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Research Article

Diagnostic accuracy of the Montreal Cognitive Assessment in screening for cognitive impairment in initially hospitalized COVID-19 patients: Findings from the prospective multicenter NeNeSCo study

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Abstract

Objective: This study aimed to investigate the prevalence and nature of cognitive impairment among severely ill COVID-19 patients and the effectiveness of the Montreal Cognitive Assessment (MoCA) in detecting it. **Method:** We evaluated cognition in COVID-19 patients hospitalized during the first wave (March to June 2020) from six Dutch hospitals, nine months post-discharge, using a comprehensive multi-domain neuropsychological test battery. Test performance was corrected for sex, age, and education differences and transformed into *z*-scores. Scores within each cognitive domain were averaged and categorized as average and above (*z*-score ≥ −0.84), low average (*z*-score −1.28 to −0.84), below average (*z*-score −1.65 to −1.28), and exceptionally low (*z*-score < −1.65). Patients were classified with cognitive impairment if at least one domain's *z*-score fell below −1.65. We assessed the MoCA's accuracy using both the original cutoff (<26) and an "optimal" cutoff determined by Youden's index. **Results:** Cognitive impairment was found in 12.1% (24/199) of patients, with verbal memory and mental speed most affected (6.5% and 7% below −1.65, respectively). The MoCA had an area under the curve of 0.84. The original cutoff showed sensitivity of 83% and specificity of 66%. Using the identified optimal cutoff of <24, maintained sensitivity while improving specificity to 81%. **Conclusions:** Cognitive impairment prevalence in initially hospitalized COVID-19 patients is lower than initially expected. Verbal memory and processing speed are primarily affected. The MoCA is a valuable screening tool for these impairments and lowering the MoCA cutoff to <24 improves specificity.

Keywords: Post-COVID-19; cognitive screening; validation; inflammatory; cognition; Montreal Cognitive Assessment

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Introduction

Shortly after the onset of the COVID-19 pandemic, concerns were raised about the potential impact of the disease on the brain and cognition due to neurological symptoms such as headache, dizziness, and alterations in taste and smell (Leonardi, et al., 2020). Various factors, including neuro-inflammation, hypoxemia, and sedation, may contribute to brain abnormalities and subsequent cognitive impairment, particularly affecting severely ill patients (Ghaderi, et al., 2023). However, the prevalence and nature of cognitive impairment, as well as the accuracy of cognitive screening tools in this population, remain unclear.

Prevalence estimates of cognitive impairment in initially hospitalized patients have been frequently reported to be around

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40% (Ferrucci, et al., 2022; Miskowiak, et al., 2023; Pihlaja, et al., 2023). Early investigations suggested a dysexecutive syndrome across the severity spectrum (Helms, et al., 2020). However, this notion has been recently challenged by a meta-analysis, suggesting a broader spectrum of cognitive impairment, encompassing learning and memory, language, and attention (Fanshawe, et al., 2024). Due to pandemic-related challenges, previous studies often had small sample sizes (N <100) and cognitive assessments were limited. These assessments mostly consisted solely of screening instruments, utilized only one test per cognitive domain, or were performed via the telephone or online (Litvan, et al., 2012; Tavares-Júnior, et al., 2022). Studies enrolled individuals across a range of severity levels, included only milder cases, or recruited patients with persistent symptoms. This likely contributed to discrepancies in findings, raising questions about the nature and prevalence of cognitive impairment in severely ill COVID-19 patients.

Previous publications that relied exclusively on screening tools such as the Montreal Cognitive Assessment (MoCA; Alemanno, et al., 2021; Ermis, et al., 2021; Evans, et al., 2021) may have overestimated cognitive impairment (Blake, et al., 2002). The MoCA, originally developed for detecting mild cognitive impairment and (Alzheimer's) dementia (Nasreddine, et al., 2005), has been validated as a cognitive screening instrument following stroke (Cumming, et al., 2013), cardiac arrest (van Gils, et al., 2022), and traumatic brain injury (Vissoci, et al., 2019). However, its validity following severe COVID-19, which may impact cognition differently, has not been assessed. Such validation would not only be beneficial for research purposes, but also for clinical practice, where the MoCA is widely adopted.

