer-Moock, et al., 2014). A score between 1.0 and 4.0 is based on the change of functional system(s) (Goldman, et al., 2010; Piri Çinar & Güven Yorgun, 2018), between 4.0 and 8.0 indicates ambulation (Piri Çinar & Güven Yorgun, 2018), 8.0 marks loss of ambulation, 8–9 distinguishes upper extremity function, 9.0–9.5 bulbar function and 10 defines death due to MS (Goldman, et al., 2010).

BBS is a reliable and effective tool for assessing problems with balance in patients with MS (Fjeldstad, et al., 2009). This performance-based measure (Berg, et al., 1989) consists of 14 tasks that assess static and dynamic activities. Individual task scores are scored from zero to four, depending on the quality of the performance of each task, with a lower score representing poorer quality of performance. The maximum total score of the scale is 56 points. The time used for administration depends on the degree of patient disability and ranges from a few to twenty minutes. To perform the test, a chair with and without armrests, a stopwatch, a step or a stool, a ruler and a

slipper or a shoe (Rugelj & Palma, 2013) are needed.

T25FW is a quantitative (Tiftikçioğlu, 2018), well-characterised specific and objective assessment tool of walking disability, which can be used to measure walking speed in MS patients with a wide range of walking disabilities (Kieseier & Pozzilli, 2012). The patient is instructed to twice walk the distance of 7.62 metres safely but as quickly as possible (Tiftikçioğlu, 2018). T25FW is a practical, highly attractive measure for clinical practice and research that is easy to administer, inexpensive and has demonstrated reliability over brief and long periods of time in a wide range of disability levels of MS (Motl, et al., 2017).

9HPT is a quantitative measure (Tiftikçioğlu, 2018), the gold standard and the optimal metric for measuring manual dexterity in MS patients (Feys, et al., 2017). Patients are required to place all the nine pegs one by one into holes arranged in a board and then remove the pegs from the holes. Two successful trials are foreseen for each hand (Tiftikçioğlu, 2018). The test is sensitive to treatment and detects progression over time which is why it is recommended to be included in clinical trials. The 20 % change in the test score is commonly used to define clinically meaningful worsening (Feys, et al., 2017).

PASAT-3 is a measure of cognitive function (Tiftikçioğlu, 2018; National Multiple Sclerosis Society, 2019) that assesses auditory information processing speed, flexibility and calculation ability (National Multiple Sclerosis Society, 2019). In the test, sixty single-digit numbers are presented to the patient by a CD-rom at a constant rate of every 3 seconds (PASAT-3). The patient must add each new number to the one immediately prior to it and the number of correct answers is recorded (Tiftikçioğlu, 2018) as a PASAT score. PASAT is a sensitive test of some specific cognitive functions frequently affected in MS (National Multiple Sclerosis Society, 2019).

Description of the sample

A convenience research sample of total 258 patients with MS regularly examined at the Outpatient Department of Neurology at the University Medical Centre (UMC) Maribor was included in the study. Patients with relapsing-remitting (RRMS), secondary progressive (SPMS), primary progressive (PPMS), and benign course of MS, of various ages, of both genders, and different duration of the disease, with EDSS ≤ 6.5, were included. We included only patients at a stable stage of the disease (patients with relapse or a month after relapse were not included).

Description of the research procedure and data analysis

Before inclusion, all participants signed a statement of voluntary participation in the study. The study was conducted at the Department of Neurology at the UMC Maribor from April to December 2015. We included patients during their regular annual examinations in the Outpatient Department of Neurology at the UMC Maribor.

The degree of disability was calculated by a neurologist in accordance with the EDSS. The patients completed a questionnaire on basic demographic data and provided a self-assessment of health-related quality of life (HRQoL) through the EQ-VAS scale. The physiotherapist performed functional assessments with BBS, T25FW, 9HPT and PASAT-3 tests. The collected data were statistically treated with a descriptive statistical method, where the arithmetic mean ($\bar{x}$) and standard deviation (s) at an interval or proportional level were calculated; for the data at the ordinal level (EDSS) and where the distribution properties did not allow the use of M (s) (in some cases BBS and 9-HPT), we used the median (Me) and interquartile intervals ($Q1–Q3$) as the measure of the central tendency ($Q1–Q3$), while in nominal variables (gender, type of MS), frequencies (f) and percentages ($\%$) were calculated. The degree of correlation between individual variables at the ratio level was calculated using the Pearson coefficient (r), and the Spearman's rank correlation (rho) coefficient was used to calculate the variables at the ordinary level. We used the Excel program for the tabulation of results, while the basic statistical analyses were made in the IBM SPSS, Version 23 (SPSS Inc., Chicago, Illinois, USA). To check the differences between individual groups, ANOVA was used for multi-category variables at the interval or proportional level, whereas the Kruskal–Wallis H-test was used for variables at the ordinal level. The 5 % alpha error risk level was used as the criterion of statistical significance.

