NÖRO PSİKİYATRİ ARŞİVİ
ARCHIVES OF NEUROPSYCHIATRY

**REVIEW/** DERLEME

Arch Neuropsychiatry 2018;55: (Supplement 1): S46–S48
https://doi.org/10.29399/npa.23330

# Multiple Sclerosis Functional Composite (MSFC): Scoring Instructions

## Multipl Skleroz Bileşik İşlevsellik Ölçütü (MSFC): Hesaplama Talimatları

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**ABSTRACT**

It is important to assess the clinical outcome in patients with multiple sclerosis (MS) both during individual clinical follow-up and in clinical trials. The National MS Society's Clinical Outcomes Assessment Task Force has developed and recommended a multidimensional clinical outcome measure, namely Multiple Sclerosis Functional Composite (MSFC). This enables to measure the impact of MS in three key clinical dimensions: leg function and ambulation, arm and hand function, and cognitive function. Raw scores in different measurement scales are transformed into standard comparable scores (z-scores) and an overall composite score is calculated. In this review, the rationale behind the MSFC, administration and calculation of the composite score is discussed in detail.

**Keywords:** multiple sclerosis, clinical outcome measure, MSFC, multiple sclerosis functional composite

**ÖZ**

Multipl sklerozda (MS) klinik sonuçların değerlendirilmesi hem bireysel hasta takibi hem de klinik çalışmalarda sonlanımın değerlendirilebilmesi açısından önemlidir. Ulusal MS Cemiyeti'nin Klinik Sonlanımı Değerlendirme Grubu "Multipl Skleroz Bileşik İşlevsellik Ölçütü (MSFC)" ismiyle çok yönlü bir klinik sonlanımı değerlendirme ölçeği geliştirmiş ve önermiştir. Bu ölçüt, MS'in üç önemli klinik alandaki etkisinin değerlendirilmesine yarar: bacak fonksiyonu ve yürüme, el ve kol fonksiyonu, bilişsel fonksiyon. Farklı ölçüm birimlerindeki ham veriler, standart karşılaştırılabilir verilere (z-skoru) dönüştürülür ve bileşik skor hesaplanır. Bu derlemede, MSFC temelindeki mantık, testin uygulanması ve bileşik skorun hesaplanması detaylı olarak tartışılmıştır.

**Anahtar Kelimeler:** multipl skleroz, klinik sonlanım ölçütü, MSFC, multipl skleroz bileşik işlevsellik ölçütü

**Cite this article as:** Tiftikçioğlu Bİ. Multiple Sclerosis Functional Composite (MSFC): Scoring Instructions. Arch Neuropsychiatry 2018;55: (Supplement 1):S46-S48. https://doi.org/10.29399/npa.23330

## MULTIPLE SCLEROSIS FUNCTIONAL COMPOSITE

Scoring systems are needed to measure the clinical status, disease severity and clinical outcome both during the individual clinical follow-up of a patient and in clinical studies. Several indexes or scoring systems have been developed to assess the clinical severity and functional deficits in patients with multiple sclerosis (MS).

Multiple Sclerosis Functional Composite (MSFC) is a multidimensional, three-component performance scale to assess the degree of impairment in MS patients. It was developed by the National MS Society (NMSS) Clinical Outcomes Assessment Task Force, after an international workshop in Charleston, South Carolina (USA), in 1994. Members of the Task Force represented five countries from different disciplines including neurology, psychology, biostatistics and epidemiology, and drug industry (1).

After a rigorous analysis of a set of various candidate outcome measures, the following tests were identified in three clinical dimensions: Timed 25-Foot Walk (T25W) for leg function and ambulation, 9-Hole Peg Test (9HPT) for arm and hand function, and Paced Auditory Serial Addition Test (PASAT-3) for cognitive function. Measures for visual function, sensory function, bowel, bladder, and sexual function were not included for various reasons. The reliability, validity, and sensitivity of these measures were analyzed using the group data from several major clinical trials and natural history studies (1–3).