By administering a standardized, comprehensive, in-person cognitive assessment in addition to the MoCA, our primary objectives are: 1. To describe the prevalence and nature of post-COVID-19 cognitive impairment in initially hospitalized patients. 2. To evaluate the accuracy (sensitivity and specificity) of the MoCA in screening for cognitive impairment as indicated by the comprehensive assessment.

Methods

Study design and participants

The analysis is based on cross-sectional data of the NeNeSCo (Neurological and Neuropsychological Sequelae of COVID-19) project, a multicenter prospective cohort study (see Klinkhammer, et al., 2023; Klinkhammer, et al., 2021 for more detail). The study included 205 COVID-19 survivors who were admitted to either the intensive care or general ward in one of six Dutch hospitals (Amsterdam University Medical Center, Maastricht University Medical Center, University Medical Center Utrecht, Zuyderland MC, Onze Lieve Vrouwe Gasthuis, and Diakonessenhuis Utrecht) during the first European infection wave (March to June 2020). Data collection took place in the three university medical centers. The study received ethical approval and was preregistered at ClinicalTrials.gov (NCT04745611). Data were obtained in compliance with the Helsinki Declaration and collected between January and August 2021.

Participants were patients admitted for confirmed (through PCR testing or inferred from radiological images) SARS-CoV-2 treatment, 18 years or older, and proficient in Dutch. Exclusions comprised MRI contraindications, pre-COVID-19 cognitive impairment (based on medical records), severe neurological damage after hospital discharge, or inability to visit the hospital for measurements. A study flow chart with detailed information about the number of patients screened and reasons for exclusion can be found in Klinkhammer, et al. (2023). Recruitment took place at least six months post-hospital discharge, with patients undergoing cognitive assessment and completing questionnaires.

Procedure

Recruiting hospitals provided lists of COVID-19 patients. The order of lists was randomized and patients meeting the criteria were invited to participate until the intended sample size (for calculation see Klinkhammer, et al. (2021)) was reached.

Cognitive screening, using the MoCA, and extensive cognitive assessment were carried out on the same day by trained research assistants at one of three university medical centers (i.e., Amsterdam UMC, Maastricht UMC, UMC Utrecht).

Measures

Demographics and clinical characteristics

Demographic variables (sex, age, and education) were collected through a paper-based questionnaire. Education level was categorized based on the Verhage scale according to the Dutch education system (1 = Less than 6 years of primary education, 2 = Finished primary education, 3 = Primary education and less than
2 years of low-level secondary education, 4 = Finished low-level secondary education, 5 = Finished average-level secondary education, 6 = Finished high-level secondary education, 7 = University degree) (Verhage, 1964). Medical data were retrieved from medical files or from the Dutch national COVID-19 database, CovidPredict (Ottenhoff, et al., 2021).

Montreal Cognitive Assessment (MoCA)

The MoCA is a widely used cognitive screening tool developed to screen for mild cognitive impairment (Nasreddine, et al., 2005). The instrument has a maximum of 30 points, whereas a score <26 indicates potential cognitive impairment. Administration takes approximately 10 min and assesses memory, attention, language, and visuospatial abilities. This study used the MoCA version 7.2 (Bruijnen, et al., 2020).

Cognitive test battery

Cognitive impairment was evaluated using a cognitive test battery consisting of internationally recognized and validated tests. The following domains were evaluated using the corresponding tests:

Mental speed and attention. Trail making part A (TMT A), Stroop color reading, and Stroop color naming.

Executive function. Trail making part B (TMT B), Trail making B/A (TMT B/A), Stroop color word, Stroop interference, Controlled Oral Word Association, and Category fluency (Animals/Occupations).

Working memory. Symbol Digit Substitution, Digit span forwards, and Digit span backwards.

Verbal memory. Rey's auditory verbal learning task (RAVLT) Trial 1–5, RAVLT Delayed Recall, and RAVLT Recognition.

Visuospatial abilities. Judgement of line orientation.

Language abilities. Boston naming task.

Administration of the test battery took approximately 90 min. Performance validity testing was employed using the Test of Memory Malingering (TOMM, score ≤ 45 on both first and second trial) to identify suboptimal performance (Tombaugh, 1996).

