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Cognitive screening improves the predictive value of stroke severity scores for functional outcome 3–6 months after mild stroke and transient ischaemic attack: an observational study

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ABSTRACT

Objectives: To investigate the prognostic value of the neurocognitive status measured by screening instruments, the Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE), individually and in combination with the stroke severity scale, the National Institute of Health Stroke Scale (NIHSS), obtained at the subacute stroke phase or the baseline (≤2 weeks), for functional outcome 3–6 months later.

Design: Prospective observational study.

Setting: Tertiary stroke neurology service.

Participants: 400 patients with a recent ischaemic stroke or transient ischaemic attack (TIA) received NIHSS, MoCA and MMSE at baseline and were followed up 3–6 months later.

Primary outcome measures: At 3–6 months following the index event, functional outcome was measured by the modified Rankin Scale (mRS) scores.

Results: Most patients (79.8%) had a mild ischaemic stroke and less disability (median NIHSS=2, median mRS=2 and median premorbid mRS=0), while a minority of patients had TIA (20.3%). Baseline NIHSS, MMSE and MoCA scores individually predicted mRS scores at 3–6 months, with NIHSS being the strongest predictor (NIHSS: R^2 change=0.043, p<0.001). Moreover, baseline MMSE scores had a small but statistically significant incremental predictive value to the baseline NIHSS for mRS scores at 3–6 months, while baseline MoCA scores did not (MMSE: R^2 changes=0.006, p=0.03; MoCA: R^2 changes=0.004, p=0.083). However, in patients with more severe stroke at baseline (defined as NIHSS>2), baseline MoCA and MMSE had a significant and moderately large incremental predictive value to the baseline NIHSS for mRS scores at 3–6 months (MMSE: R^2 changes=0.021, p=0.010; MoCA: R^2 changes=0.017, p=0.021).

Conclusions: Cognitive screening at the subacute stroke phase can predict functional outcome independently and improve the predictive value of stroke severity scores for functional outcome 3–6 months later, particularly in patients with more severe stroke.

ARTICLE SUMMARY

Article focus

- The prognostic value of neurocognitive status measured by brief screening instruments, the Montreal Cognitive Assessment (MoCA) and the Mini-Mental State Examination (MMSE), individually and in combination with the stroke severity scale, the National Institute of Health Stroke Scale (NIHSS), at the subacute stroke phase for functional outcomes at 3–6 months is unknown.
- We examined the predictive ability of MMSE and MoCA individually and in combination with the NIHSS for functional outcome 3–6 months after mild stroke and transient ischaemic attack.
- We also explored the predictive ability of these measures in patients with differing stroke severity.

Key messages

- Cognitive screening at the subacute stroke phase can predict functional outcome independently. Neurocognitive status measured by baseline MMSE scores adds a small incremental prediction to baseline stroke severity scores for functional outcomes at 3–6 months patients with stroke.
- Additionally, in patients with more severe strokes defined by baseline NIHSS score ≥2, neurocognitive status measured by baseline MMSE and MoCA improve the predictive value of stroke severity scores for functional outcome 3–6 months later. However, the incremental predictive value of the MMSE and MoCA is relatively smaller than the NIHSS.

ARTICLE SUMMARY

Strengths and limitations of this study

- We examined the prognostic value of neurocognitive status (MoCA and MMSE) and stroke severity (NIHSS) at the subacute stroke phase systematically as a singular measure and in combination for mRS scores 3–6 months later in a large sample of patients with stroke and in patients with differing stroke severity.
- An additional strength is the choice of 3–6 months of follow-up because patients were more likely to resume their daily activities and usual roles within this time frame. Hence, the findings established in this study can guide early intervention from baseline to 3–6 months after stroke.
- We did not systematically examine rehabilitation services provided for patients from the subacute stroke phase for 3–6 months of follow-up.

