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Review article

Improvement of gait and balance in patients with multiple sclerosis after multidisciplinary physical rehabilitation: Analysis of real-world data in Russia

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1. Introduction

Multiple sclerosis (MS) is a chronic immune-mediated inflammatory disease of the central nervous system (CNS) in which inflammation, demyelination, and axonal loss occurs in even early stages of the disease. Immunological disturbances lead to a complex of disabilities including disorders of strength, sensation, coordination and balance, as well as visual, cognitive and affective deficits (Lemus et al., 2018; Khan et al., 2006). The disease course can be extremely variable across individual patients, and although significant treatment advances have been made in recent years, MS remains one of the most frequent causes of neurological disability in young people (Oh et al., 2018). High variability of disease course, fluctuation of symptoms, and steady progression make rehabilitation necessary already in the early stages of the disease.

The main task of rehabilitation is to help patients to maintain daily activity, efficiency and social life in new conditions. Physical therapy is important part of intervention along with psychological and occupational therapy. Various exercises such as strengthening, stretching, aerobic training and robot-assisted training may reduce symptoms (fatigue, weakness, pain, balance impairment) and improve walking issues and mobility status of patients.

The effectiveness of multidisciplinary rehabilitation on improvement of the physical function of patients has been proven in numerous studies. In Hvid et al. (2021) study significant and clinically relevant improvements were found in all measures of walking capacity (6MWT, SSST, 5STS, DGI and MSWS-12). Interesting and solid data were also obtained from the multicenter study by Baert et al. (2014) in which, besides to confirming the effectiveness of rehabilitation, the validity of scales for assessing the results of interventions was considered. Long walking tests (2MWT and 6MWT) and patient-reported measures of walking ability (MSWS-12) proved to be more accurate compared to short walking tests (T25FW at either usual or fast speed) in detecting improvement after physical rehabilitation.

To our knowledge, no major (including multicenter) studies have been conducted in Russia to assess various rehabilitation methods and their results. In Russia, rehabilitation is available for all patients with multiple sclerosis under the compulsory health insurance program. Rehabilitation centers provide both outpatient and inpatient services. The aim of our study was to evaluate the efficacy of physical rehabilitation methods, applied in the Russian Federation, in patients with balance and walking disturbances caused by MS and to reveal predictors of positive outcomes.

2. Materials and methods

2.1. Patients

The study involved patients undergoing inpatient medical rehabilitation in the rehabilitation department of the Saint-Petersburg Center of Multiple Sclerosis and Autoimmune diseases (SBIH City Clinical

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Hospital #31) from October 2019 to August 2020. The study was approved by the local independent Ethical Committee of the City Clinical Hospital №31. Patients gave their written informed consent before participation.

The primary endpoint of the study was MCID achievement in the 6MWT. Several objectives were settled based on the aim of the study: to assess changes in tests' results before and after rehabilitation course; to evaluate the proportion of patients improved using minimally clinically important difference (MCID) in each test and in combinations of tests; to find out which baseline characteristics (demographic and clinical) contribute to improvement in tests.

Participants were required to meet the following criteria: >18 years of age, any gender with clinically definite diagnosis of MS of any type (established by clinical, laboratory and MRI criteria, matching 2017 McDonald et al. criteria) and any EDSS score with complaints of imbalance and/or walking impairment (). The criterion for exclusion was the duration of rehabilitation treatment of less than 5 weeks. Patients agreed to follow recommendations of their treating specialists and perform special tests before and after rehabilitation.

2.2. Intervention

Within 5 weeks patients underwent a multidisciplinary rehabilitation course. All patients received a physical therapy (PT) in groups and individually, machine-assisted therapy (treadmill, balance platform and bicycle ergometer) total duration of 1.5 h for 5 consecutive days. PT included aerobic exercises, strengthening, balance training, stretching and aquatic therapy (optional). Individual sessions with an occupational therapist and neuropsychologist were performed if necessary. Depending on the indications, occupational therapy could include the following methods: positioning (sourcing of a posture for effective and safe performance of the activities selected by the patient), adaptation of the environment, sourcing or adjustment of assistive devices, training of hand functions, of which using orthoses; mastering of activities of daily living, biofeedback therapy (ANIKA), gaze training etc. Neuropsychologist evaluated cognitive and emotional disorders in patients. The following scales were used to assess the corresponding domains: California Verbal Learning Test-II (CVLT-II), Brief Visuospatial Memory Test Revised (BVMRT), Symbol Digit Modalities Test (SDMT), Hospital Anxiety and Depression Scale (HADS), Patient Health Questionnaire (PHQ-9) and General Anxiety Disorder (GAD-7). When problems were detected, the following treatment protocols were applied: attention process training, word list, visual mnemonics, training in the use of notebooks, ect.