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Analyses

MoCA

Individuals with ≤ 12 years of formal education were granted an additional point on the MoCA to correct for educational differences (Nasreddine, et al., 2005). Subsequently, MoCA scores were categorized as either normal or below the cutoff (<26).

Cognitive test battery

Univariate normative comparisons were performed using the Advanced Neuropsychological Diagnostics Infrastructure (ANDI; http://www.andi.nl; de Vent et al., 2016), which transformed each cognitive test score into an age, sex, and education adjusted *z*-score. Domain composite scores were calculated by averaging *z*-scores of tests within the same domain. It is recommended that a domain should comprise at least two tests (Litvan, et al., 2012). However, two domains (visuospatial abilities and language function) consisted of only one test each, and thus, they were excluded from the MoCA accuracy analyses and only included in the performance tables.

Each participant's performance was evaluated based on the scores of every cognitive test separately, as well as based on each of the cognitive domain composite scores, using the following categories:

Average and above (*z*-score ≥ -0.84 or $\geq 20^{th}$ percentile)

low average (z-score < -0.84 to ≥ -1.28 or $< 20^{th}$ to $\geq 10^{th}$ percentile)

below average (z-score < -1.28 to ≥ -1.65 or $< 10^{th}$ to $\geq 5^{th}$ percentile), and

exceptionally low (z-score < -1.65 or $< 5^{th}$ percentile).

These categories are anchored in the classification of the "exceptionally low" group, which we also used to define cognitive impairment: A participant was classified as having cognitive impairment if one or more cognitive domains were categorized as exceptionally low (z-score < -1.65 which corresponds to $<5^{th}$ percentile). This threshold, also used in previous research, balances sensitivity and health care resources (Reukers, et al., 2020; Van den Berg, et al., 2005). To maintain consistency, the subsequent categories were based on percentile rankings (<5th, <10th, <20th), ensuring practical applicability while aligning with established norms. Grouping everyone who performs at an average level or better into a single category was done because the MoCA is designed to identify cognitive impairments, not to distinguish among varying levels of higher cognitive functioning.

MoCA accuracy

The MoCA's discriminative power was assessed using the area under the curve (AUC) and its accuracy (i.e., sensitivity, specificity, false negative rate, false positive rate, and correct classification rate) was determined using both the original cutoff (<26) and the optimal cutoff as indicated by the highest Youden's index (sensitivity + specificity − 1; range = 0–100%; Youden, 1950).

Sensitivity analysis

After our initial analyses which included TOMM low scorers, we conducted a sensitivity analysis excluding them ($N = 3$). This analysis followed the same methodology as the primary analyses.

Exclusion due to missing data

Participants were excluded from analyses if the MoCA was missing or if a cognitive domain included in the gold standard (i.e., mental speed/attention, executive function, working memory, and verbal memory) consisted of less than two tests.

Significance was assessed at a one-sided (subnormal) alpha-level of 0.05. Analyses were executed using R version 4.2.2 (R Core Team, 2023).

Results

Of the 205 participants, six were excluded due to missing data, leaving 199 patients for analysis. Among these, 49% were treated in intensive care and received mechanical ventilation for a median duration of 14 days [IQR: 8–23]. The most prevalent preexisting comorbidities were hypertension (33%), chronic cardiac disease (21.3%), and diabetes (13.5%). Additionally, 25.6% of the patients reported having received psychological care prior to COVID-19, with burnout being the most commonly named reason (28%). Patient characteristics are summarized in Table 1, while details on the excluded patients are provided in Supplemental Appendix S1.

The median MoCA score was 26 [IQR = 23–28] and 39.7% (79/199) scored below the cutoff. Cognitive impairment (defined as ≥1 cognitive domain *z*-scores < −1.65) was identified in 12.1% (24/199) of the sample.

Cognitive profile

Table 2 shows the percentages of patients scoring average and above, low average, below average, and exceptionally low per test and per cognitive domain.

Verbal memory has the highest percentage of scores falling into the non-average categories, with 6.5% of exceptionally low, 7.5% of below average scores and 12.6% of low average scores. This is followed by mental speed with 7% of exceptionally low, 4.5% of below average scores and 8.5% of low average scores.