INTRODUCTION

It is important for early intervention and focused management to have instruments available during the subacute stroke phase for predicting functional outcome 3–6 months later. Cognitive performance measured by the Montreal Cognitive Assessment (MoCA) and the Mini-Mental State Examination (MMSE) administered at the subacute stroke phase predicted patients' functional outcomes at inpatient discharge.[1 2] Furthermore, patients' poststroke cognitive functioning measured by a brief neuropsychological battery 2–3 weeks following a stroke predicted their functional outcomes 13 months later.[3] No study has as yet investigated the utility of patients' neurocognitive status at the subacute stroke phase for predicting functional outcome at 3–6 months. A widely used stroke severity scale, the National Institute of Health Stroke Scale (NIHSS), administered at the subacute stroke phase is predictive of patients' functional outcomes 3–6 months later,[4] but has limited representation of cognitive function.[5] Hence, whether the NIHSS and neurocognitive status at baseline are independently predictive or have additive predictive value for functional outcomes at 3–6 months is unknown.

We therefore examined the predictive ability of MMSE and MoCA individually and in combination with the NIHSS at the subacute stroke phase for functional outcome 3–6 months later. In addition, we explored the predictive ability of these measures in patients with differing stroke severity.

METHODS

Subjects

The methodology of this study has been described previously.[6] Briefly, we recruited 400 consecutive patients (≥21 years old) with a recent ischaemic stroke or transient ischaemic attack (TIA; ≤14 days) during their inpatient admission (subacute stroke phase or baseline) at the National University Health System in Singapore. Patients were excluded if they had a major physical disability or an active psychiatric disorder that would impede cognitive testing.

Standard protocol approvals and patient consent

This study was conducted in conformity with the Declaration of Helsinki. Written informed consent was obtained from all participants and/or legally acceptable representatives.

Procedures

Patients were assessed using the NIHSS, modified Rankin Scale (mRS; premorbid and baseline functioning), MMSE[7] and MoCA[8] at baseline. In addition, their mRS scores were collected 3–6 months later. The NIHSS and mRS were administered by certified research personnel blinded to the patients' neurocognitive status at baseline and at 3–6 months follow-up. Similarly, the cognitive screening tests were administered by trained research psychologists blinded to the patients' NIHSS and mRS scores. The patients' functional outcome was defined by the continuous scores of mRS.

Statistical analyses

Between-group differences were examined using an independent-sample t test for quantitative variables and Pearson's χ^2 test for categorical variables. Hierarchical regression analyses were conducted to examine the incremental contributions of baseline MMSE and MoCA compared with the baseline NIHSS in predicting functional outcomes defined by mRS scores at 3–6 months after stroke. In the initial analysis, the clinically relevant or significant covariates (ie, age, sex, years of education, number of cardiovascular risk factors, premorbid and baseline mRS) were entered in the first block. The cognitive screening variables (MMSE or MoCA) at baseline were entered in the second block and the NIHSS scores at baseline were entered in the third block (Model A1 and B1 for MMSE and MoCA, respectively). Subsequently, the order of entry was altered, with the baseline NIHSS scores being entered in the second block and either baseline MMSE or MoCA being entered at the third block (Model A2 and B2 for MMSE and MoCA, respectively). In order to explore the predictive value in patients with differing stroke severity, we dichotomised the baseline NIHSS scores using a median split and repeated these analyses.

All statistical analyses were performed with IBM SPSS Statistics V.20.0 for Windows.

RESULTS

Subject characteristics

The recruited patients were mostly Chinese (70.3%) and male (69.8%), with a mean age of 59.8 (11.6) years and a mean of 7.7 (4.3) years of formal education. Most patients (79.8%) had a mild ischaemic stroke and less disability (median NIHSS=2, median mRS=2 and median premorbid mRS=0), while a minority of patients had TIA (20.3%). The median interval between the stroke or TIA event and assessment was 2 days (range 0–14).