Results

Table 1 shows basic demographic and clinical data. Differences in scores between the groups with different types of the disease are shown in Table 2. These differences are statistically significant regarding the BBS ($p < 0.001$), 9 HPT ($p < 0.001$), T25-FW ($p < 0.001$), and PASAT-3 ($p < 0.001$). We also found statistically significant differences in the rates of disability regarding the EDSS ($p < 0.001$) and in self-assessed health state according to EQ-VAS ($p < 0.001$).

Table 3 depicts the association of individual assessments of functional tests in all patients with MS and various courses of MS and the quality of life (EQ-VAS). The results show that achievements in a single functional test in patients with MS correlate with the self-assessment of the quality of life. A higher degree of functionality (better achievements in the BBS and PASAT-3) is correlated with a higher quality of life according to EQ-VAS (positive correlations between instruments). These correlations were demonstrated in the whole research sample and partially in RRMS and

Table 1: *Demographic and clinical characteristics of the study group*
Tabela 1: *Demografske in klinične značilnosti raziskovalnega vzorca*

MS type / Oblika MS	*Gender / Spol*		*Age (years) / Starost (leta)* $\bar{x}$ *(s)*	*Duration of the disease (years) / Trajanje bolezni (leta)* $\bar{x}$ *(s)*	*DMT*	
	Males / Moški n (%)	*Females / Ženske n (%)*			*No / Ne (%)*	*Yes / Da (%)*
RRMS	44 (26.19)	124 (73.80)	43.7 (11.80)	10.11 (7.69)	54 (32.14)	114 (67.85)
SPMS	9 (18.00)	41 (82.00)	58.5 (9.92)	18.3 (10.36)	33 (66.00)	17 (34.00)
PPMS	5 (45.45)	6 (54.54)	56.8 (5.19)	6.5 (4.28)	11 (100.00)	0 (0.00)
BENIGN	8 (27.58)	21 (72.41)	55.5 (8.70)	18.8 (9.71)	26 (89.65)	3 (10.34)
TOTAL / SKUPAJ	66 (25.58)	192 (74.41)	48.5 (12.69)	12.5 (9.28)	124 (48.06)	134 (51.93)

Legend / Legenda: n – number of patients / število bolnikov; $\bar{x}$ *– average / povprečje; s – standard deviation / odklon; % – percentage / odstotek; DMT – disease modifying-treatment / imunomodulatorno zdravljenje; MS – multiple sclerosis / multipla skleroza; RRMS – relapsing-remitting multiple sclerosis / recidivno-remitentna oblika multiple skleroze; SPMS – secondary progressive multiple sclerosis / sekundarno progresivna multipla skleroza; PPMS – primary progressive multiple sclerosis / primarno progresivna multipla skleroza; BENIGN – benign course of multiple sclerosis / benigni potek multiple skleroze*

Table 2: *Overview of the differences in various test scores in patients with different types of MS*
Tabela 2: *Pregled razlik v ocenah testov pri bolnikih z različnimi oblikami MS*

MS type / oblika	*EDSS* Me (IQ1–IQ3)*	*BBS* Me (IQ1–IQ3)*	*9-HPT* Me (IQ1–IQ3)*	*T25-FW* $\bar{x}$ *(s)*	*PASAT-3* $\bar{x}$ *(s)*	*EQ-VAS* $\bar{x}$ *(s)*
RRMS	2.0 (1.1–3.5)	56.0 (53.0–56.0)	24.2 (7.10)	5.9 (2.41)	39.7 (12.60)	74.2 (17.89)
SPMS	6.0 (4.5–6.0)	39.9 (10.80)	34.1 (14.57)	12.7 (6.23)	34.7 (11.53)	57.0 (17.28)
PPMS	5.0 (3.5-6.0)	37.2 (9.52)	30.6 (25.8–80.5)	11.7 (4.48)	30.8 (11.00)	53.0 (9.59)
BENIGN	1.5 (1.0–2.0)	56.0 (52.0–56.0)	22.5 (3.8)	5.6 (1.33)	40.7 (10.81)	81.1 (19.47)

