Cerebral Circulation - Cognition and Behavior 2 (2021) 100008

Contents lists available at ScienceDirect

Cerebral Circulation - Cognition and Behavior

journal homepage: www.elsevier.com/locate/cccb

Longitudinal changes in MoCA performances in patients with mild cognitive impairment and small vessel disease. Results from the VMCI-Tuscany Study

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ARTICLE INFO

Keywords:
Montreal Cognitive Assessment
Cerebral small vessel disease
Mild cognitive impairment
Major neurocognitive disorder

ABSTRACT

Objectives: The Montreal Cognitive Assessment (MoCA) is a cognitive screening test largely employed in vascular cognitive impairment, but there are no data about MoCA longitudinal changes in patients with cerebral small vessel disease (SVD). We aimed to describe changes in MoCA performance in patients with mild cognitive impairment (MCI) and SVD during a 2-year follow-up, and to evaluate their association with transition to major neurocognitive disorder (NCD).

Materials and Methods: Within the prospective observational VMCI-Tuscany Study, patients with MCI and SVD underwent a comprehensive clinical, neuropsychological, and functional evaluation at baseline, and after 1 and 2 years.

Results: Among the 138 patients (mean age 74.4 ± 6.9 years; males: 57%) who completed the study follow-up, 44 (32%) received a major NCD diagnosis. Baseline MoCA scores (mean±SD) were lower in major NCD patients (20.5 ± 5) than in reverter/stable MCI (22.2 ± 4.3), and the difference approached the statistical threshold of significance (p=.051). The total cohort presented a decrease in MoCA score (mean±SD) of -1.3 ± 4.2 points (-2.6 ± 4.7 in major NCD patients, -0.7 ± 3.9 in reverter/stable MCI). A multivariate logistic model on the predictors of transition from MCI to major NCD, showed MoCA approaching the statistical significance (OR=1.09, 95% CI=1.00–1.19, p=.049).

Discussion: In our sample of MCI patients with SVD, longitudinal changes in MoCA performances were consistent with an expected more pronounced deterioration in patients who received a diagnosis of major NCD. MoCA sensitivity to change and predictive utility need to be further explored in VCI studies based on larger samples and longer follow-up periods.

1. Introduction

Subcortical ischemic vascular disease caused by small vessel disease (SVD) has been demonstrated to be associated with cognitive impairment [1-3], particularly with deficits in attention and executive functions, and slowing of information processing [4,5]. The clinical spectrum of vascular cognitive impairment (VCI), i.e. a cognitive impairment pri-

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https://doi.org/10.1016/j.cccb.2021.100008
Received 23 December 2020; Received in revised form 2 March 2021; Accepted 3 March 2021
Available online 21 March 2021

marily caused by or associated with cerebrovascular lesions, ranges from mild cognitive impairment (MCI) to dementia [1].

The Montreal Cognitive Assessment (MoCA) is a brief cognitive test originally designed to identify MCI [6]. Because MoCA specifically evaluates cognitive domains affected in SVD, it has been increasingly utilized as an effective screening measure in VCI.

The application of measures of cognitive function in clinical and research longitudinal settings poses a question on how likely it is that an observed change in an individual is due to chance or is clinically relevant. Hence, the interpretation of long-term changes in cognitive measures is of great relevance to determine their reliability [7].

MoCA longitudinal trajectories and their potential as a measure or predictor of cognitive change and decline over time may be useful from both clinical and research perspectives, but experience on this issue is limited. Studies in healthy older adults gained contrasting evidence: in some studies, MoCA performances remained relatively stable over time [8,9], while in others an increase in MoCA scores suggested the influence of a test-retest practice effect, particularly for relatively short time intervals between the evaluations [10,11]. Taking into account the few studies on MCI patients, Costa et al. [11] and Krishnan et al. [12] found that MoCA seemed a valid tool for detecting cognitive change over 1 and 3.5 years, respectively, while Phua et al. [13] found that MoCA had low accuracy in tracking longitudinal decline in a mixed cohort of cognitively intact participants, MCI, and demented patients over a 3-year follow-up period. In one study in Parkinson disease, Lessing et al. [14] found no significant change in MoCA performances over a 3-year period.

Our aim was to describe the changes in MoCA performance over a 2-year period in patients with MCI and SVD, and to evaluate its sensitivity to change and its predictive value on the transition from MCI to major neurocognitive disorder (NCD).