The total duration of daily rehabilitation procedures lasted from 1.5 to 3 h with breaks.

2.3. Assessment

Data were collected before and after physical rehabilitation course (Baseline – BL) by a neurologist (e.g., disease course and duration, EDSS score and pyramidal, sensory and cerebellum functional system score,) and a physical therapist (only gait and balance tests) during a physical examination. We used 4 tests to assess balance and walking performance in patients: Timed 25-Foot Walk (T25FW), 6 Min Walking Test (6MWT), 5 Times Sit-to-Stand Test (5TSST), Test Up-and-Go (TUG). The cognitive and emotional status of patients, as well as the occupational therapy implementation, were not taken into account in this study.

Minimal clinically important difference (MCID) was established according to recent research data to define if changes in gait and balance were clinically significant.

2.3.1. Timed 25-Foot walk (T25FW)

The test measures gait speed in patients with multiple sclerosis, and has been validated in several studies. A study by Kieseier and Pozzilli (2012) reported a high reliability (intra-class correlation coefficient (ICC)>0,9 in inter-rater, intra-rater and test-retest assessment) and validity of T25FW in pwMS. Same data were obtained in observational study Motl et al. (2017).

Patients were directed to one end of a clearly marked 25-foot course and were instructed to walk 25 feet as quickly as possible, but safely, being allowed to use any mobility aid (in this case, patient used same aid at BL and AR). The time was calculated from the instruction to start and ended when the patient reached the 25-foot mark.

MCID was defined as decrease of time on more than 20% from baseline (Hobart et al., 2013). Despite the fact, that such data from clinical trial on fampridine should be used with caution, these data seem the most appropriate to use as MCID to our knowledge.

Minutes walking test (6MWT). 6MWT is a widely approved test for measuring aerobic capacity and endurance while walking in patients with stroke (Kosak and Smith, 2004), Parkinson's disease (Steffen and Seney, 2008), spinal injuries (Van Hedel et al., 2005). The test was validated for MS in studies by Kieseier and Pozzilli (2012) and Goldman et al. (2008) and was recommended as an outcome measure (OM) by the American Physical Therapy Association (Potter et al., 2014).

Patients were instructed to walk as far as possible for 6 min. They were allowed to have rest stops, but it was forbidden to sit down. The patient could use any mobility aid (same at BL and AR).

MCID was defined as an increase of distance for more than 21.6 m from baseline based on the improvement from the patients' perspective in the study by Baert et al. (2014).

Times sit-to-stand test (5TSST). 5TSST was used as a measure of balance for MS patients in several studies. It's validity for MS patients has been studied in paper by Møller et al. (2012).

Patients set with arms folded across the chest with back against the chair. Patients were instructed to stand up and sit down for 5 times as fast as possible. The time was calculated upon therapist's instruction to start and ended when a patient was safely seated in the chair after 5th repetition. MCID was defined as a decrease in time on ≥34.6% from baseline (Jencen et al., 2016).

2.3.2. Timed up-and-go (TUG)

TUG was used to determine a risk fall and to measure a progress of ambulation and balance in patients. The test was validated in Sebastião et al. (2016) study and showed high/moderate associations with measures of ambulatory mobility and EDSS, balance confidence, and postural control. TUG is recommended to use in MS research as outcome measure (Potter et al., 2014; Cohen et al., 2015).

Patients started in a seated position, then stood up upon therapist's command, walked 3 m, turned around, walked back to the chair and set down. Measurement stopped when patients set with their back completely lying on a back of a chair.

MCID was defined as a decrease in time on ≥31% from baseline (Nilsagard et al., 2007).

2.4. Statistical analysis

All data are presented as median (25th and 75th quartiles; interquartile range) or mean (95 CI), depending on the type of distribution. Wilcoxon signed rank test was used for comparison of results at BL and AR. A multivariate linear regression analysis (logistic regression) was performed to assess the significance of baseline factors affecting improvement for each test. The endpoint was the patient's achievement of improvement relative to the MCID. Sex, age, disease duration, BL EDSS score and BL scores of pyramidal, sensory, and cerebellar functional systems were used as coefficients. Statistica 13 (http://statsoft.ru) and R (https://www.r-project.org) were used for calculations.