Legend / Legenda: $\bar{x}$ *– average / povprečje; s – standard deviation / standardni odklon; Me – median / mediana; (Q1-Q3) – interquartile range / interkvartilni razmik; EDSS – Expanded Disability Status Scale / razširjena lestvica stopnje prizadetosti; BBS – Berg balance scale / Bergova lestvica za oceno ravnotežja; 9-HPT – Nine hole peg test / Test devetih zatičev; T25-FW – Timed 25-Foot Walk test / Časovno merjeni test hoje 7,62 metra; PASAT-3 – Paced Auditory Serial Additional Test / Trisekundni test kognitivnih funkcij; EQ-VAS – Visual analogue scale for assessing health-related quality of life / Vizualna analogna lestvica za oceno z zdravjem povezane kakovosti življenja; MS – multiple sclerosis / multipla skleroza; RRMS – relapsing-remitting multiple sclerosis / recidivno-remitentna oblika multiple skleroze; SPMS – secondary progressive multiple sclerosiss / sekundarno progresivna multipla skleroza; PPMS – primary progressive multiple sclerosis / primarno progresivna multipla skleroza; BENIGN – benign course of multiple sclerosis / benigni potek multiple skleroze; * – for groups where the distribution of results was not similar to the normal, the median with interquartile intervals is shown instead of the arithmetic mean and standard deviation / pri skupinah, kjer distribucija rezultatov ni podobna normalni, je namesto aritmetične sredine in standardne devijacije prikazana mediana z interkvartilnimi razmiki*

a benign course of MS. A higher degree of disability (worse achievements in the 9-HPT and T25-FW) on the other hand, is correlated with a lower quality of life according to EQ-VAS (negative correlations between instruments). These correlations were demonstrated in the whole research sample and RRMS, and partially in SPMS and benign course of MS.

We found a significant association between the assessment of individual functional tests (degree of functionality) in patients with MS and the degree of neurological disability (Table 4). At a higher level of functionality, the degree of disability assessed by the EDSS is lower (negative correlation between the achievements in the BBS or PASAT-3 test with the EDSS), while at a higher level of non-functionality, a higher degree of neurological disability is found (positive correlation of the EDSS with the 9-HPT and the T25-FW). The described correlations are present in all the courses of the disease when the functionality is assessed with the BBS or the T25-FW test.

Table 3: *Correlation between individual functional test scores and the quality-of-life assessment (EQ-VAS) in patients with MS*
Tabela 3: *Stopnja povezanosti med oceno posameznega funkcionalnega testa in oceno kakovosti življenja (EQ-VAS) pri pacientih z MS*

EQ-VAS	***BBS***	***9-HPT***	***T25-FW***	***PASAT-3***
EQ-VAS (TOTAL / SKUPAJ)	0.43**	–0.40**	–0.42**	0.19**
EQ-VAS (RRMS)	0.32**	–0.33**	–0.33**	0.14
EQ-VAS (SPMS)	0.100	–0.34**	–0.18	0.01
EQ-VAS (PPMS)	0.07	–0.57	–0.12	–0.56
EQ-VAS (BENIGN)	0.65**	–0.31	–0.45*	0.09

*Legend / Legenda: BBS – Berg balance scale / Bergova lestvica za oceno ravnotežja; 9-HPT – Nine hole peg test / Test devetih zatičev; T25-FW – Timed 25-Foot Walk test / Časovno merjeni test hoje 7,62 metra; PASAT-3 – Paced Auditory Serial Additional Test / Trisekundni test kognitivnih funkcij; EQ-VAS – Visual Analogue Scale for Assessing health-related quality of life / Vizualna analogna lestvica za oceno z zdravjem povezane kakovosti življenja; RRMS – relapsing-remitting multiple sclerosis / recidivno-remitentna oblika multiple skleroze; SPMS – secondary progressive multiple sclerosis / sekundarno progresivna multipla skleroza; PPMS – primary progressive multiple sclerosis / primarno progresivna multipla skleroza; BENIGN – benign course of multiple sclerosis / benigni potek multiple skleroze; * – $p < 0.05$; ** – $p < 0.01$.*

Table 4: *Correlation between individual functional test scores and the degree of disability (EDSS) in patients with MS*
Tabela 4: *Povezava med oceno posameznega funkcionalnega testa ter stopnjo prizadetosti (po EDSS) pri pacientih z MS*

EDSS	***BBS***	***9-HPT***	***T25-FW***	***PASAT-3***
EDSS (TOTAL / SKUPAJ)	–0.77*	0.67**	0.80**	–0.25**
EDSS (RRMS)	–0.60**	0.64**	0.67**	–0.19*
EDSS (SPMS)	–0.55**	0.05	0.64**	–0.02
EDSS (PPMS)	–0.68*	–0.03	0.81**	–0.09
EDSS (BENIGN)	–0.64**	0.57**	0.74**	–0.27