MoCA accuracy

Table 3 displays the diagnostic properties of the MoCA at the original and optimal cutoffs. The MoCA's area under the curve was calculated to be 0.84 (see Figure 1). The optimal cutoff was determined to be <24, which maintained the same sensitivity (83.3%) as the original cutoff while improving specificity from 66.3% to 80.6%. Using the optimal cutoff, the percentage of patients scoring low was reduced by 12.6% to 27.1% (54/199). Figure 2 shows the confusion matrices comparing potential cognitive impairment as suggested by the MoCA using the original and optimal cutoff with cognitive impairment as indicated by the extensive cognitive testing.

Secondary analyses

All three patients who scored low on the TOMM also scored below the original cutoff on the MoCA and were identified as having cognitive impairment in the primary analysis. Consequently, excluding these patients reduced the percentage of low scorers on the MoCA from 39.7% to 38.8% (76/196) and the observed cognitive impairment rate from 12.1% to 10.7% (21/196). Verbal memory (5.6% exceptionally low, 7.1% below average scores, 12.8% low average scores) and mental speed (6.1% exceptionally low, 4.6% below average, 8.2% low average scores) remained to be the domains with the highest percentage of impaired scores. The accuracy of the MoCA was only mildly affected with the AUC decreasing from 0.84 to 0.81. Details can be found in supplemental appendix S2.

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Table 1. Demographic and clinical characteristics

Variable	*n*/*N* (%) or Mean (SD) or Median (IQR)
Characteristics	
Age, years; median [IQR]	63 [53–69]
Sex, female; *n*/*N* (%)	61/199 (30.7%)
Education level[a]	
Low; *n*/*N* (%)	36/199 (18.1%)
Medium; *n*/*N* (%)	82/199 (41.2%)
High; *n*/*N* (%)	81/199 (40.7%)
Received care after hospital discharge	
Physical therapy; *n*/*N* (%)	141/198 (71.2%)
Occupational therapy; *n*/*N* (%)	53/198 (26.8%)
Rehabilitation[b]; *n*/*N* (%)	86/198 (43.4%)
Psychology; *n*/*N* (%)	47/198 (23.7%)
Comorbidities[c]	
Chronic cardiac disease; *n*/*N* (%)	38/178 (21.3%)
Chronic pulmonary disease; *n*/*N* (%)	17/178 (9.6%)
Chronic kidney disease; *n*/*N* (%)	10/178 (5.6%)
Diabetes; *n*/*N* (%)	24/178 (13.5%)
Body-mass index[d], kg/m2; median [IQR]	27.5 [53.0–69.0]
Hypertension; *n*/*N* (%)	58/178 (32.6%)
Pre-COVID-19 psychological care[e]	51/199 (25.6%)
Burnout	14/51 (27.5%)
Grief	6/51 (11.8%)
Trauma	6/51 (11.8%)
Depression	6/51 (11.8%)
Anxiety	3/51 (5.9%)
Disease-related parameters	
ICU stay, *n*/*N* (%)	97/199 (48.7%)
Length of ICU stay, days; median [IQR]	14 [7–24]
Invasive ventilation[f], days; median [IQR]	14 [8–23]
Coagulation disorder, n/N (%)	27/179 (15.1%)
Delirium, *n*/*N* (%)	42/175 (24.0%)
Highest SOFA score; mean (SD)	6.9 (2.9)
APACHE IV; mean (SD)	55.6 (16.6)
MoCA score, median [IQR]	26 [23–28]
MoCA low, *n*/*N* (%)	79/199 (39.7%)
MoCA education corrected (<12 years of education), *n*/*N* (%)	40/199 (20.1%)

Note: kg/m2 = kilogram per square meter. ICU = intensive care unit. SOFA = sequential organ failure score. APACHE IV = Acute Physiology and Chronic Health Evaluation IV. *n* = number of individuals. SD = standard deviation. IQR = interquartile range. Values are median [Interquartile range] or *n*/total *N* (%).

[a]Education level was separated into low, medium, and high based on guidelines of the Dutch Central Bureau of Statistics.[17]

[b]Includes in- and outclinic rehabilitation and may include cognitive rehabilitation.