3. Results

3.1. Patients baseline characteristics

126 patients undergone the full course of inpatient multidisciplinary rehabilitation. The mean (SD) age of patients was 45.07 (10.83) years. Female patients prevailed with 86/126 (68.25%) included (binom test $p = 0.00005$). The median duration of the disease was 130.5 (71; 183.75) months. The clinical course was distributed among patients in following proportions: RRMS – 77/126 (61,11%), SPMS – 30/126 (23,81%), PPMS – 19/126 (15,08%) (pairwise comparisons using chi-squared test: RRMS vs SPMS $p = 0.00001$, RRMS vs PPMS $p = 0.00000001$, SPMS vs PPMS $p = 0.12$). The median EDSS score was 5.25 (25th, 75th percentiles; range: 4, 6; 2.5 – 6.5). 58/126 (45.03%) of patients had EDSS ≥ 6.0.

3.2. Efficacy analysis of physical rehabilitation

There were significant differences in results of performed tests before and after a rehabilitation course. Patients showed a significant positive dynamic in TUG ($p=1.329e^{-14}$), 6MWT ($p = 1.786e^{-12}$), 5-TSST ($p = 1.878e^{-12}$) and T25FW ($p = 3.927e^{-10}$). The median EDSS score also significantly decreased (5.25 at BL vs. 4.0 post rehabilitation, $p = 2.457e^{-11}$). Clinical data of our patients are summarized in the Table 1.

In total, 37/126 (29,4%) of patients showed improvement in T25FW, 88/126 (69,8%) - in 6MWT; only 17/126 (13,5%) of patients achieved MCID after rehabilitation in TUG, and 18/126 (14,3%) – in 5-TSST. We also assessed the distribution of patients based on the number of tests where improvements above MCID were achieved. Thus, 29/126 (23,0%) patients had improvement in 6MWT and T25FW, 12/126 (9,5%) – in 6MWT, T25FW and TUG, 8/126 (6,3%) – in all 4 tests.

3.2.1. Predictors of improvement

Cross-validation analysis was performed to define possible factors contributing to outcomes of the rehabilitation. For all tests, disease duration and the age of patients were significant predictors of improvement above the MCID. Baseline EDSS score had a weighty impact on positive outcome (Fig. 1). Our decision tree model based on three major variables (disease duration, age and EDSS) showed more accuracy in outcomes prediction compared to a model based on all BL characteristics for tests (more data in Table 2).

Our statistical model showed the greatest accuracy in predicting a true negative outcome in T25FW, TUG, 5TSST. The 6MWT was the only test where the model predicted improvement above MCID with adequate accuracy. In the 6MWT, positive outcome significantly depended on the total disease duration and the age of patients. Thus, with disease duration <45 months and age <43 years, improvement is achievable for a significant number of patients (Fig. 2). Variables' importance scores generated in the decision tree are presented in the Fig. 2. More data are available in the Appendix A.

MS – multiple sclerosis; EDSS – Expanded disability status scale; FS - functional scale in the EDSS score; RRMS – relapsing-remitting multiple sclerosis; SPMS – secondary progressive multiple sclerosis; T25FW – Times 25-foot walk test, TUG – Timed Up-and-Go, 5TSST – 5 Times Sit-to-Stand Test, 6MWT – 6 Min Walking Test

To define if any of baseline characteristics had a significant impact on the *magnitude* of changes, we performed the multiple regression analysis. No significant correlates were revealed for T25FW and 6MWT. Sensory component of EDSS showed a significant impact on the TUG test magnitude of change ($p = 0.0005$) and a pyramidal functional system score showed a trend to significant changes. For the 5TSST, only the baseline EDSS score had a significant impact ($p = 0.0029$). Data are presented in the Table 3.

Table 1
Changes in EDSS, balance and gait measurements following physical rehabilitation program.

