Original Article

Relationship Between Corpus Callusom Index and Clinical Subtypes, Severity of Cognitive Disorders, and Disability in Multiple Sclerosis

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Abstract

Background: Brain magnetic resonance imaging (MRI) is crucial to determine the prognosis of multiple sclerosis (MS). The use of simple and accessible techniques that can be used for examining and managing the cognitive status and disability of patients with MS is one of the important concerns. This study aimed to investigate the relationship between corpus callosum index in brain MRI and clinical subgroups of MS, severity of cognitive disorders, and disability in multiple sclerosis.

Materials and Methods: This cross-sectional study was conducted to determine the relationship between CCI and clinical subgroups of MS, the severity of cognitive disorders, and disability in patients with MS referred to Imam Hossein Hospital in 2020. The maximum length of the corpus callosum (anterior, posterior diameter) was measured, and the height of the corpus callosum was measured on a line perpendicular to its long axis. Corpus callosum index (CCI), symbol digit modalities test (SDMT), and expanded disability status scale (EDSS) were assessed in patients. A significance level of less than 0.05 was considered.

Results: A total of 85 patients with a mean age of 40.73 ± 8.45 years were assessed, and 65.9% were women. The CCI value was significantly lower in women (P-value: 0.001). The mean value of EDSS in all participants was 2.64±2.49. There was a statistically significant difference between the different subgroups of MS with the EDSS score, age of disease onset, SDMT score, CCI index, and mean disease duration (all P-values<0.05). There was a significant negative correlation between the CCI index and age (P:0.02, r:-0.24), duration of the disease (P:0.001, r:-0.38), EDSS (P:0.001, r:-0.71), while the correlation between SDMT and CCI was positive (P:0.001, r:0.67).

Conclusion: CCI is a quick and cost-beneficial parameter to evaluate cognitive disorders and disability in patients with MS.

Keywords: Multiple sclerosis, Corpus callosum, Magnetic resonance imaging

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Introduction

Multiple sclerosis (MS) is one of the most common neurological diseases of the central nervous system, which has various clinical manifestations and affects the sensory, motor, cerebellum, brainstem, and autonomic systems. MS progression leads to disability that can affect quality of life[4-7]. In 2013, the global prevalence of MS was 33 per 100,000, an increase from

about 30 per 100,000 in 2008[5].

Several studies found that visual and verbal episodic memory reduction, as well as cognitive processing speed reduction, are the most common cognitive complications in multiple sclerosis. In one study, impairments in the symbol digit modality test (SDMT) (up to 50%), the California verbal learning test-II (27.5%), and the brief visuospatial memory test (32.5%) were found in MS patients[6,7].

The corpus callosum is the largest communicating pathway between the cerebral hemispheres. Recent studies revealed this structure's structural and functional changes in many neurological diseases[8]. Magnetic resonance imaging (MRI) is an important imaging method in diagnosing, evaluating response to treatment, and follow-up in patients with MS. Corpus callosum measurements can be used as an alternative method for brain atrophy evaluations[9]. There is increasing evidence that structural evaluations of the corpus callosum are valuable as a marker in multiple sclerosis. These assessments may help demonstrate corticospinal tract atrophy and lesion load[10].

It has been found that damage to the corpus callosum is related to cognitive disorders in patients with multiple sclerosis[11,12]. Limited studies have investigated the relationship between structural characteristics of the corpus callosum, clinical characteristics, and disability in MS. Therefore, this study aimed to investigate the relationship between the corpus callosum index as an available marker, with clinical subgroups, cognitive disorders, and the disability of the disease.

Methods

This cross-sectional study investigated the relationship between the corpus callosum index in brain MRI and the clinical subgroups, severity of cognitive disorders, and disability in MS. All MS patients referred to Imam Hossein Hospital in 2023 were examined.

The inclusion criteria were age between 18 and 50, confirmed multiple sclerosis diagnosis based on McDonald's criteria[13], and performed brain MRI in Imam Hossein Hospital in 2023. The exclusion criteria were images that lacked the necessary quality for interpretation, any bleeding lesion or mass in the brain or skull area, chronic brain diseases like seizures or non-brain disease such as diabetes that can cause brain atrophy, and not having consent to participate in the study.

Clinical data, including (the clinical subgroup of the disease, age of onset of the disease, and expanded disability status scale (EDSS) test) were evaluated by the neurologist. The interval between brain MRI and EDSS test was over 2 weeks. An MS MRI was re-examined and evaluated by a neurologist. The subgroups of MS were classified as Relapsing-Remitting MS (RRMS), Secondary Progressive MS (SPMS), and Primary Progressive MS (PPMS)[13].

The formula [Genu+trancus+splenium/AP diameter] was used in the sagittal sections of the T1-weighted brain MRI sequence to calculate the corpus callosum index[14].