[c]Definitions are based on a World Health Organization template.[18]

[d]$N = 118$

[e]Based on patient self-report. The percentages correspond to the five most-reported categories.

[f]All intensive care unit patients received invasive ventilation during their treatment.

Discussion

After an extensive in-person cognitive assessment, we observed long-term cognitive impairment in 12% of our initially hospitalized COVID-19 sample. These impairments mainly affected verbal memory and mental speed. The MoCA's discriminative ability, defined by the AUC exceeding 0.80, was high (de Hond, et al., 2022). The MoCA met the recommended minimum sensitivity (>80%) and specificity (>60%) required for cognitive screening instruments with both the original and the optimal cutoff (Blake, et al., 2002). However, the optimal cutoff (<24) increased the specificity substantially compared to the original cutoff (<26).

Our findings suggest a lower prevalence of cognitive impairment than initially suggested, as an earlier meta-analysis reported estimates ranging from 18 to 36% (Ceban, et al., 2022). This is particularly noteworthy given that our findings are derived from a sample of patients who were initially severely ill, placing them at a higher biological risk for brain damage and consequent cognitive impairments. While we did not find support for dysexecutive syndrome as reported in earlier studies (Helms, et al., 2020), our results align with a recent meta-analysis, showing impairments across all cognitive domains (Fanshawe, et al., 2024). Notably, mental speed and verbal memory impairments were slightly more prevalent. This could impact the MoCA's accuracy, as it does not include a measure of mental speed, potentially resulting in false negatives for this patient group. Accuracy could be improved by adding an extra speed task, which has also proven effective in stroke patients (Zaidi, et al., 2020). The prevalence of processing speed impairments may be attributed to widespread brain impacts such as inflammation and hypoxia (reduced oxygen levels), common to COVID-19, which could compromise brain integrity and slow down information transmission (Felmingham, et al., 2004; Hofmeijer, et al., 2014; Liu, et al., 2022). Additionally, mood disorders and post-traumatic stress may negatively impact cognitive functions, and this relationship warrants further investigation.

Despite the relatively low rates of cognitive impairment identified in the current analysis, previous analyses of the same patients revealed cognitive complaints that far exceeded these cognitive impairments (Klinkhammer, et al., 2023). Furthermore, cognitive complaints were not found to be associated with cognitive impairments (Duindam, et al., 2022; Klinkhammer, et al., 2024). This discrepancy could be the result of decrements in cognition that do not meet the criteria for cognitive impairment but are still experienced as functional decline by the patients. Cognitive complaints could also indicate future cognitive decline, but also psychosocial factors could play a role in their development (Klinkhammer, et al., 2024; Pike, et al., 2022).

Since cognitive complaints do not reliably predict current cognitive impairment, screening serves two crucial purposes: Firstly, it ensures that cognitive impairments are not overlooked, a problem that frequently occurs (Stiekema, et al., 2024). Secondly, when patients present with cognitive complaints, screening enables the differentiation between those who currently show signs for cognitive impairment and those without. Extensive neuropsychological testing is resource-intensive. Therefore, effective screening instruments not only reduce healthcare costs but also mitigate lengthy waiting periods for assessments. The MoCA is widely adopted in clinical settings, and our study validated it as a screening tool for probable cognitive impairment following severe COVID-19. Lowering the cutoff to <24 would improve specificity while maintaining sensitivity at the same level as the original cutoff. Moreover, using the optimal cutoff, the percentage of patients classified with probable impairment reduced from 40 to 27%, aligning more closely with the prevalence determined through extensive assessment. Previous studies have similarly shown that lowering the cutoff can also enhance accuracy in non-COVID-19 samples (Angermann, et al., 2017; Tiffin-Richards, et al., 2014). However, as clinicians are accustomed to the current cutoff, implementing an adaptation may prove impractical. As screening instruments prioritize sensitivity, which remained unaffected by the lowered cutoff in our sample, a change of cutoff would not have a big clinical impact. While the MoCA proves valuable, users must remain aware of its limitations. Despite its high sensitivity, it carries a false negative rate of approximately 17% with both cutoffs. This rate is higher than that reported for other similar populations (e.g., 14% for cardiac arrest (van Gils, et al., 2022), 8% for stroke (Cumming, et al., 2013)). However, it is worth noting that these conditions benefit from more comprehensive knowledge regarding