*Legend / Legenda: BBS – Berg balance scale / Bergova lestvica za oceno ravnotežja; 9-HPT – Nine hole peg test / Test devetih zatičev; T25-FW – Timed 25-Foot Walk test / Časovno merjeni test hoje 7.62 metra; PASAT-3 – Paced Auditory Serial Additional Test / Trisekundni test kognitivnih funkcij; EDSS – Expanded Disability Status Scale / Razširjena lestvica stopnje prizadetosti; RRMS – relapsing-remitting multiple sclerosis / recidivno-remitentna oblika multiple skleroze; SPMS – secondary progressive multiple sclerosis / sekundarno progresivna multipla skleroza; PPMS – primary progressive multiple sclerosis / primarno progresivna multipla skleroza; BENIGN – benign course of multiple sclerosis / benigni potek multiple skleroze; * – $p<0.05$; ** – $p<0.01$.*

Discussion

We found the average highest level of disability measured by EDSS, the most reduced quality of life (EQ-VAS), greatest cognitive impairment (PASAT-3), walking disability (T25-FW), loss of coordination in the upper extremities (9-HPT) and the presence of impaired balance (BBS) in patients with progressive forms of MS. Differences in scores between different courses of MS were statistically significant. The obtained results are quite similar to other studies. Matias-Guiu and colleagues (2017) found that the frequency of cognitive impairment varies among different clinical forms of MS and that it is significantly more frequent in patients with progressive forms of MS. Furthermore, Opara and colleagues (2010) found that patients with progressive forms of MS have more cognitive impairment than patients with RRMS. As could be seen from Papuć and Stelmasiak's (2012) study, the quality of life is better in patients with RRMS compared with patients with SPMS and PPMS. Łabuz-Roszak and colleagues (2013) concluded that the quality of life is especially worse in older MS patients with secondary progressive course of the disease. In the study by Reese and colleagues (2013), it is reported that patients with progressive forms of MS have a reduced quality of life (EQ-VAS), a higher level of disability (EDSS) and lower Multiple Sclerosis Functional Composite Z-composite scores, which consists of subtests of PASAT-3, T25-FW and 9-HPT scores (Fischer, et al., 2001). This trend is also evident in the study of Atteya and colleagues (2019), who found significant differences in BBS scores between RRMS and SPMS patients, with more present instability in SPMS than in RRMS patients.

Because MS considerably impairs patients' health status, it is very important to comprehensively assess the factors related to the quality of life (Reese, et al., 2013). Lysandropoulos and Havrdova (2015) think that the elements of the quality of life are not defined enough. For this reason, we wanted to discover the possible correlations between the quality of life (EQ-VAS) and functional tests (BBS, 9-HPT, T25-FW, PASAT-3) scores for the whole research sample

and individual course of MS. We found that a better quality of life (EQ-VAS) was associated with a higher score of balance measures (BBS) in the entire research sample, RRMS and a benign course of MS. Prosperini and Castelli (2018) report that balance problems, among others, negatively affect the quality of life, but in general the literature in this area is very scarce. We found negative correlations between the EQ-VAS and 9-HPT instruments in the entire research sample and RRMS and SPMS forms of disease. Højsgaard Chow and colleagues (2018), did not find a statistically significant correlation between 9-HPT and the quality of life based on SF-36 in patients with progressive forms of MS. Also, in patients with RRMS and progressive MS, Yalachkov and colleagues (2019) did not find a significant correlation between upper extremities functions (9-HPT) and the quality of life according to EQ-5D index and EQ-VAS score either. We also observed possible correlations between the quality of life (EQ-VAS) and the T25-FW test. A negative correlation trend was found between these two variables in the entire research sample, in RRMS form and benign course of MS. Bethoux and colleagues (2016) did not find any significant correlation between the quality of life according to the EQ-5D (European Quality of Life) questionnaire and walking speed measured by the T25-FW. In SPMS and PPMS patients Højsgaard Chow and colleagues (2018) found statistically significant moderately negative correlation between T25-FW and the quality of life measured by the Physical Component Summary of the SF-36 questionnaire. Only in the entire research sample we found that a better quality of life (EQ-VAS) was associated with better cognitive functions (PASAT-3), but the correlation between these two variables was weak. In progressive forms of MS (SPMS and PPMS) Højsgaard Chow and colleagues (2018) found a statistically significant positive correlation between cognitive functions (PASAT) and the quality of life measured by the Short Form 36 questionnaire (SF-36). In patients with RRMS, SPMS, PPMS and CIS Baumstarck-Barrau and colleagues (2011) found a statistically significant correlation between PASAT and the quality of life based on the Mental Component Summary Score of the SF-36. However, the literature does not provide information about associations between the quality of life measured by EQ-VAS and cognitive functions measured by PASAT-3.