The symbol digit modalities test (SDMT) was used to check the brain's cognitive function. This test consists of an encrypted key of 9 abstract symbols, each paired with a number from 1 to 9. The subject must quickly scan the key and write the number corresponding to each symbol. In this test, printed on a sheet, we consider the maximum number of shapes the patient pairs with the correct number in 90 seconds as the test answer[15].

EDSS test was used to check the severity of disability in these patients. The EDSS increases from 0 to 10 in increments of 0.5 units, indicating higher levels of disability[16]. Scoring was based on the examination by a neurologist, and all patient data were entered into the researcher's checklist.

Statistical analysis: Mean, standard deviation, median, range, frequency, and percentage were used to describe the data. We used the ANOVA test to compare numerical variables and Pearson's correlation coefficient to check the relationship between variables. Analyzes were performed by SPSS v.25.0 statistical software. A P-value less than 0.05 was considered statistically significant.

Ethical consideration: This study was approved by the ethical committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1402.312).

Results

In this study, 85 patients with MS were examined. In Table 1, information on demographic characteristics is seen.

Table 1. Demographic information of patients**.**

Parameters	Mean ± SD	Median N (%)
Age	40.73 ± 8.45	42 (4.56)
Sex	Male	29 (34.1)
	Female	56 (65.9)

Table 2 shows the demographic and clinical characteristics of the patients based on the disease subgroups. This table81tshows statistically significant differences between different subgroups regarding EDSS score, age of disease onset, SDMT score, CCI index, and disease duration.

Table 3 shows the correlation between CCI and various clinical and demographic characteristics. These results show statistically significant correlations between CCI and age, disease duration, EDSS score, and SDMT score, while no significant correlation was observed between CCI and age of disease onset.

We also assessed the association of mean CCI with gender. The mean CCI was 0.33 ± 0.08 in men and 0.27 ± 0.08 in women. These two groups' differences were statistically significant (P-value = 0.001).

Discussion

In the present study, which was conducted to determine the relationship between CCI and clinical subgroups, the severity of cognitive disorders, and disability in patients with MS, 85 patients with a mean age of 40.73 ± 8.45 years and 65.9% women were investigated. A statistically significant difference was seen in the mean CCI between the two sexes, and the CCI value was significantly lower in women. The mean EDSS score of all participants was 2.64 ± 2.49.

Table 3. Correlation between CCI and various clinical and demographic characteristics (N=85)**.**

Parameters	Statistical test	CCI
Age	Pearson Correlation	-0.241*
	P-value	0.026
Moderate disease	Pearson Correlation	-0.388
	P-value	0<0.001
EDSS score	Pearson Correlation	-0.719
	P-value	0<0.001
Age start disease	Pearson Correlation	-0.030
	P-value	0.786
SDMT score	Pearson Correlation	0.676
	P-value	0<0.001

There was a statistically significant difference between the different subgroups of MS with the EDSS score, age of disease onset, SDMT score, CCI, and disease duration. Regarding the correlation of CCI with other parameters, it was seen that a significant negative correlation was observed between CCI and age, disease duration, and EDSS, while the correlation between SDMT and CCI was significantly positive.

Demir et al. evaluated the relationship between structural measurements of the corpus callosum (CC) and disability in patients with multiple sclerosis. A total of 40 patients (29 women, 11 men) with a mean age of 36.47 ± 11.14 years were investigated. In CC morphometric measurements of patients, CC genu was 11.46±1.60 mm, truncus was 5.29 mm, splenium was 11.09±1.82 mm, anterior-posterior diameter was 65.20 mm, and CCI was 0.43±0.05. A negative correlation was determined between CCI and disease duration, number of attacks, and EDSS scores in MS. In the severe disability group, CC splenium, AP diameter, and CCI were lower. The conclusion was that corpus callosum changes can be evaluated as a parameter in the evaluation of the disease process in MS[17]. In the current study, 85 patients with a mean age of 40.73±8.45 years

Table 2. Demographic and clinical characteristics of participants according to subgroups**.**

		Subgroup			
	Total	**SPMS**	**RRMS**	**PPMS**	**P-value**
EDSS.score	2.64 ± 2.49	4.83 ± 1.57	0.76 ± 1.11	5.5 ± 1.02	<0.001
Age at the start of the disease	32.78 ± 8.76	33.13 ± 8.53	30.42 ± 8.56	40.29 ± 5.17	0.001
SDMT score	20.32 ± 10.19	12.22 ± 7.54	27.19 ± 6.33	10.07 ± 5.14	<0.001
CCI	0.29 ± 0.08	0.22 ± 0.05	0.34 ± 0.05	0.24 ± 0.07	<0.001
Disease duration	8 ± 5.51	10.83 ± 6.66	6.85 ± 5.14	7.29 ± 2.55	0.014

and 65.9% women were examined, and from the perspective of the number of examined patients, the present study has an advantage over Demir et al.'s study. Our study also showed that the mean CCI was equal to 0.29±0.08, which seems to be a remarkable difference from Demir et al.'s study (0.43±0.05 vs. 0.29±0.08). This difference could be due to the difference in the initial volume of CC between different genetics, but this issue needs to be investigated in future studies. In the current study, it was seen that there was a statistically significant difference in the mean CCI between the two sexes, and this finding was similar to the study by Demir et al. Demir et al. reported that a negative correlation was determined between CCI and disease duration, number of attacks, and EDSS scores in MS. In the current study, it was seen that there were significant negative correlations between the CCI with the duration of the disease and the EDSS score, and in this sense, these two studies were similar.