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Table 2. Average and above, low average, below average, and exceptionally low scores on cognitive tests and domains ($N = 199$)

	N	Average and above	Low average	Below average	Exceptionally low
Z-scores		> -0.84	< -0.84 to ≥ -1.28	< -1.28 to ≥ -1.65	< -1.65
Percentiles		$>20^{th}$	$<20^{th}$ to $\geq 10^{th}$	$<10^{th}$ to $\geq 5^{th}$	$<5^{th}$
Mental speed / attention[a]	**199**	159 (79.9%)	17 (8.5%)	9 (4.5%)	14 (7%)
Trail making A	197	167 (84.8%)	12 (6.1%)	4 (2%)	14 (7.1%)
Stroop color reading	199	141 (70.9%)	17 (8.5%)	15 (7.5%)	26 (13.1%)
Stroop color naming	199	140 (70.4%)	24 (12.1%)	10 (5%)	25 (12.6%)
Executive function[a]	**199**	177 (88.9%)	13 (6.5%)	4 (2%)	5 (2.5%)
Trail making B	194	144 (74.2%)	23 (11.9%)	11 (5.7%)	16 (8.2%)
Trail making B/A	195	136 (69.7%)	20 (10.3%)	14 (7.2%)	25 (12.8%)
Stroop color word	196	151 (77%)	15 (8%)	15 (8%)	15 (8%)
Stroop interference	196	193 (98%)	1 (0%)	1 (0%)	1 (0%)
Controlled Oral Word Association	198	134 (67.7%)	23 (11.6%)	20 (10.1%)	21 (10.6%)
Category fluency (Animals)	199	150 (75.4%)	21 (10.6%)	16 (8%)	12 (6%)
Category fluency (Occupations)	197	148 (75.1%)	25 (12.7%)	11 (5.6%)	13 (6.6%)
Working memory[a]	**199**	166 (83.4%)	24 (12.1%)	7 (3.5%)	2 (1%)
Symbol Digit Substitution	199	170 (85.4%)	7 (3.5%)	8 (4%)	14 (7%)
Digit span forwards	199	103 (51.8%)	43 (21.6%)	30 (15.1%)	23 (11.6%)
Digit span backwards	198	150 (75.8%)	17 (8.6%)	16 (8.1%)	15 (7.6%)
Verbal memory[a]	**199**	146 (73.4%)	25 (12.6%)	15 (7.5%)	13 (6.5%)
Rey's auditory verbal learning task (Trial 1–5)	199	139 (69.8%)	25 (12.6%)	19 (9.5%)	16 (8%)
Rey's auditory verbal learning task (Delayed Recall)	198	143 (72.2%)	24 (12.1%)	10 (5.1%)	21 (10.6%)
Rey's auditory verbal learning task (Recognition)	199	131 (65.8%)	27 (13.6%)	16 (8%)	25 (12.6%)
Visuospatial function (Judgement of line orientation)	**199**	179 (89.9%)	0 (0%)	8 (4%)	12 (6%)
Language function (Boston naming task)	**199**	178 (89.4%)	9 (4.5%)	5 (2.5%)	7 (3.5%)

[a]Averaged *z*-score across the cognitive tests within this domain. Cases with <2 tests per cognitive domain were excluded.

Table 3. Accuracy of the MoCA at the original and optimal cutoff

	Cognitive dysfunction
AUC [95% CI]	0.84 [0.74–0.94]
Original cutoff	<26
Youden	49.6
False positive rate	33.7
False negative rate	16.7
Accuracy	68.3
Sensitivity [95% CI]	83.3 [66.7–95.8]
Specificity [95% CI]	66.3 [59.4–73.1]
Optimal cutoff (Youden's index)	<24
Youden	63.9
False positive rate	19.4
False negative rate	16.6
Accuracy	80.9
Sensitivity [95% CI]	83.3 [66.7–95.8]
Specificity [95% CI]	80.6 [74.3–86.3]

Note: AUC = area under the curve. CI = confidence interval.