Variables	Baseline	Post Rehabilitation	*p*-value
EDSS, median (25th and 75th percentiles), range	5.25 (4; 6) 2.5 – 6.5	4 (3.5; 6) 2.0 – 6.5	***p* < 0.0001***
TUG, median (25th and 75th percentiles), range, seconds	11.95 (8.89; 16.78) 5.41 – 66	9.72 (7.98; 15) 5.35 – 46	***p* < 0.0001****
6MWT, mean (SD) in meters, seconds	285.13 (144.59)	328.15 (146.35)	***p* < 0.0001*****
5-TSST, median (25th and 75th percentiles), range, seconds	14.19 (10.74; 17.79) 6.21 – 87	12.13 (10; 15.29) 5.9 – 30.78	***p* < 0.0001†**
T25FW, median (25th and 75th percentiles), range, seconds	7.61 (6.12; 10.66) 3.81 – 60	6.58 (5.56; 9.58) 3.36 – 46	***p* < 0.0001‡**

T25FW – Times 25-foot walk test, TUG – Timed Up-and-Go, 5TSST – 5 Times Sit-to-Stand Test, 6MWT – 6 Min Walking Test, EDSS – Expanded Disability Status Scale, * $p = 0.00000000002457$, ** - $p = 0.00000000000001329$, *** - $p = 0.000000000001786$, † - $p = 0.000000000001878$, ‡- $p = 0.0000000003927$.

4. Discussion

This study focused on the effect of physical rehabilitation on walking and balance dysfunctions in MS patients. We also aimed to find predictors of a positive response to these interventions from simple clinical and demographical data, collected in the routine practice.

In this study, a significant improvement was reached for all tests of balance and gait efficiency. Our data are in line with a number of other studies reporting a positive effect of different physical rehabilitation program on walking, balance and ambulation in people with multiple sclerosis. Thus, patients generally show significant improvements in TUG, 6MWT, 5-TSST and T25FW after rehabilitation programs (Møller et al., 2012; Kalron et al., 2015; Baert et al., 2018). However, a clear discrepancy was evident: among our patients, 69,8% achieved an improvement in 6MWT (the primary endpoint reached), that more than doubled the number of patients who improved their T25FW results (29, 4%). This confirms previous results on Baert et al. (2014).

Key factors influencing the improvement in our study were age of patients, disease duration and baseline EDSS score. To our knowledge, not so many studies investigated the impact of age on rehabilitation outcomes. In the study by Langdon and Thompson (1999) the age of patients with MS was not predictive of an improvement in both motor and cognitive tests. In the study of patients with spinal cord trauma by New and Epi (2007), the age of patients increased the risk of complications during rehabilitation (e.g. pressure ulcer), but showed no impact on benefits of rehabilitation. Age alone was a significant predictor of total FIM score and Motor FIM score after rehabilitation at discharge in the study by Bagg et al. (2002) and Bindawas et al. (2017) in patients with stroke. Hence, no straightforward associations with age were described until now. The influence of age on the course of MS and the level of disability is described in detail in many studies. Predominance of gliosis and axonal damage over remyelination processes increases with age (Frischer et al., 2009; Lassman, 2011). The lack of adequate remyelination leads to the progression of the disease, which is accompanied by a steady increase in walking difficulties, impaired hand function, and a decrease in cognitive functions. Post-relapse recovery potential declines with senescence leading to more likely accumulation of disability due to relapses (Conway et al., 2018). The effectiveness of disease-modifying therapy also decreases with aging, while increasing the risk of adverse events (Weideman et al., 2017). Given these conditions, the association of rehabilitation outcomes with age described in our study seem logically justified.

The impact of the disease duration is somewhat contradictory. In the study of Gaber et al. (2010), no relationship was found between the disease duration and the achievement of rehabilitation goals. In this study, the assessment of benefit was made based on the achievement of