### 1. Description of MSFC Component Measures

T25W is a quantitative measure of lower extremity function and ambulation. The patient is instructed to walk a distance of 25 feet (7.62 meters), clearly marked at both ends with prominent signs, as quickly as possible, but safely. It should be noted if the patient requires his/her assistive device for walking. As the patient completes first timed walk (Trial 1), he/she is instructed to walk the way back to the starting point (Trial 2). The amount of time required for walking this standard distance in both trials is recorded in seconds. Time limit per trial is 180 seconds (3 minutes). If the patient cannot complete a trial in 3 minutes, or completes

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**Received/Geliş Tarihi:** 31.07.2018, **Accepted/Kabul Tarihi:** 14.09.2018

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the first trial but cannot complete trial 2 after a 5-minute rest period, then the test is discontinued.

9HPT is a quantitative measure of upper extremity (hand and arm) function. The patient is instructed to place pegs one by one into each of nine holes arranged in a board stabilized with a plastic nonslip sheet on a solid table, and then to remove these pegs from the holes. Both the dominant and non-dominant hands are tested twice (two consecutive trials for each hand). The side of the board with pegs should be in front of the hand being tested. The patient is required to complete two successful trials for each hand. The amount of time (in seconds) required to place and remove all nine pegs is recorded for each trial.

PASAT-3 is the last test included in MSFC, which is a measure of cognitive function, enabling the assessment of concentration, speed of auditory information processing, flexibility and calculation. A total of sixty single digit numbers are presented by an audiotape/CD-rom at a constant rate in every 3 seconds (PASAT-3). Patient is required to add each new number to the one immediately prior to it. Due to the relative complexity of this test, a practice trial with a set of 10 numbers should be performed prior to the original test. The patient is allowed up to three practice trials. At east two correct answers on any three trials is sufficient to proceed with the original test. Two sets of numbers (forms A and B) have been developed to be used alternatively in every visit to minimize memorizing. The number of correct answers is recorded. PASAT-2 (stimuli every 2 seconds) test might be administered after PASAT-3 if desired.

## 2. MSFC Administration

Ideally, a standardized protocol should be assigned and a single examining physician/technician with adequate training should administer all three tests to avoid inter-rater variability, which could significantly alter the results.

Tests should be explained to the patient in a clear and understandable way. Full instructions should be given to the patient exactly as is given in the instruction manual of test (4).

The testing room settings and environmental conditions should be standardized and any change should be avoided. All equipment (stopwatch, marked 25-foot line, 9HPT apparatus, CD player, PASAT-3 stimulus records, pen and patient forms) should be kept readily available. Any effort should be made to avoid any unnecessary stimulus that could distract the patient. Only the examiner and the patient should be in the testing room during 9HPT and PASAT-3. The space for T25W should be cleared off any obstacles.

The patient should feel comfortable with the situation. Examiner should explain the instructions in a professional but friendly way and let the patient ask any questions before starting the tests.

Examiner should write down the test results, as well as any situation that disturbs the performance of patient.

Examiner should not provide direct feedback to the patient about his/her performance.

## 3. Scoring the MSFC

Since the units of three variables measured by three tests are different (time for T25W and 9HPT and number of correct answers in PASAT-3), raw scores should be converted to a common metric, namely z-scores. The overall composite score (MSFC score) is calculated by adding the z-scores for each test.

### *Transforming The Raw Data into Z-scores*

Z-score enables addition of various measurements with different units by converting the data into a standardized value. Table 1 shows the general formula for calculating the MSFC score.

**Table 1.** The formula for creating the MSFC score

$$\text{MSFC Score} = \frac{(Z_{arm,average} + Z_{leg,average} + Z_{cognitive})}{3}$$

Z-score compares each variable with the outcome of a reference population and indicates a location (point) for each variable according to that population. Z-score is expressed in units of standard deviation. In other words, z-score enables us to understand the distance of our data according to the mean value of a reference population in units of standard deviation. Here, it is important to define the reference population. Reference population could be the patient cohort in a particular study, where the test results from the baseline visit from all patients in a particular study cohort is selected. Another method is to use the data of all multiple sclerosis patients in a pooled dataset. The most preferred reference dataset is the data from NMSS Task Force database (1, 2). Using results from normal subjects could be another option, however this leads to lower z-scores, making most patients worse than normal. Although the population choice does not affect comparisons of a single variable over time, but affects the overall composite score when single z-scores are summed up (2).