According to Fjeldstad and colleagues (2009), postural instability is common in MS patients, even with a low disability score. Furthermore, with a BSS bedside instrument it is possible to properly identify postural instability problems in MS patients. We found that a negative correlation between the EDSS and BBS scores was stronger in SPMS followed by RRMS and a benign course of MS. In a study that included only patients with RRMS and SPMS disease course, Atteya and colleagues (2019) also found a negative correlation between the BBS and EDSS scores. We also found a positive correlation between EDSS and 9-HPT in patients with RRMS, but not in patients with PPMS or SPMS. It follows that a higher degree of neurological impairement (EDSS) is associated with greater problems in the area of upper limb dexterity. Ozakbas and colleagues (2004) also found moderate correlations between 9-HPT and EDSS score in patients with the RRMS and SPMS forms of the disease. In all the studied groups, we found a high positive correlation between neurological disability (EDSS) and non-functionality in the field of ambulation (T25-FW). In a cross-sectional study, Bethoux and colleagues (2016) also found that the EDSS score is significantly correlated with walking speed measured by the T25-FW test. Ozakbas and colleagues (2004) reported positive correlations between T25-FW and EDSS score in patients with the RRMS and SPMS forms of the disease. In our study a weak negative correlation trend was also present between the EDSS and PASAT-3 scores. It follows that a lower level of disability was associated with better cognitive functions in the entire research sample and in RRMS. In a cross-sectional, multi-centre study that included 487 patients with RRMS, Ozakbas and colleagues (2018) also revealed a significant negative correlation of PASAT-3 and EDSS scores. In a cross-sectional study including 357 patients with the most common forms of MS, Matias-Guiu and colleagues (2017) report that the disability score (EDSS) is independently associated with cognitive impairment. However, it should be noted that in their case cognitive assessment was performed with the comprehensive neuropsychological assessment protocol.

As we already know, the effects of the treatment of MS patients should be monitored with different instruments that vary depending on the goal of the therapy (Amato & Portaccio, 2007). For assessing outcomes in the field of MS there are many specific, symptom-targeted and generic measurement options available that could be used for research and clinical purposes (Nowinski, et al., 2017). This is even more important because rehabilitation measures not only monitor but also improve the quality of care and coordinated treatment of MS patients (Hutchinson, et al., 2009). As van Winsen and colleagues (2010) pointed out, the use of combinations of outcome measures in MS should be further explored. As a result of these findings and the importance of the professional and rational monitoring of MS patients, the findings from our study should be interpreted with caution; we must be aware that before implementing them in clinical practice, long-term correlations and predictive values among the used instruments must also be verified. Moreover, we should point out that in our study only Caucasian individuals from northeastern part of Slovenia were included, so our findings do not necessarily reflect the status (condition) of all MS patients.

Conclusion

As evident, the differences in scores of all the instruments used in the study are statistically significant among the diverse courses of MS. There are also dependencies among the instrument scores used, which are only partly reflected in individual types of MS. In this context, it should be noted that the described results relate only to the short-term correlation between instrument scores and it is, therefore, also necessary to verify their short-term predictive values, and before implementing these lessons in clinical practice, it is also necessary to verify their long-term correlation and predictive values. Our findings also pointed out the need for proper, complex, personalized and rational monitoring of MS patients in daily clinical practice. It is evident that using only the quality of life or disability measure does not provide information on all considerable segments of patients (perceived) health status. Use of different functional tests is also required to provide more detailed and complex information about patients' abilities.

Conflict of interest / Nasprotje interesov

The authors declare that no conflicts of interest exist. / Avtorja izjavljata, da ni nasprotja interesov.

Funding / Financiranje

The study received no funding. / Raziskava ni bila finančno podprta.

Ethical approval / Etika raziskovanja

The study was approved by the Commission for Medical Ethics UMC Maribor (Decision No. UKC-MB-KME-10-2/15). / Soglasje za raziskavo je odobrila Komisija za medicinsko etiko UKC Maribor (Sklep št. UKC-MB-KME-10-2/15).

Author contributions / Prispevek avtorjev

Both authors participated in the conceptual planning, writing and reviewing of the introduction, methodology, results, interpretation, discussion and conclusion of the research. / Oba avtorja sta sodelovala pri idejnem načrtovanju, pisanju in pregledu uvoda, metodologije, rezultatov, interpretacije, diskusije in zaključka raziskave.