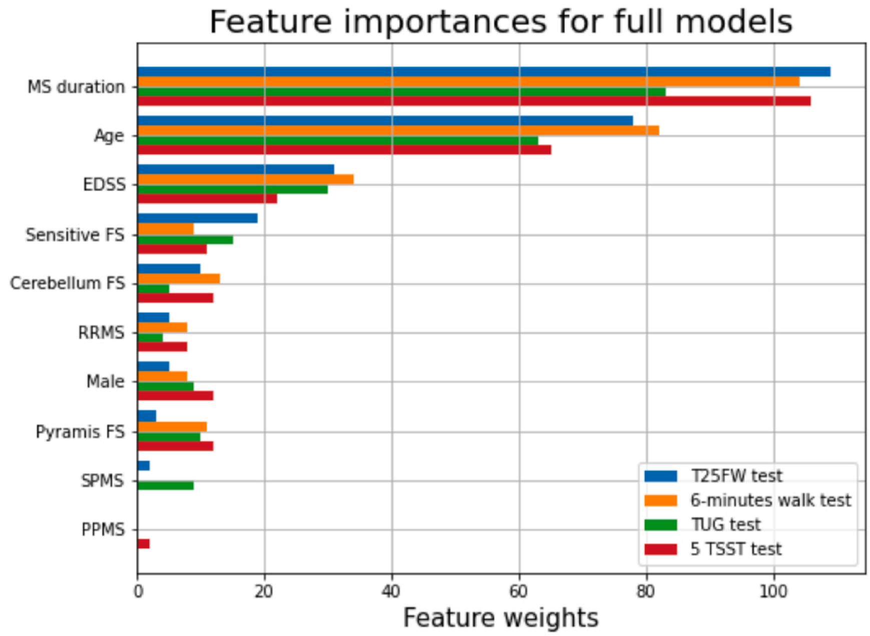

Fig. 1. Variables' importance scores generated in the decision tree to describe the improvement for each test.

Table 2
Accuracy of statistical models.

Tests	Model 1 (for all BL variables)	Model 2 (disease duration, age and EDSS)
T25FW	57.95% (6.72%)	61.36% (6.82%)
TUG	78.41% (5.90%)	80.68% (1.97%)
5TSST	82.95% (8.12%)	80.68% (4.95%)
6MWT	55.68% (8.12%)	61.36% (8.19%)

T25FW – Times 25-foot walk test, TUG – Timed Up-and-Go, 5TSST – 5 Times Sit-to-Stand Test, 6MWT – 6 Min Walking Test, BL – baseline.

rehabilitation goals, in contrast to our study. In the study by Liberatore et al. (2013) patients with a longer disease duration had a poorer response to rehabilitation, that corresponds with finding of our study. This tendency was also true in the study Grasso et al. (2005), where patients with a short disease duration (less than 15 years) had a nearly twice as high probability of improvement of the Barthel Index (BI) than other patients. Long-term disease duration affects cognitive functions (Brochet and Ruet, 2019) as well as fatigue (Ghajarzadeh et al., 2013) and the quality of life (QoL) (Rezapour et al., 2017). These symptoms are difficult to treat with medication and, to our point of view, can significantly reduce the effectiveness and adherence to rehabilitation measures.

The effect of baseline EDSS score on outcomes is controversial as well. Grasso et al. (2009) observed a greater effectiveness in patients with mildly (EDSS score 2–5.5) and moderately (EDSS score 6.0–6.5) disabled MS patients in BI and Rivermead Mobility Index (RMI). In the study by Groppo et al. (2019) EDSS improvement was significantly more frequent in patients with a shorter disease duration, female gender, RRMS course and longer admission duration, that is in line with our data.

Additionally, this is the first study, to our knowledge, that used the decision-tree algorithm to evaluate the impact of predictors. This neural network algorithm may find additional associations, not previously shown by a regression analysis or other methods. We also used MCIDs to describe a rehabilitation effectiveness, that is not also a common strategy.

6MWT is designed to assess a tolerance to aerobic exercise and adaptability of patient to a usual life activity. Endurance is related to the neurological status of patients, but also to the efficiency of respiratory

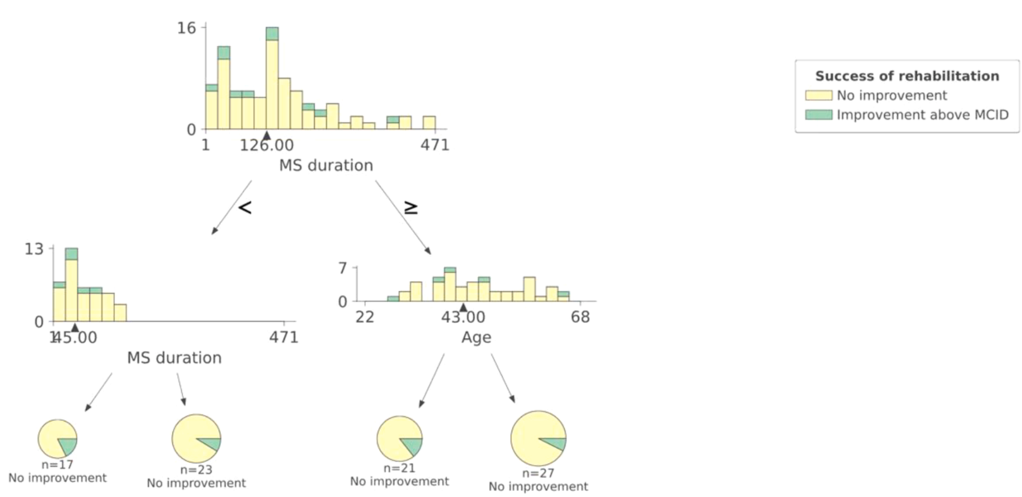

Fig. 2. The decision tree classifier of improvement in the 6 min walking test.