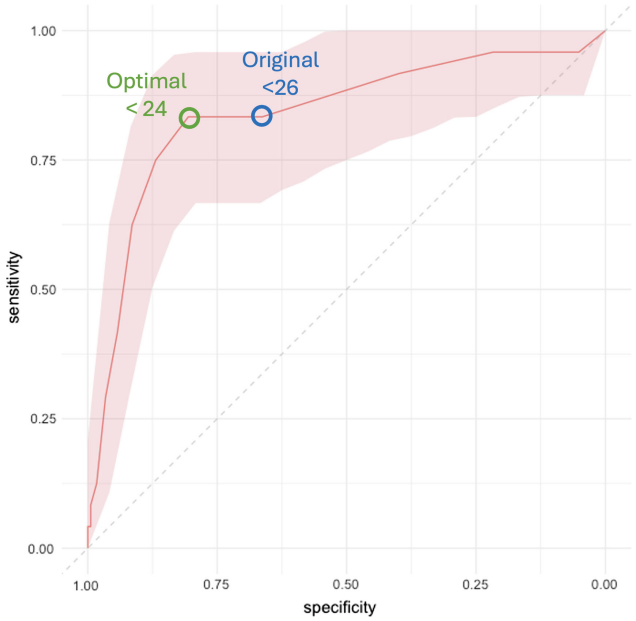

Figure 1. Receiver Operating Characteristic Curve for the Montreal Cognitive Assessment (MoCA) in detecting cognitive dysfunction, defined as at least one domain z-score falling below -1.65 (5th percentile). The dashed line represents a random classifier, while the solid red line illustrates the MoCA's performance at varying cutoffs, with a 95% confidence interval. The circles denote the optimal (on the left) and original (on the right) cutoffs.

potential brain consequences and associated impairments. While the MoCA is a valid screening tool for clinical practice, research should refrain from reporting prevalences of cognitive impairment based on the MoCA, as this leads to an overestimation. In practice, the MoCA should always be interpreted in the context of a clinical evaluation, in which other factors like demographic characteristics, premorbid level of functioning, or mood problems are taken into consideration.

Two previous studies suggested that the MoCA is less suitable in screening for cognitive impairment in individuals with persistent cognitive complaints who initially had a milder COVID-19 course (Lynch, et al., 2022; Schild, et al., 2023). However, only one of those formally investigated the accuracy of the MoCA (Lynch, et al., 2022). One reason for the observed inaccuracy could be the classification of cognitive impairment, which relied on *at least two test z-scores below −1.0* for low performance and *at least one test z-score below −2.0* for extremely low performance, criteria that may be considered rather lenient (Lynch, et al., 2022). Findings in this sample could therefore reflect the MoCA's inability to screen for mild cognitive abnormalities or may be a consequence of a different brain impact and consequent cognitive impairment in less severely ill patients.

While the MoCA may be more appropriate in screening for cognitive impairment following severe COVID-19, our findings

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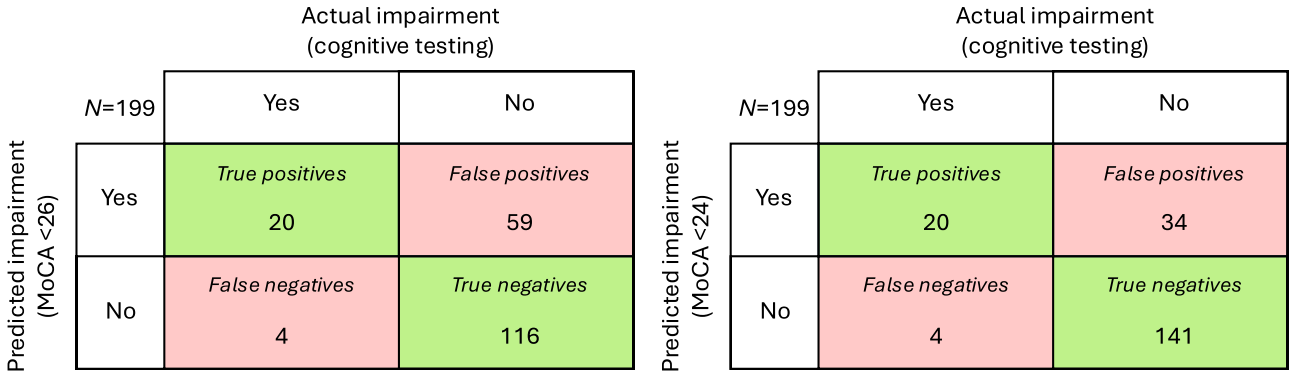