2. Material and methods

The Vascular MCI-Tuscany Study is a multicenter, prospective, observational study aimed at examining the determinants of transition from vascular MCI to dementia in patients with SVD. The study methodology has been reported in detail elsewhere [15]. The study was conducted in accordance with the Helsinki Declaration, was approved by the local ethics committee, and each patient gave a written informed consent. To be included, patients had to be classified as affected by: (1) MCI according to Winblad et al. criteria [16], and operationalized according to Salvadori et al. [17]; and (2) evidence on magnetic resonance imaging (MRI) of moderate to severe white matter hyperintensities (WMH) according to a modified version of the Fazekas scale [18]. The degree of WMH severity was rated on Fluid Attenuated Inversion Recovery (FLAIR) sequences taking into account only deep and subcortical white matter lesions. The modified Fazekas scale is a visual scale based on a categorization into 3 severity classes: grade 1 (mild WMH) = single lesions below 10 mm, areas of 'grouped' lesions smaller than 20 mm in any diameter; grade 2 (moderate WMH) = single lesions between 10 and 20 mm, areas of 'grouped' lesions more than 20 mm in any diameter, no more than 'connecting bridges' between individual lesions; grade 3 (severe WMH) = single lesions or confluent areas of hyperintensity 20 mm or more in any diameter. According to the study protocol, at baseline each patient underwent a comprehensive clinical, neuropsychological, and functional evaluation that was repeated after 12 and 24 months.

At baseline evaluation the diagnosis of MCI required at least one borderline score (an adjusted score between the outer and inner 95% confidence limits for the 5th percentile of the normal population according to Italian normative data) among the 12 scores deriving from the 9 neuropsychological tests included in the VMCI-Tuscany neuropsychological battery [19]. The main outcome of the VMCI-Tuscany study protocol was the transition from MCI to major NCD, and has been operationalized according to the DSM-5 criteria for major NCDs [20–21]. According to the diagnostic algorithm, a major NCD diagnosis was assigned in case of a worsened functional and cognitive outcome. In case of a worsened functional outcome and a stable cognitive one, the major NCD diagnosis was made only if the functional status was not consequent to other diseases or physical limitations. Patients were classified as reverter if all cognitive tests resulted within the normal range and functional outcome was improved. In all other cases, patients were classified as stable MCI [21].

The MoCA score was not taken into account for the initial MCI diagnosis, nor for the final one. MoCA performance was evaluated according to the Italian normative data, and demographically adjusted scores were classified as impaired (below the outer 95% confidence limits), borderline (between the outer and inner 95% confidence limits for the 5th percentile), and normal (above the inner 95% confidence limits for the 5th percentile) [22]. A delta score (Δ-MoCA), corresponding to the difference in MoCA demographically adjusted scores between the basal evaluation and the longitudinal diagnosis, was computed.

The neuroimaging variables used in the present study were WMH (modified Fazekas scale moderate, grade 2, vs. severe, grade 3) and lacunar infarcts (absent vs. present).

2.1. Statistical analysis

Descriptive analyses (frequencies and percentages or means and standard deviations) were used to describe the cohort in terms of demographics, frequencies distributions of longitudinal diagnostic categories, and MoCA performances.

Univariate analyses (independent t and chi square tests) were employed to compare basal MoCA performances between reverter/stable MCI vs. demented patients. A multivariate logistic model was used to evaluate the predictors of transition from MCI to major NCD, and included basal MoCA demographically adjusted total score and other relevant demographic, clinical, and neuroimaging variables such as age, sex, hypertension, diabetes, history of stroke, WMH, and lacunar infarcts. All analyses were done using the SPSS software version 26, and a significance threshold of 0.05 was applied.

3. Results

After a median follow-up of 24 months (interquartile range 15–25 months), out of the 153 patients of the VMCI-Tuscany baseline cohort, 138 (mean age 74.4 ± 6.9 years; males: 57%) had follow-up information sufficient to formulate a cognitive diagnosis: 10 (7%) reverted to normal cognition, 84 (61%) remained MCI, and 44 (32%) had a diagnosis of major NCD. Out of these 138 patients, 37 received their last evaluation at 12 months (18 for incomplete evaluation at 2 years, and 19 for transition to major NCD), and 101 at 24 months.

The demographically adjusted basal MoCA mean (±SD) total score was lower in patients diagnosed as demented (20.5 ± 5) than in reverter/stable MCI patients (22.2 ± 4.3), and the distributions of patients that presented an impaired baseline MoCA performance were higher in patients diagnosed as demented (27%) than in reverter/stable MCI patients (15%). Despite a mean baseline MoCA difference of approximately 1.7 points, comparisons between major NCD and reverter/stable MCI ones approached but did not reach the statistical threshold of significance (p=.051).

The total cohort presented a mean (±SD) decrease in MoCA scores (Δ-MoCA) of −1.3 ± 4.2 points, with a Δ-MoCA=−2.6 ± 4.7 in patients diagnosed as major NCD, and a Δ-MoCA=−0.7 ± 3.9 in reverter/stable patients (Fig. 1). Taking into account changes in MoCA performances over time, percentages of patients with impaired performance increased from 19% (basal evaluation) to 32% (last evaluation), while percentages of patients with normal performance decreased from 66% to 57%, respectively (Fig. 2).