Literature

Amato, M.P. & Portaccio, E., 2007. Clinical outcome measures in multiple sclerosis. *Journal of the Neurological Sciences,* 259(1/2), pp. 118–122.
https://doi.org/10.1016/j.jns.2006.06.031
PMid:17376487

Atteya, A., Elwishy, A., Kishk, N., Ismail, S.R. & Badawy, R., 2019. Assessment of postural balance in multiple sclerosis patients. *The Egyptian Journal of Neurology, Psychiatry and Neurosurgery,* 55(7), pp. 1–5.
https://doi.org/10.1186/s41983-018-0049-4

Baumstarck-Barrau, K., Simeoni, M.C., Reuter, F., Klemina, I., Aghababian, V., Pelletier, J., et al., 2011. Cognitive function and quality of life in multiple sclerosis patients: a cross-sectional study. *BMC Neurology,* 11(17), pp. 1–10.
https://doi.org/10.1186/1471-2377-11-17
PMid:1288343; PMCid:PMC3039581

Berg, K., Wood-Dauphinee, S., Williams, J.I. & Gayton, D., 1989. Measuring balance in the elderly: preliminary development of an instrument. *Physiotherapy Canada,* 41(6), pp. 304–311.
https://doi.org/10.3138/ptc.41.6.304

Bethoux, F.A., Palfy, D.M. & Plow M.A., 2016. Correlates of the timed 25 foot walk in a multiple sclerosis outpatient rehabilitation clinic. *International Journal of Rehabilitation Research,* 39(2), pp. 134–139.
https://doi.org/10.1097/MRR.0000000000000157
PMid:26926380; PMCid:PMC4850097

Cohen, J.A., Reingold, S.C., Polman, C.H., Wolinsky, J.S. & International Advisory Committee on Clinical Trials in Multiple Sclerosis, 2012. Disability outcome measures in multiple sclerosis clinical trials: current status and future prospects. *Lacent Neurology,* 11(5), pp. 467–476.
https://doi.org/10.1016/S1474-4422(12)70059-5

Cutter, G.R., Baier, M.L., Rudick, R.A., Cookfair, D.L., Fischer, J.S., Petkau, J., et al., 1999. Development of a multiple sclerosis functional composite as a clinical trial outcome measure. *Brain*, 122(5), pp. 871–882.
https://doi.org/10.1093/brain/122.5.871
PMid:10355672

EuroQol Group, 2017. *EQ-5D-3L /About.* Rotterdam: EuroQol Group. Available at: https://euroqol.org/eq-5d-instruments/eq-5d-3l-about/ [11. 11. 2019].

European Multiple Sclerosis Platform & Rehabilitation in Multiple Sclerosis, 2012. *Recommendations on rehabilitation services for persons with Multiple Sclerosis in Europe.* Brussels: European Multiple Sclerosis Platform, p. 59. Available at: http://www.emsp.org/wp-content/uploads/2015/11/12-0431_Henze-30-04-12.pdf [6. 7. 2019].

Feys, P., Lamers, I., Francis, G., Benedict, R., Phillips, G., LaRocca, N., et al., 2017. The Nine-Hole Peg Test as a manual dexterity performance measure for multiple sclerosis. *Multiple Sclerosis Journal,* 23(5), pp. 711–720.
https://doi.org/10.1177/1352458517690824
PMid:28206826; PMCid:PMC5405844

Fischer, J.S, Jak, A.J., Kniker, J.E., Rudick, R.A. & Cutter, G., 2001. *Multiple Sclerosis Functional Composite (MSFC). Administration and scoring manual.* National Multiple Sclerosis Society, pp. 1–44. Available at: http://main.nationalmssociety.org/docs/HOM/MSFC_Manual_and_Forms.pdf [16. 11. 2019].

Fjeldstad-Pardo, C., Pardo, G., Frederiksen, C., Bemben, D.A. & Bemben, M., 2009. Assessment of postural balance in multiple sclerosis. *International Journal of MS Care*, 11, pp. 1–5. https://doi.org/10.7224/1537-2073-11.1.1

Goldman, M.D., Motl, R.W. & Rudick, R.A., 2010. Possible clinical outcome measures for clinical trials in patients with multiple sclerosis. *Therapeutic Advances in Neurological Disorders,* 3(4), pp. 229–239. https://doi.org/10.1177/1756285610374117 PMid:21179614; PMCid:PMC3002657

Højsgaard Chow, H., Schreiber, K., Magyari, M., Ammitzbøll, C., Börnsen, L., Romme Christensen, J., et al., 2018. Progressive multiple sclerosis, cognitive function, and quality of life. *Brain and Behavior,* 8(2), pp. 1–7. https://doi.org/10.1002/brb3.875 PMid:29484253; PMCid:PMC5822575