Another important issue in transforming z-scores is the direction (sign) of z-score, which should be same in all three variables to determine the deterioration in all three tests. Sign of z-score indicates whether the result is better or worse than the mean value of reference population. Decreased z-scores in PASAT-3 indicate deterioration, however, decreased z-scores in T25W and 9HPT indicate improvement. When calculating the composite score, different directions would alter the composite score, unintentionally. Therefore, proper adjustments should be made to z-scores according to the tests. One method is to multiply z-score by -1. This method is recommended to transform z-scores of T25W test. Another method is to take the reciprocal of the test value while calculating z-score. This method is recommended for values where small increases are important for a variable, such as 9HPT. These adjustments are explained, below.

The formulas for calculating z-scores for each test are shown in Table 2.

**Table 2.** The formulas for calculating z-scores for each test

$$Z_{arm,\ average} = \frac{\text{Average (1/9HPT)} - \text{Mean}_{\text{Reference cohort}}\text{(1/9HPT)}}{\text{Std Dev}_{\text{Reference cohort}}\text{(1/9HPT)}}$$

$$Z_{leg,\ average} = \frac{\text{Average T25W} - \text{Mean}_{\text{Reference cohort}}\text{T25W}}{\text{Std Dev}_{\text{Reference cohort}}\text{T25W}}$$

$$Z_{cognitive} = \frac{\text{PASAT-3} - \text{Mean}_{\text{Reference cohort}}\text{PASAT-3}}{\text{Std Dev}_{\text{Reference cohort}}\text{PASAT-3}}$$

An example could help us to better understand. Suppose that a 25-year-old female, diagnosed with RRMS, has completed two trials of T25W test in 4.7 and 5.6 seconds. She has performed the two trials of 9HPT with

dominant hand in 18.7 and 19.2 seconds and with non-dominant in 20.7 and 20.4 seconds. Her number of correct answers in PASAT-3 Form A was 42. Reference population is the NMSS Task Force Database. If we put these data in to the formula and standardize the results of our patient to the Task Force database:

$$Z_{arm,\ average} = \frac{[(1/19.0) + (1/20.6)] / 2 - 0.0439}{0.0101}$$

$$Z_{leg,\ average} = -\left\{\frac{[(4.7 + 5.6) / 2] - 9.5353}{11.4058}\right\}$$

$$Z_{cognitive} = \frac{42 - 45.0311}{12.0771}$$

MSFC score = (0.693 + 0.377 – 0.251) / 3 = 0.273

It is important to remember that MSFC score changes according to the reference population selected. Therefore, the same reference population should be selected for follow-up visits.

Finally, attention is needed for special situations, such as the inability of the patient to complete a test due to disability or fatigue. If the patient is unable to perform 9HPT, instead of leaving blank, or scoring zero, the result is coded as 777, as recommended in MSFC instructions, providing a number pretty close to zero. If the patient is unable to perform T25W test, the z-score of 13.7 (adjusted: -13.7) is recorded, which is the largest z-score calculated in the NMSS Task Force database. If the patient does not get at least one correct answer on PASAT-3, which means unable to complete PASAT-3 test, a score of zero is recorded.

**This review was presented during "MSFC Session" at 2nd Assessment of Physical Disability in Multiple Sclerosis Symposium, May19-20th, 2018, İzmir, Turkey.**

**Peer-review:** Externally peer-reviewed.

**Financial Disclosure:** The author declared that this study has received no financial support.

**Bu derleme "2. Multipl Sklerozda Fiziksel Engelliliğin Ölçümü Sempozyumu" sırasında "MSFC oturumu"ndaki konuşmadan hazırlanmıştır.**

**Hakem Değerlendirmesi:** Dış Bağımsız.

**Finansal Destek:** Yazar bu çalışma için finansal destek almadığını beyan etmiştir.

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