At 3–6 months following the index event, patients who were lost to follow-up (n=12) were younger and their clinical condition stabilised faster than those who completed the follow-up (age: 52.8±12.9 vs 60.0±11.5, p=0.03; interval days: 2.91±2.31 vs 2.08±0.90, p=0.01). We defined favourable functional outcome as mRS score ≤1 and poor functional outcome as mRS score ≥2. Dichotomised mRS scores for favourable and poor functional outcomes are commonly used, which is in keeping with the recommendation from previous analyses.[9] The majority of the patients (n=252, 64.9%) had good functional outcomes (mRS score ≤1) while approximately one-third of the patients (n=136, 35.1%) had poor functional outcomes (mRS score ≥2). Patients with poor functional outcome were significantly older women of Malay ethnicity, less educated, more neurologically impaired with poorer premorbid and baseline functioning and assessed later following a cerebrovascular event. They also had more stroke classification of large artery occlusion and cardioembolic stroke, as well as a higher number of cardiovascular risk factors. In addition, patients with poorer functional outcome had significantly lower scores of the MMSE and the MoCA. The population characteristics of patients with favourable and poor functional outcomes can be found in table 1.

The predictive ability of the MoCA, MMSE and NIHSS

Using hierarchical regression analyses and controlling for baseline characteristics, the MMSE, MoCA and NIHSS—as singular measures—predicted mRS scores at 3–6 months after stroke (R^2 changes of 0.012, 0.007 and 0.043, with p values 0.004, 0.029 and <0.001, respectively; table 2). Baseline MMSE scores added a small but statistically significant prediction of functional outcomes in addition to baseline NIHSS scores, while baseline MoCA scores did not (MMSE: R^2 changes=0.006, p=0.03; MoCA: R^2 changes=0.004, p=0.083).

Using a median split of baseline NIHSS scores at 2, patients with NIHSS scores ≤2 (median=1, range 0–2) were defined as having less severe strokes and those with an NIHSS score >2 (median=5, range 3–18) were defined as having more severe strokes. As shown in table 3, in patients with an NIHSS score >2, baseline MMSE and MoCA had a significant and considerable incremental prediction for functional outcomes at 3–6 months in addition to baseline NIHSS scores (MMSE: R^2 changes=0.021, p=0.010; MoCA: R^2 changes=0.017, p=0.021), while neither baseline neurocognitive measure nor baseline NIHSS showed an incremental prediction for functional outcomes in patients with less severe stroke (NIHSS score ≤2).

DISCUSSION

Cognitive screening at the subacute stroke phase can independently predict functional outcome at the early convalescent stroke phase. Baseline MMSE scores add a small incremental prediction to baseline stroke severity

Table 1 Population characteristics according to the functional outcome defined by mRS scores at 3–6 months after stroke

Characteristic N (%)	mRS 0–1 (N=252)	mRS ≥2 (N=136)	Univariate analysis, p value
Age, mean (SD)	57.9 (10.8)	63.8 (11.8)	<0.001
Gender, female	68 (27.0%)	52 (38.2%)	0.02
Education, years (mean, SD)	9.8 (4.3)	6.3 (3.7)	<0.001
Ethnicity			0.039
Chinese	188 (74.6%)	87 (64.0%)	
Malay	40 (15.9%)	36 (26.5%)	
Indian and others	24 (9.5%)	13 (9.6%)	
Stroke classification			<0.001
SAO	114 (45.2%)	60 (44.1%)	
LAA	29 (11.5%)	30 (22.1%)	
CE	31 (12.3%)	25 (18.4%)	
UND and OC	12 (4.8%)	8 (5.9%)	
TIA	66 (26.2%)	13 (9.6%)	
NIHSS (mean, SD)	1.46 (1.83)	5.04 (3.68)	<0.001
Premorbid mRS (median)	0.06 (0.29)	0.54 (1.05)	<0.001
Baseline mRS (median)	1.28 (1.20)	3.04 (1.21)	<0.001
Mean interval (days) between stroke/TIA and assessment	2.4 (2.0)	3.8 (2.5)	<0.001
Cognitive screening tests			
MMSE (mean, SD)	25.7 (3.3)	22.6 (4.3)	<0.001
MoCA (mean, SD)	22.0 (4.8)	18.1 (5.5)	<0.001
Number of cardiovascular risk factors (median)	2	3	<0.001
Recurrent vascular events (N, %)	10 (4.0%)	8 (6.0%)	0.37

CE, cardioembolism; LAA, large artery atherosclerosis; MMSE, Mini-mental State Examination; MoCA, Montreal Cognitive Assessment; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Score; OC, other determined aetiology; SAO, small artery occlusion; TIA, transient ischaemic attack; UND, undetermined aetiology.