Figure 2. Confusion matrices showing the Montreal Cognitive Assessment (MoCA) performance in predicting cognitive impairment, as determined by extensive cognitive testing. The matrices compare MoCA predictions using the original cutoff score (<26, left) and the optimized cutoff based on the Youden index (<24, right). Correct predictions (true positives and true negatives) are highlighted in green, while incorrect predictions (false positives and false negatives) are highlighted in red.

may be applicable to similar populations. Common reasons for admission to critical care units in COVID-19 include sepsis, pneumonia, and acute respiratory distress syndrome, which are also frequent reasons for general critical care admission (Grasselli, et al., 2020). All conditions are characterized by an extreme inflammatory response and impaired oxygen delivery, two mechanisms assumed to contribute to COVID-19 brain abnormalities and potential consequential cognitive impairment (Pezzini & Padovani, 2020; Wilson, et al., 2020). In line with this, MRI findings of COVID-19 patients largely resemble those of other critically ill patients (e.g., presence of microbleeds; Klinkhammer, et al., 2023). Although the MoCA has not been validated in patients following other severe inflammatory diseases, it is commonly used as screening instrument in these populations. Given the similarities to severe COVID-19 patients, this approach appears warranted.

Study strengths and limitations

The present study evaluated the effectiveness of the MoCA as a screening tool by comparing its performance with that of a comprehensive neuropsychological test battery administered by trained professionals to a sizable cohort of initially hospitalized COVID-19 patients. While the number of hospitalized COVID-19 cases has declined over time, individuals continue to experience the consequences. Additionally, similarities to other patient populations suggest that our findings could have broader relevance to other conditions characterized by significant inflammatory responses. Recently, normative data for the MoCA, correcting for age, education, and sex differences, were published (Kessels, et al., 2022). We applied these corrections to our data (results not presented but available upon request); however this did not enhance the accuracy of the MoCA or alter our conclusions.

In interpreting our results, it is important to acknowledge the lack of a consensus in defining cognitive impairment, leading to variations in criteria used. Some define impairment based on test performance level, while others use composite domain scores. Further, *z*-score cutoffs vary widely (e.g., <−1.0, <−1.5, <−1.65, <−2.0). This can result in different outcomes. There are no strict guidelines for categorizing cognitive tests into domains, and conventional cognitive domains often overlap (Harvey, 2019). As a result, most tests can fit into multiple domains. For example, the Symbol Digit Substitution Test, categorized in this study as a task of working memory, can also serve as an indicator of psychomotor speed. Similarly, the Controlled Oral Word Association Task, used as a measure of executive function, may also be classified as an indicator of language function. In clinical settings, additional factors such as self-reported cognitive complaints, impact on daily functioning, and proxy reports are considered when diagnosing cognitive impairment. Consequently, classified cognitive impairments in the current study represent only low test performance rather than definitive diagnoses. Further, cognitive impairment is most accurately detected by observing changes over time, as comparisons to normative samples only estimate pre-illness cognitive function, making it likely that small decrements will go unnoticed (Schaeverbeke, et al., 2021). Lastly, patients excluded due to preexistent cognitive impairment or severe neurological damage may have been more prone to new/worsening neurological damage and new/worsening cognitive impairment. However, it would have been impossible to differentiate new/worsening from existing problems without a pre-illness measurement.

Conclusion/Implications

We found that cognitive impairment in COVID-19 patients approximately 9 months after hospital discharge is 12%, which is lower than initially expected. While present across all domains, it primarily affects verbal memory and processing speed. The MoCA serves as a valuable screening tool for these impairments. However, caution is warranted when estimating impairment prevalence, as the MoCA tends to overestimate these. Although lowering the MoCA cutoff to <24 enhances specificity, the original cutoff of <26 remains sufficiently effective.

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