The multivariate logistic model on the predictors of transition from MCI to major NCD (table 1) showed that MoCA score bordered the statistical significance (OR=1.09, 95% CI=1.00–1.19, p=.049).

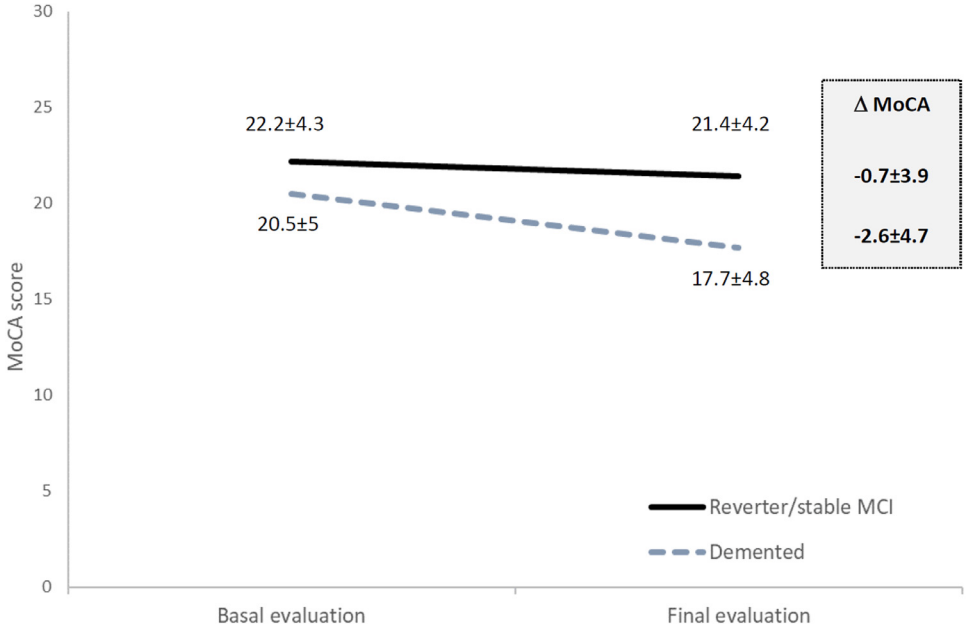

Fig. 1. Changes in MoCA scores in reverter/stable MCI and demented patients.