Hutchinson, B., Forwell, S.J., Bennett, S., Brown, T., Karpatkin, H. & Miller, D., 2009. Toward a consensus on rehabilitation outcomes in MS: gait and fatigue. Report of a CMSC Consensus Conference, November 28-29, 2007. *International Journal of MS Care*, 11, pp. 67–78. https://doi.org/10.7224/1537-2073-11.2.67

Jones, K.H., Ford, D.V., Jones, P.A., John, A., Middelton, R.M., Lackhart Jones, H., et al., 2013. How people with multiple sclerosis rate their quality of life: an EQ-5D survey via the UK MS Register. *PLoS One,* 8(6), pp. 1–8. https://doi.org/10.1371/journal.pone.0065640 PMid:23776516; PMCid:PMC3679154

Karabudak, R., Dahdaleh, M., Aljumah, M., Alroughani, R., Alsharoqi, I.A., AlTahan, A.M., et al., 2015. Functional clinical outcomes in multiple sclerosis: current status and future prospects. *Multiple Sclerosis and Related Disorders,* 4(3), pp. 192–201. https://doi.org/10.1016/j.msard.2015.03.004 PMid:26008936

Kieseier, B.C. & Pozzilli, C., 2012. Assessing walking disability in multiple sclerosis. *Multiple Sclerosis Journal,* 18(7), pp. 914–924. https://doi.org/10.1177/1352458512444498 PMid:22740603

Kurtzke, J.F., 1983. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology,* 33(11), pp. 1444–1452. https://doi.org/10.1212/WNL.33.11.1444 PMid:6685237

Łabuz Roszak, B., Kubicka-Bączyk, K., Pierzchała, K., Horyniecki, M., Machowska-Majchrzak, A., Augustyńska-Mutryn, D., et al., 2013. Quality of life in multiple sclerosis – association with clinical features, fatigue and depressive syndrome. *Psychiatria Polska,* 47(3), pp. 433–441.

Lysandropoulos, A.P. & Havrdova, E., 2015. 'Hidden' factors influencing quality of life in patients with multiple sclerosis. *European Journal of Neurology,* 22(Suppl 2), pp. 28–33. https://doi.org/10.1111/ene.12801 PMid:26374511

Matias-Guiu, J.A., Cortés-Martínez, A., Valles-Salgado, M., Oreja-Guevara, C., Pytel, V. & Montero, P., 2017. Functional components of cognitive impairment in multiple sclerosis: a cross-sectional investigation. *Frontiers in Neurology,* 8(643), pp. 1–9. https://doi.org/10.3389/fneur.2017.00643 PMid:29234305; PMCid:PMC5712315

Meyer-Moock, S., Feng, Y.S., Maeurer, M., Dippel, F.W. & Kohlmann, T., 2014. Systematic literature review and validity evaluation of the Expanded Disability Status Scale (EDSS) and the Multiple Sclerosis Functional Composite (MSFC) in patients with multiple sclerosis. *BMC Neurology,* 14(58), pp. 1–10. https://doi.org/10.1186/1471-2377-14-58 PMid:24666846; PMCid:PMC3986942

Motl, R.W., Cohen, J.A., Benedict, R., Phillips, G., LaRocca, N., Hudson, L.D., et al., 2017. Validity of the timed 25-foot walk as an ambulatory performance outcome measure for multiple sclerosis. *Multiple Sclerosis Journal,* 23(5), pp. 704–710. https://doi.org/10.1177/1352458517690823 PMid:28206828; PMCid:PMC5405807

National Multiple Sclerosis Society, 2019. *Paced Auditory Serial Addition Test (PASAT).* Available at: https://www.nationalmssociety.org/For-Professionals/Researchers/Resources-for-Researchers/Clinical-Study-Measures/Paced-Auditory-Serial-Addition-Test-(PASAT) [12. 11. 2019].

Nowinski, C.J., Miller, D.M. & Cella, D., 2017. Evolution of patient-reported outcomes and their role in multiple sclerosis clinical trials. *Neurotherapeutics,* 14, pp. 934–944. https://doi.org/10.1007/s13311-017-0571-6 PMid:28913785; PMCid:PMC5722775

Opara, J.A., Jaracz, K. & Brola, W., 2010. Quality of life in multiple sclerosis. *Journal of Medicine and Life,* 3(4), pp. 352–358.

