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Prognosis prediction of motor outcome in hemiparetic patients with anterior choroidal artery infarction

Radiologic and transcranial magnetic stimulation prognostic validation studies (STROBE)

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Abstract

To investigate prognosis prediction of motor outcome in anterior choroidal artery (AChA) infarction patients using radiologic and transcranial magnetic stimulation (TMS) studies.

Twenty six patients with complete weakness of the affected hand were recruited. The Motricity Index (MI), Medical Research Council (MRC) scores for the affected finger extensors, Modified Brunnstrom classification (MBC) and Functional Ambulation Category (FAC) were evaluated twice: at onset and the chronic stage (3–4 months after onset). Patients were assigned according to the presence of infarction at the corona radiata (CR); the CR-positive group (infarct presence at the CR and posterior limb of internal capsule [PLIC], 11 patients) and CR-negative group (infarct presence at the PLIC, 15 patients), and the presence of motor evoked potentials at the affected hand muscle: the TMS-positive group (11 patients) and the TMS-negative group (15 patients).

At the second evaluation, the MI scores were significantly different between the CR-positive (45.10 ± 7.06) and CR-negative groups (57.90 ± 11.56), and between the TMS-positive (60.37 ± 11.53) and TMS-negative groups (46.70 ± 7.99) ($P < .05$). The MRC scores for the finger extensors were also significantly different between the CR-positive (0.95 ± 1.01) and CR-negative (2.57 ± 1.33) groups and between the TMS-positive (3.05 ± 0.88) and TMS-negative (1.03 ± 1.14) groups ($P < .05$). Fourteen (53.85%) of the 26 patients recovered to have a functional hand score (MBC ≥5) and 19 (73.07%) of the 26 patients recovered to have an independent gait score (FAC ≥3) on their second evaluation.

The results show that CR involvement in addition to the presence of a PLIC lesion and a TMS-negative response were related to poor motor outcomes in patients with an AChA infarction. Consequently, radiologic and TMS studies can be considered for motor outcome prognosis prediction in patients with an AChA infarction.

Abbreviations: AChA = anterior choroidal artery, APB = abductor pollicis brevis, CR = corona radiate, CST = corticospinal tract, DTI = diffusion tensor imaging, FAC = functional ambulatory category, MBC = modified Brunnstrom classification, MEP = motor evoked potential, MI = motricity index, MRC = medical research council, PLIC = posterior limb of internal capsule, TMS = transcranial magnetic stimulation.

Keywords: anterior choroidal artery, cerebral infarction, hemiparesis, prognosis, transcranial magnetic stimulation

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1. Introduction

Motor weakness is a common and serious disabling sequela of stroke and over 50% of stroke patients present with a residual motor deficit.[1] Prognosis prediction of motor weakness in stroke patients is clinically important because it can provide information useful in determining the necessity of neurological interventions, estimating the duration of the rehabilitation period, predicting residual sequelae, and establishing neuro-rehabilitation strategies.[2,3]

The lateral corticospinal tract (CST) is reported to be the most important neural tract associated with motor function. Many previous studies have demonstrated that the lateral CST controls a major portion of the motor functions of proximal muscles as well as the distal muscles of the fingers and ankles; in particular, a functioning lateral CST is mandatory for hand function.[4–8] Many studies have attempted to predict motor outcome in stroke patients by estimating the status of the lateral CST using clinical observations, radiological findings, electrophysiological results, and functional neuroimaging and diffusion tensor imaging (DTI) results.[9–15]

Hemiparesis is a major clinical manifestation of infarction in the territory of the anterior choroidal artery (AChA), which comprises mainly the posterior limb of the internal capsule (PLIC) and the posterior portion of the corona radiata (CR).[12,14–19] It was reported that the PLIC was involved in 98% of AChA infarction.[19] The PLIC and the posterior portion of the CR are areas of importance to motor function because the lateral CST descends through these areas.[20–22] The anterior cerebral artery perforators supply the anterior limb of the IC, middle cerebral artery supplies the superior part of IC, and AChA perforators supply posterior two-third of PLIC which the CST is located.[21,23] By contrast, various perforators from the middle cerebral artery, anterior cerebral artery, and AChA supply CR area.[24] In addition, the PLIC is the narrowest area for that portion of the CST descending through the supratentorial area.[21,25] As a result, among infarction locations in the supratentorial areas, the PLIC has been deemed the area producing the worst effects on motor outcome.[14]