Table 3
Multiple regression analysis to evaluate the associations of baseline predictors on the magnitude of changes after rehabilitation.

Tests	Coefficients	Estimate	Standard. Error	*p*-value
T25FW	EDSS (BL)	0.4845	0.2978	0.106
	Pyramidal Functions	−0.9636	2.2142	0.664
TUG	Sex	−1.5545	0.9568	0.1070
	Disease duration	0.0065	0.0041	0.1181
	Pyramidal Functions	5.9017	2.9899	0.0508
	Sensory Functions	18.1749	5.0871	**0.0005**
5TSST	Sex	1.9110	1.2625	0.1327
	EDSS (BL)	1.5017	0.4937	**0.0029**
6MWT	Sex	−3.8583	15.4243	0.803
	Age	−0.4149	0.6750	0.540
	Disease duration	−0.01220	0.0700	0.862
	Pyramidal Functions	58.5363	51.9831	0.263
	Sensory Functions	−56.0910	54.1795	0.303
	Cerebellar Functions	−91.48388	86.79430	0.294

T25FW – Times 25-foot walk test, TUG – Timed Up-and-Go, 5TSST – 5 Times Sit-to-Stand Test, 6MWT – 6 Min Walking Test, EDSS – Expanded Disability Status Scale, BL – baseline.

and cardiovascular systems function. Regular aerobic exercise has a significant effect on muscle strength, balance, as well as latent symptoms of MS progression (depression and fatigue) and significantly improves patients' QoL (Swank et al., 2013; Giesser, 2015). There are a number of studies on the effect of aerobic exercise indirectly through neurotrophic factors in patients and animal models (Devasahayam et al., 2017; Banitalebi et al., 2020; Bansi et al., 2012). This multidirectional effect of exercise is especially important for patients with progressive type of MS. Exercises performed by patients during our rehabilitation interventions (treadmill, bicycle ergometer, physical therapy) were attributed to aerobic training, that certainly led to an increase in walking distance.

The magnitude of improvement in 6MWT results wasn't associated with any baseline characteristics in patients. Understanding the factors that influence the results in 6MWT seems important, since this particular test reflects the patients' tolerance to aerobic exercise, which is necessary for daily activity.

T25FW is used for assessing gait velocity, which may be affected by balance confidence, fatigue and motor planning (Nogueira et al., 2013). The gait speed is related to factors other than aerobic capacity in 6WMT, such as muscle power, neural drive and dual-task performance, that are impaired in MS patients (Nogueira et al., 2013; Fimland et al., 2010; Güner et al., 2015). Improvements in this test may require different approach in training that was not the primary aim for the majority of patients. They were trained to increase mostly their walking distance, than the speed of gait, and the accent was made on the safety of their gait. This may have had led to improvements in only 17.1% of patients in T25FW test. Our data are in line with other studies. In a study by Baert et al. (2014), the improvement of fastest speed in T25FW was −6.5% in the whole group which is below the chosen MCID in our study.

We didn't find any statistically significant association of baseline characteristics with magnitude of T25FW improvement. Motl et al. (2017) noted that the T25FW is not universally applicable across the MS spectrum, as it might have ceiling effects for those with EDSS of 6.5 or above (i.e. not able to walk 25 feet). Similar data were obtained by Baert et al. (2014). They showed that T25FW is less responsive than 6MWT, especially in moderately to severely disabled patients (EDSS 4.5–6.5). The proportion of patients improved above MCID in our cohort is only 17.1%, probably related to a relatively high proportion of severe disability (EDSS$\geq$ 6.0 in 58/127 (45.67%) patients). Thus, despite the simplicity of implementation for therapists, doctors and patients, this test showed a significant limitation for the use in a group of disabled MS patients as a rehabilitation outcome.