Ozakbas, S., Cagiran, I., Ormeci, B. & Idiman, E., 2004. Correlations between multiple sclerosis functional composite, expanded disability status scale and health-related quality of life during and after treatment of relapses in patients with multiple sclerosis. *Journal of the Neurological Sciences,* 218(1/2), pp. 3–7. https://doi.org/10.1016/j.jns.2003.09.015 PMid:14759626

Ozakbas, S., Turkoglu, R., Tamam, Y., Terzi, M., Taskapilioglu, O., Yucesan, C., et al., 2018. Prevalence of and risk factors for cognitive impairment in patients with relapsing-remitting multiple sclerosis: multi-center, controlled trial. *Multiple Sclerosis and Related Disorders,* 22(2018), pp. 70–76. https://doi.org/10.1016/j.msard.2018.03.009 PMid:29605801

Papuć, E. & Stelmasiak, Z., 2012. Factors predicting quality of life in a group of Polish subjects with multiple sclerosis: accounting for functional state, socio-demographic and clinical factors. *Clinical Neurology and Neurosurgery,* 114(4), pp. 341–346. https://doi.org/10.1016/j.clineuro.2011.11.012 PMid:22137087

Piri Çinar, B. & Güven Yorgun, Y., 2018. What we learned from the history of multiple sclerosis measurement: expanded disability status scale. *Archives of Neuropsychiatry,* 55(Suppl 1), pp. 69–75. https://doi.org/10.29399/npa.23343 PMid:30692861; PMCid:PMC6278618

Prosperini, L. & Castelli, L., 2018. Spotlight on postural control in patients with multiple sclerosis. *Degenerative Neurological and Neuromuscular Disease,* 8, pp. 25–34. https://doi.org/10.2147/DNND.S135755 PMid:30050386; PMCid:PMC6053902

Reese, J.P., Wienemann, G., John, A., Linnemann, A., Balzer-Geldsetzer, M., Mueller, U.O., et al., 2013. Preference-based health status in a German outpatient cohort with multiple sclerosis. *Health and Quality of Life Outcomes,* 11(162), pp. 1–9. https://doi.org/10.1186/1477-7525-11-162 PMid:24089999; PMCid:PMC3851447

Rugelj, D. & Palma, P., 2013. Bergova lestvica za oceno ravnotežja. Berg balance scale. *Fizioterapija,* 21(1), pp. 15–25.

Shapiro, R.T., 2011. Best practices in comprehensive MS symptomatic management. Reports from a CMSC Consensus Conference: team approach to complex symptomatic management in multiple sclerosis. *International Journal of MS Care*, 13(Suppl 4), p. 12. https://doi.org/10.7224/1537-2073-13.S4.1 PMid:24453699; PMCid:PMC3882948

Slavkovic, S., Golubovic, S., Vojnovic, M. & Nadj, C., 2019. Influence of cognitive and motor abilities on the level of current functioning in people with multiple sclerosis. *Zdravstveno Varstvo,* 58(2), pp. 54–61. https://doi.org/10.2478/sjph-2019-0007 PMid:30984295; PMCid:PMC6455014

Tiftikçioğlu, B.I., 2018. Multiple Sclerosis Functional Composite (MSFC): scoring instructions. *Archives of Neuropsychiatry,* 55(Suppl 1), pp. S46–S48. https://doi.org/10.29399/npa.23330

van Winsen, L.M.L., Kragt, J.J., Hoogervorst, E.L.J., Polman, C.H. & Uitdehaag, B.M.J., 2010. Outcome measurement in multiple sclerosis: detection of clinicaly relevant improvement. *Multiple Sclerosis,* 16(5), pp. 604–610. https://doi.org/10.1177/1352458509359922 PMid:20086019

Yalachkov, Y., Soydas, D., Bergmann, J., Frisch, S., Behrens, M., Foerch, et al., J. 2019. Determinants of quality of life in relapsing-remitting and progressive multiple sclerosis. *Multiple Sclerosis and Related Disorders,* 30, pp. 33–37. https://doi.org/10.1016/j.msard.2019.01.049 PMid:30735970

Ysrraelit, M.C., Fiol, M.P., Gaitán, M.I. & Correale, J., 2018. Quality of life assessment in multiple sclerosis: different perception between patients and neurologists. *Frontiers in Neurology,* 8(729), pp. 1–6. https://doi.org/10.3389/fneur.2017.00729 PMid:29375468; PMCid:PMC5769192

Cite as / Citirajte kot:
Koprivnik, M. & Hojs Fabjan, T., 2020. Clinical features in adult multiple sclerosis patients: a cross-sectional study. *Obzornik zdravstvene nege*, 54(2), 104–112. https://doi.org/10.14528/snr.2020.54.2.3016