Despite the above indications of the clinical significance of AChA infarction, only a few studies have used clinical observations, radiologic findings, and DTI results for motor outcome prognosis prediction in patients with AChA infarction.[12,14,17] In 2001, Shelton & Reding investigated motor outcome in 41 patients with infarctions in the supratentorial area who showed severe weakness of the affected upper extremity, characteristics that were similar to those of the patients in our study.[12] The authors reported that 75% of the patients with lesions in the cerebral cortex and 38.5% of the patients with subcortical or mixed cortical plus subcortical lesions without involvement of the PLIC showed isolated upper limb movement at approximately 2 months after onset. By contrast, only 3.6% of the patients with a PLIC lesion exhibited isolated upper limb movement whereas none of the patients with PLIC and CR lesions showed isolated upper limb movement. In 2005, Wenezelburger et al investigated the hand function motor outcomes in 18 patients with PLIC infarction at a mean of 2.4 years after onset.[16] They reported that the more posteriorly the acute lesion was located within the PLIC, the more pronounced were the chronic motor deficits, which had been measured by examining kinematic recordings of the subjects' reaching to grasp movement. In 2008, Nelles et al investigated the correlation between motor outcome and the characteristics of the affected CST, as determined by DTI, in 25 patients with AChA infarction.[14] They reported that the patients with the greater the involvement of the affected CST (more reduction of anisotropy in terms of fractional anisotropy value and fiber disruption of the affected CST) revealed the poorer the motor outcome. Therefore, there are few descriptions of prognosis prediction of motor outcome in patients with AChA infarction. In particular, there are no reports describing the use of transcranial magnetic stimulation (TMS) for elucidating motor outcome prognosis prediction for AChA infarction.

Brain MRI has an advantage to estimate the integrity of the lateral CST anatomically at the PLIC and the posterior portion of CR.[12,14–19] By contrast, TMS has an unique advantage for determining the integrity of the lateral CST neurophysiologically through assessment of motor evoked potential (MEP) presence.[15,26–29] Hence, TMS has been widely used for prognosis prediction of motor outcome in other stroke types.[15,26–29] In this study, we hypothesized the combined studies of radiologic findings and TMS could be useful for prognosis prediction of motor outcome in AChA infarction.

In the current study, we investigated prognosis prediction of motor outcome in patients with AChA infarction by performing radiologic- and TMS-based studies.

2. Methods

This study was conducted retrospectively, and the institutional review board of a university hospital approved the study protocol. Because this study used a retrospective review of existing administrative data, the waiver of written informed consent was approved by the institutional review board (Access Code: YUMC-2019–04–050). Also, this study conforms to all STROBE guidelines and reports the required information accordingly (see Supplementary Checklist)

2.1. Subjects

Twenty six consecutive patients, who had been admitted to the rehabilitation department of a university hospital (14 men, 12 women; mean age 62.2 ± 9.2 years) with no history of neurologic/psychiatric disease or head trauma were recruited according to the following inclusive criteria:

1. first-ever stroke;
2. complete weakness of the affected hand (finger flexors and extensors) and severe weakness of the upper limb (mean Medical Research Council [MRC] score: less than 2 [full score: 5] of the shoulder abductors, elbow flexors and wrist extensors) at the day of stroke onset[30];
3. an infarct, which was confirmed by a neuro-radiologist, in the territory of the AChA including PLIC[16,24,31]; and
4. absence of serious medical complications, such as pneumonia or cardiac problems, from stroke onset to final evaluation.

Patients who showed apraxia, severe somatosensory problems (less than 12 points [full mark: 24] on the subscale for kinesthetic sensation of the Nottingham Sensory Assessment), were aged older than 80 years, or had severe cognitive problems (Mini-Mental State Examination score <25) were excluded from the study.[32,33] In addition, the patients who underwent procedures to get inserted metallic hardware, such as internal pulse generator, were excluded from this study.[34]

Table 1

Demographic and clinical data of the patients.

Variables	Sub-variables	Number	Sub-variables	Number
Patients, n		26		
Age, yrs, mean (SD)		62.2 (9.2)		
Sex, n (%)	Male	14 (53.8)	Female	12 (46.2)
Lesion side, n (%)	Right	14 (53.8)	Left	12 (46.2)
Days to TMS evaluation (SD)		12.9 (2.5)		
Days to the sec evaluation (SD)		108.4 (9.3)		
Risk factor, n (%)	DM	10 (38.5)	HTN	17 (65.4)
	HCL	15 (57.7)		

DM = diabetes mellitus, HCL = hypercholesterolemia, HTN = hypertension, TMS = transcranial magnetic stimulation.