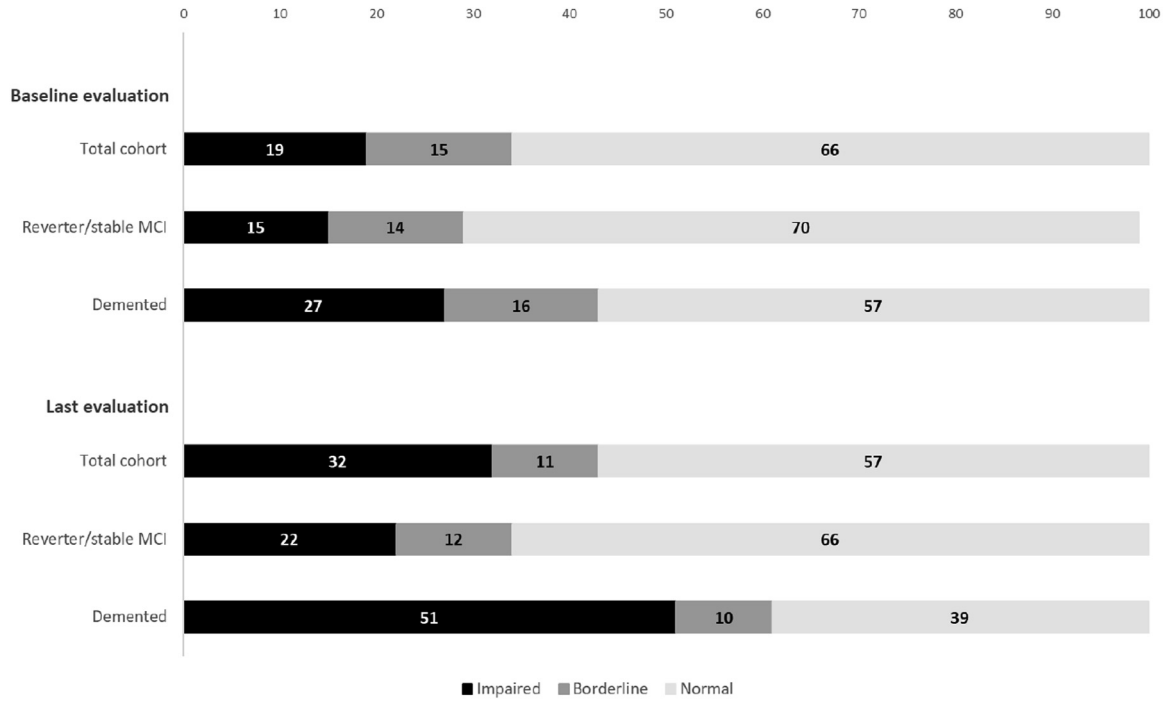

Fig. 2. Percentage distributions of MoCA performances at baseline and final evaluations in the total cohort and in reverter/stable MCI and demented patients.

Table 1
Predictors of transition from mild cognitive impairment to major neurocognitive disorder (logistic regression).

	Transition to major NCD Reverter/stable MCI vs. NCD		
	OR	95% CI	p
Age (years)	.98	.92–1.03	.426
Sex (female)	.94	.42–2.07	.871
Hypertension	1.60	.51–5.05	.421
Diabetes	1.55	.54–4.38	.413
History of stroke	2.06	.93–4.59	.076
White matter hyperintensities (severe)	.74	.34–1.60	.448
Lacunar infarcts (present)	.78	.34–1.79	.556
MoCA score	1.09	1.00–1.19	.049

4. Discussion

In our sample of patients with MCI and SVD evaluated over a 2-year follow-up period, MoCA performances decreased over time with a mean loss of approximately 1.3 points in the total sample, and 2.6 points in patients who then received a major NCD diagnosis. Longitudinal changes in MoCA performances were consistent with the different trajectories of cognitive decline observed in our patients, thus confirming its potentials in terms of sensitivity to change. Baseline MoCA performances resulted worse in patients who developed a major NCD compared to those who did not. Despite from the statistical point of view this evidence represents only a trend, MoCA revealed some predictive significance on progression of cognitive status in patients with MCI.

Taking into account rates of change in MoCA scores estimated from previous studies, results for the overall cohort were in line with the annualized change of 0.52 point found by Krishnan et al. in MCI patients [12]. Moreover, in our cohort, patients who received a major NCD diagnosis largely exceeded the clinically meaningful thresholds of 1.73 points found in the MCI sample by Krishnan et al. [12]. This seems to point toward the hypothesis that, despite the fact that basal MoCA performance was only partially accurate in discriminating between patients at risk of major NCD and those who were not, its longitudinal trajectory could have the potential to be sensitive to cognitive changes in cerebrovascular patients' populations, as well as in neurodegenerative ones. Evidence on the validity of cognitive screening instruments is highly relevant in the healthcare setting, where a more comprehensive and sensitive neuropsychological assessment cannot be provided.

Limitations of our study need to be considered. In our sample MoCA only approached the significance threshold in differentiating between patients who received a major NCD diagnosis and those who did not. The small sample size is a major limitation that could have negatively influenced statistical power, and thus the probability to effectively detecting a predictive role of MoCA. A further limitation is that almost a quarter of the subjects had their evaluation at 12 months (i.e. a year earlier than 75% of the subjects), and thus some of them might have converted to NCD with a longer follow-up time.

Another limitation of our study is the possible effect of test-retest in MoCA performances, particularly in patients with the milder profiles of cognitive impairment. Despite the fact that a decrease in mean MoCA score was found over time, the large variability in our delta scores revealed that a proportion of patients had a higher MoCA score at follow-up. From a statistical point of view, these large deviations further reduced statistical power. Methodological issues related to practice effects in serial cognitive assessments are known to influence cognitive performance both in healthy elderly and neurological disease populations. When the cognitive protocol of the present study was developed, only one Italian validated version of the MoCA test was available [22,23]. Recently, two alternative forms of the Italian version of the MoCA have been validated [24], and their use in longitudinal studies could be of potential utility to overcome the test-retest influence.

One last possible limitation was the lack of imaging and biological markers of neurodegenerative burden that could better define the etiology of our sample. However, this patients sample likely represents what is encountered in clinical practice, but we cannot be completely sure that it was composed of patients with pure vascular MCI. As a result, our conclusions refer to a sample of patients with MCI and SVD, and cannot be generalized to the global MCI population.

Despite having been proposed as a screening tool for vascular cognitive impairment, the predictive value of MoCA for detecting patients who are likely going to show cognitive deterioration still needs further study with larger samples and longer follow-up periods. Parallel versions of the test could be used to address the issue of test-retest effects.

Declaration of Competing Interest

None

Funding sources

The VMCI-Tuscany study was funded by Tuscany region (Programma per la Ricerca Regionale in Materia di Salute 2009).

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