Table 2 Hierarchical regression of mRS scores at 3–6 months after stroke on baseline MMSE, MoCA and NIHSS scores

Model	Block	Variables	Final β (p value)	R^2	R^2 change	F change	p Value
	1	Controls*		0.46	0.460	54.10	<0.001
A1	2	Baseline MMSE	−0.1 (0.031)	0.47	0.012	8.48	0.004
	3	Baseline NIHSS	0.3 (<0.001)	0.51	0.038	29.00	<0.001
A2	2	Baseline NIHSS	0.3 (<0.001)	0.50	0.043	33.00	<0.001
	3	Baseline MMSE	−0.1 (0.031)	0.51	0.006	4.71	0.031
B1	2	Baseline MoCA	−0.08 (0.083)	0.47	0.007	4.80	0.029
	3	Baseline NIHSS	0.31 (<0.001)	0.51	0.040	31.10	<0.001
B2	2	Baseline NIHSS	0.31 (<0.001)	0.50	0.043	33.00	<0.001
	3	Baseline MoCA	−0.08 (0.083)	0.51	0.004	3.02	0.083

*Block 1 variables for blocks 2 and 3 variables in the models (A1, A2, B1 and B2) include age, sex, education, composite of cardiovascular risk factors, premorbid mRS and baseline mRS.
MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; mRS, modified Rankin scale; NIHSS, National Institute of Health Stroke Score.

scores for functional outcomes at 3–6 months patients with stroke. Additionally, in patients with more severe stroke defined by baseline NIHSS score ≥2, baseline MMSE and MoCA improve the predictive value of stroke severity scores for a functional outcome 3–6 months later. However, the incremental predictive value of the MMSE and MoCA is relatively smaller than the NIHSS.

The contributions of our study are threefold. First, our finding that neurocognitive status at the subacute stroke phase predicts functional outcome at 3–6 months is novel and consistent with previous studies in inpatient rehabilitation[1 2] and at 13 months after stroke.[3] Second, MMSE scores at baseline add a small incremental prediction to baseline stroke severity scores for functional outcomes 3–6 months later. Third, baseline MMSE and MoCA showed a considerable incremental effect to the baseline NIHSS scores in predicting functional outcomes in patients with more severe strokes (NIHSS>2) while neither neurocognitive measures nor stroke severity scores at baseline were predictive for functional outcomes in patients with less severe strokes (NIHSS score ≤2). This may be explained by the higher recovery potential of patients with more neurological deficits compared to patients with less severe deficits.

There are several strengths of our study. First, we examined the prognostic value of NIHSS and cognitive status by systematically assessing baseline values individually and in combination in predicting patients' mRS scores 3–6 months after stroke. Although previous studies that investigated the predictive power of cognition included baseline NIHSS as a control variable (along with other baseline characteristics), they did not explore the role of baseline NIHSS *as a predictor* itself.[1–3] Second, we chose 3–6 months of follow-up period because prognosis of functional recovery can be made reliably within 12 weeks after stroke,[10] and patients were more likely to resume their daily activities and usual roles within this time frame. Therefore, the findings established in this study can guide early intervention from baseline to 3–6 months after stroke. Third, we examined the predictive ability of neurocognitive status and stroke severity measures at baseline for functional outcomes at 3–6 months in patients with differing stroke severity.