The TUG test has been established as an indicator of fall risk and basic functional mobility (Schoene et al., 2013). Sustained implementation of tasks requires the coordinated work of several systems at once: muscle strength, balance, and motor control of walking. Significant associations were observed between TUG and Sensory (p = 0.0005) functional scale score and a trend was revealed for the Pyramidal functional scale score (p = 0.0508). In Sebastião et al. (2016) study same strong correlation was revealed for Pyramidal and Cerebellar functions as well. Indeed, the TUG includes elements that mimic commonly performed movements present in everyday life, which are not captured by other valid mobility measures such as T25FW and 6MWT.

The significant association between the magnitude of improvement of 5TSST and baseline EDSS score is also consistent with other reports. Rising from a seated to a standing position is one of the most common activities of daily living, that reflects maintaining physical independence and functional mobility. Significant correlations were found between the 5TSST and knee flexor and extensor muscle strength, and between the 5TSST and balance performance in Møller et al. (2012) research. Thus, the increase in muscle strength is reflected in both the EDSS score and improved test time. In a study by Møller et al. (2012) they used a different MCID (25,5%), which seems to be a more achievable and equally tangible change for patients. More data on this test are needed for MS patients.

From our point of view, the use of rehabilitation outcomes should be based on the level of patients' disability. A similar hypothesis was tested in the Baert et al. (2014) study where patients were divided in groups based on EDSS score. According to their data, MSWS- 12 and long walking capacity tests (e.g. 6MWT) may be more appropriate than short walking tests (e.g. T25FW) for detecting change in mildly as well as moderate–severe disabled patients. The objectives of our study did not include dividing patients into groups depending on the EDSS score. However, the statistical model (decision tree classifier, see Appendix) predicted a truly negative outcome in T25FW for patients with EDSS<4, mild disability level, while positive outcomes in 6MWT had no such connection with EDSS score. The general conclusion of the observational data is that walking distance (endurance) can be improved across the disability spectrum, but gait speed - in the moderate MS stage.

The limitation of our study is the absence of control group; however, this was a study in a routine clinical practice setting. Adding a follow-up period to assess the longevity of the effect of rehabilitation would add an additional value, however this was not the scope of this study.

Clear outcome measures should be implemented into clinical practice to estimate the impact of rehabilitation. From this study, however, we can see that for the majority of tests taken, the results were below the level of MCID despite highly significant changes of absolute values for the group in general. This may stem from the methods used to determine the MCIDs. Determination of MCID is a cornerstone aspect of any test, however, the methodology of counting MCID in tests for MS rehabilitation may differ significantly. Thus, a study by Learmonth et al., (2013) estimated MCID as a function of standard error of mean (SEM), reflecting real changes in tests after 6 months. However, in their study no rehabilitation intervention was applied, so these data may be more suitable for long-term follow-up studies when worsening of disability is mostly expected Learmonth et al., (2013). In the study by Baert et al. (2014), MCIDs were counted after rehabilitation and used external validation by patients' and experts' opinion, presenting appropriate MCID for 6MWT. MCID for T25FW and 5TSST were taken from studies of fampridine and, so, should be interpreted with caution, however, they were also found in studies where improvement in function was the main outcome (Hobart et al., 2013; Jensen et al., 2016). We could not find same data for TUG test, so it was taken from the study with no rehabilitation intervention (Nilsagard et al., 2007). MCIDs for T25FW, 5TSST and TUG seem quite high for many patients, especially those with significant disability, to reach them. Conversely, MCID for the 6MWT (+21, 6 m) was determined based on patients' perspective and this test showed the greatest percentage of improvement. Thus, more harmonization in measuring rehabilitation outcomes is required in order to claim that methods we study really work.

In this study we showed the beneficial impact of multidisciplinary rehabilitation on gait and balance parameters, however, this was above the selected MCIDs only for a limited number of patients. Since rehabilitation is a goal-oriented process, a careful selection of measurements in specific domains of goals should be implemented in the routine clinical practice. Many outcomes correlate with measures of disability (EDSS), so using of goals may be stratified based on baseline EDSS score.

Author statement

A.Stepanova has nothing to declare

G.Makshakov has received honoraria for lectures and speaking in the past 2 years from Roche, Novartis, Valenta and Ipsen.

A. Kulyakhtin has nothing to declare

I.Kalinin has nothing to declare

P. Feys has nothing to declare. Editorial board member of MSJ, NNR and Frontiers in Rehabilitation Sciences

E.Evdoshenko has nothing to declare.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.msard.2022.103640.

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