Yaldizil et al. investigated the relationship between general and regional atrophy of the CC, neuropsychological test performance, and fatigue in MS patients. A cross-sectional study on 113 MS patients with a mean age of 48±11 years, 75/113 women, 84/113 relapsing-remitting MS, a mean disease duration of 21±9 years, and a mean EDSS score of 3.2±1.7 was done. CCI was highly correlated with SDMT. Posterior CC segment atrophy was significantly associated with poor outcomes in SDMT. In contrast, atrophy of the anterior part of the CC was significantly associated with fatigue severity and poor performance in the long-term memory test. It was concluded that CC atrophy is associated with cognitive impairment and fatigue. Regional CCI results show that these relationships are somewhat spatially segregated[18]. In the present study, the mean age was 40.73±8.45 years, and it was seen that there was a statistically significant difference between the two genders in the mean CCI, and the CCI value was significantly lower in women. The mean EDSS score of all participants was 2.64±2.49. There was a statistically significant difference between the different subgroups of MS with the EDSS score, age of disease onset, SDMT score, CCI, and disease duration. A significant negative correlation was observed between CCI index, age, disease duration, and EDSS score. In contrast, the correlation between SDMT and CCI was positive and significant, and these findings were similar between the two studies. Based on these two studies, it was seen that there is a relationship between the CCI and parameters related to cognitive impairment and ability of patients with MS, which indicates the importance of using this method in the management of patients with MS.

Caligori et al. reported that an increase in EDSS was associated with a decrease in CC diameter. It was concluded that regional CC imaging features differentially explain disability in RRMS patients, revealing strong and distinct correlation patterns with the clinical and cognitive status of patients affected by this specific clinical phenotype[19]. In our study, it was seen that the CCI, defined as Genu + trancus + splenium /AP diameter, has a significant correlation with parameters related to MS, and these findings were similar to the study of Caligori et al. The findings of the current study and the study of Caligori et al. show that CCI is a proper method for evaluating and managing cognitive impairment and disability in MS, and this evaluation method is even related to the type of disease. It can be used in different subtypes of MS.

Gunberg et al. longitudinally investigated the normalized CC area (nCCA) as a marker of cognitive function and disability in MS. Their findings indicated that the annual rate of CC atrophy decreased with the duration of the disease. nCCA was strongly correlated with SDMT and moderately correlated with EDSS. It was concluded that nCCA correlates well with physical and cognitive disability. The nCCA is rapid and can be applied to clinical practice, where it may help identify patients needing neuropsychological evaluation[11]. The current study observed a significant negative correlation between CCI and EDSS score, while the correlation between SDMT and CCI was positive and significant. Our study also showed that CCI is correlated with EDSS and SDMT, and this finding was similar between these two studies. Of course, it is important to mention that CCI was measured in the current study, but nCCA was measured in Gunberg et al.'s study, which differed between the two studies. The evaluating method of the corpus callosum was different between the two studies. However, two studies showed that the evaluation of the corpus callosum in MRI is related to the neuropsychological impact of MS disease

and is correlated with cognitive findings and disability, which shows that the evaluation of CC parameters in MRI is valuable.

Llufriu et al. investigated the impact of CC damage on physical disability and cognitive dysfunction in MS. Twenty-one RRMS patients and 13 healthy subjects underwent structural MRI and CC diffusion tensor. They concluded that CC structural and microstructural abnormalities were associated with impaired motor callosal inhibitory conduction in MS. CC damage may contribute to cognitive dysfunction and physical disability[20]. In the current study, it was seen that changes in the CC were related to cognitive disorders and disability in MS patients, and this finding was also confirmed in the study of Llufriu et al.

Akaike et al. evaluated the relationship of corpus callosum area (CCA) with dysfunction of cognitive processing in MS. They found that CCA has the potential to act as a dependable indicator of cognitive impairment in MS and can be readily integrated into clinical practice, thereby offering a valuable diagnostic resource for identifying cognitive impairment in this patient population[21]. Based on the findings of this study and the current study, it can be said that CC-related parameters have different potential diagnostic values in patients with MS, and further studies should be done in this respect because the data about the different relationships of CC-related parameters with MS are limited[22-24].

Conclusion

It is concluded that CCI is a suitable parameter to evaluate cognitive impairment and disability in patients with MS, which is both quick and cheap and provides useful information based on the type of MS disease. CCI has a negative and significant correlation with age, disease duration, and EDSS score, but it has a positive and significant correlation with SDMT.

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Conflict of interest

The authors further declare that they have no conflict of interest.

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