Table 3 Hierarchical regression of mRS scores at 3–6 months after stroke on baseline MMSE, MoCA and NIHSS for a subsample of patients with NIHSS scores >2 at baseline

Model	Block	Variables	Final β (p value)	R^2	R^2 change	F change	p Value
	1	Controls*		0.46	0.460	21.68	<0.001
A1	2	Baseline MMSE	−0.18 (0.010)	0.49	0.036	10.94	0.001
	3	Baseline NIHSS	0.22 (0.001)	0.53	0.034	11.07	0.001
A2	2	Baseline NIHSS	0.22 (0.001)	0.51	0.049	15.33	<0.001
	3	Baseline MMSE	−0.18 (0.010)	0.53	0.021	6.83	0.010
B1	2	Baseline MoCA	−0.16 (0.021)	0.49	0.029	8.51	0.004
	3	Baseline NIHSS	0.22 (0.001)	0.52	0.040	12.07	0.001
B2	2	Baseline NIHSS	0.22 (0.001)	0.51	0.049	15.33	<0.001
	3	Baseline MoCA	−0.16 (0.021)	0.52	0.017	5.42	0.021

*Block 1 variables for blocks 2 and 3 variables in the models (A1, A2, B1 and B2) include age, sex, education, composite of cardiovascular risk factors, premorbid mRS and baseline mRS.
MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Score.

There are several limitations of this study. First, our results may not be generalisable as the majority of patients had less severe stroke; nevertheless, one-third of the patients had poor functional outcomes 3–6 months after stroke, so better prognostic tools are required. Second, we employed cognitive screening tests at baseline, rather than formal neuropsychological assessments, for their brevity and utility by non-specialist personnel. Third, we did not examine rehabilitation services systematically as this information was not collected. However, all patients received standard rehabilitation according to the institutional pathway. Fourth, mRS has been criticised for its lack of specificity[5]; however, it is a summary of outcomes in functioning and has been widely used in clinical trials as a primary efficacy measure. Lastly, we did not consider other predictive scores (eg, PLAN score,[11] iScore,[12] six simple variable[13] and five simple variable scores[14]) for our models primarily due to the following reasons: (1) none of these scores include a cognitive measure; (2) PLAN scores are developed using a more severe functional outcome measure, such as mRS scores of 5–6 at discharge. Similarly, iScore has been used to estimate poor functional outcome defined by mRS 3–5; (3) six simple variable and five simple variable scores require the Glasgow Coma Scale, which we did not collect in this study. Therefore, we are unable to adopt these models to predict functional outcome in this study. However, in line with our aims, we included significant and clinically relevant predictors as control variables (age, sex, education, composite of cardiovascular risk factors, premorbid mRS and baseline mRS) in our models. Our prediction models can be applied to patients with mild ischaemic stroke and TIA, especially in those with an NIHSS score >2. The routine cognitive screening at the subacute stroke phase with either MoCA or MMSE could add incremental predictive value to the NIHSS of patients with an NIHSS score >2 for functional outcomes at 3–6 months. However, this model has yet to be validated externally, and therefore it may not be generalisable to other stroke populations.

In conclusion, 4.3% of the functional outcome after 3–6 months can be predicted early after admission by NIHSS, with its many functional and only few cognitive items. Premorbid and baseline factors alone, however, explain almost half of the variance. In addition, neurocognitive status at the subacute stroke phase is independently predictive of functioning at the early convalescent stroke phase. Baseline MMSE scores can add incremental prediction to the baseline stroke severity score for functional outcome 3–6 months later. Moreover, in patients with more recovery potential, baseline MMSE and MoCA can improve the baseline stroke severity score in predicting functional outcomes 3–6 months later. We have previously shown that these screening tests administered at the subacute stroke phase could also predict cognitive outcomes 3–6 months later.[6] In addition, MoCA administration has been reported to be applicable to the majority of patients with acute stroke (ischaemic or haemorrhagic; 82.5%) and therefore feasible to be used in acute stroke phase.[15] Therefore, the predictive value and brevity of the MMSE and MoCA warrants their routine use in the subacute stroke phase in clinical service and early acute stroke trials. However, the current instruments (NIHSS in combination with MMSE or MoCA) could only predict for 51% of the functional outcome. Therefore, it would be helpful if a better prognostic tool can improve the prediction for functional outcome to 70–80%. Future studies may establish a modified scale combining the NIHSS and items from the MMSE and MoCA to improve the predictive ability for functional outcome.

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