Fourteen of the patients (53.8%) had lesions in the right hemispheres and the remainder (12 patients: 46.2%) had lesions in the left hemisphere (Table 1). The risk factors associated with the strokes were: hypertension (17 patients: 65.4%), diabetes mellitus (10 patients: 38.5%), and hypercholesterolemia (15 patients: 57.7%). Distributions for all types of risk factors did not differ statistically between mild and severe groups. All patients received similar rehabilitative therapy including movement therapy at sections of the physical and occupational therapy: motor strengthening of the trunk and affected extremities, and exercises for trunk stability and control, static and dynamic balance training on sitting and standing positions, and neuromuscular electrical stimulation of the affected knee extensor and ankle dorsiflexor muscles.

2.2. Clinical evaluation

The motor function and functional status of the patients were evaluated twice: first, at onset (within 24 hours after symptom onset) and second, during the chronic stage after onset (between 3 and 4 months after onset: the mean duration between first and second evaluations; 108.4 ± 9.3 days). Evaluation methods included the Motricity Index (MI), the MRC for the affected finger extensors, the modified Brunnstrom classification (MBC), and the Functional Ambulation Category (FAC).[35–41] The MI was used to measure motor function for the entire motor function system of the affected upper and lower extremities and has a maximum index value of 100.[36] The MRC score for the finger extensors was determined as follows: 0 (no contraction); 1 (palpable contraction, but no visible movement); 2 (movement without gravity); 3 (movement against gravity); 4 (movement against a resistance lower than the resistance overcome by the healthy side); and 5 (movement against a resistance equal to the maximum resistance overcome by the healthy side).[13,30,42] The function of the affected hand was categorized according to the MBC and scored as 1 (unable to move fingers voluntarily), 2 (able to move fingers voluntarily), 3 (able to close hand voluntarily; unable to open hand), 4 (able to grasp a card between thumb and medial side of index finger; able to extend fingers slightly), 5 (able to pick up and hold a glass; able to extend fingers), and 6 (able to catch and throw a ball in a near-normal fashion; able to button and unbutton a shirt).[35] We defined the patients who showed MBC: 5 to 6 at the second evaluation as the mild group and the patients who revealed MBC: 1 to 4 as the severe group. Walking ability was categorized by determining the patient's FAC.[38] The 6 categories in the FAC were: 0 (non-ambulatory), 1 (needs continuous support from 1 person), 2 (needs intermittent support from 1 person), 3 (needs only verbal supervision), 4 (help is required on stairs and uneven surfaces), and 5 (can walk independently anywhere). The reliabilities and validities of the MI, MRC, MBC, and FAC methods have been well-established.[30,35–40,45]

2.3. Infarct localization

Magnetic resonance images were acquired using a 1.5 T Philips Gyroscan Intera (Hoffman-LaRoche, Ltd, Best, Netherlands). Patients were assigned to 1 of 2 subgroups according to the presence of infarction at the CR; the CR-positive group included patients with infarct presence at the CR and PLIC levels (5 men, 6 women; mean age, 61.1 ± 9.8 years, range, 48–76 years), whereas the CR-negative group included patients with infarct presence only at the PLIC level (9 men, 6 women; mean age, 63.0 ± 8.9 years, range, 48–74 years) (Fig. 1). No significant differences in mean age or sex ratio were observed between these 2 groups ($P > .05$).

2.4. Transcranial magnetic stimulation

TMS was performed at an average of 12.9 ± 2.5 days after onset by using a Magstim Novametrix 200 magnetic stimulator (Novametrix Inc., Wallingford, CT, USA) with a 9 cm mean diameter circular coil. Cortical stimulation was performed with the coil held tangentially over the vertex. The left hemisphere was stimulated by using a counter clockwise current, and the right hemisphere was stimulated by using a clockwise current. MEPs were obtained from both abductor pollicis brevis (APBs) muscles while in a relaxed state during TMS. The excitatory threshold was defined as the minimum stimulus required to elicit a MEP with a peak-to-peak amplitude of 50 μV or greater in 2 of 4 stimulation episodes.[25] Stimulation intensity was set at 100% of the maximum stimulator output. Each hemisphere was stimulated 4 times with a minimum interval of 10 second and the MEP with the shortest latency and the largest amplitude was selected. Patients were assigned to 1 of 2 TMS-based subgroups according to the presence of MEPs at the affected APB muscle: the TMS-positive group in which there was presence of a MEP at the affected APB muscle (6 men, 5 women; mean age, 62.3 ± 9.0 years, range, 50–76 years), and the TMS-negative group in which there was an absence of a MEP at the affected APB muscle (8 men, 7 women; mean age, 62.1 ± 9.6 years, range, 46–74 years). No significant differences in mean age or sex ratio were detected between the 2 TMS subgroups ($P > .05$).

2.5. Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) 23.0 software (SPSS Inc., Chicago, IL).

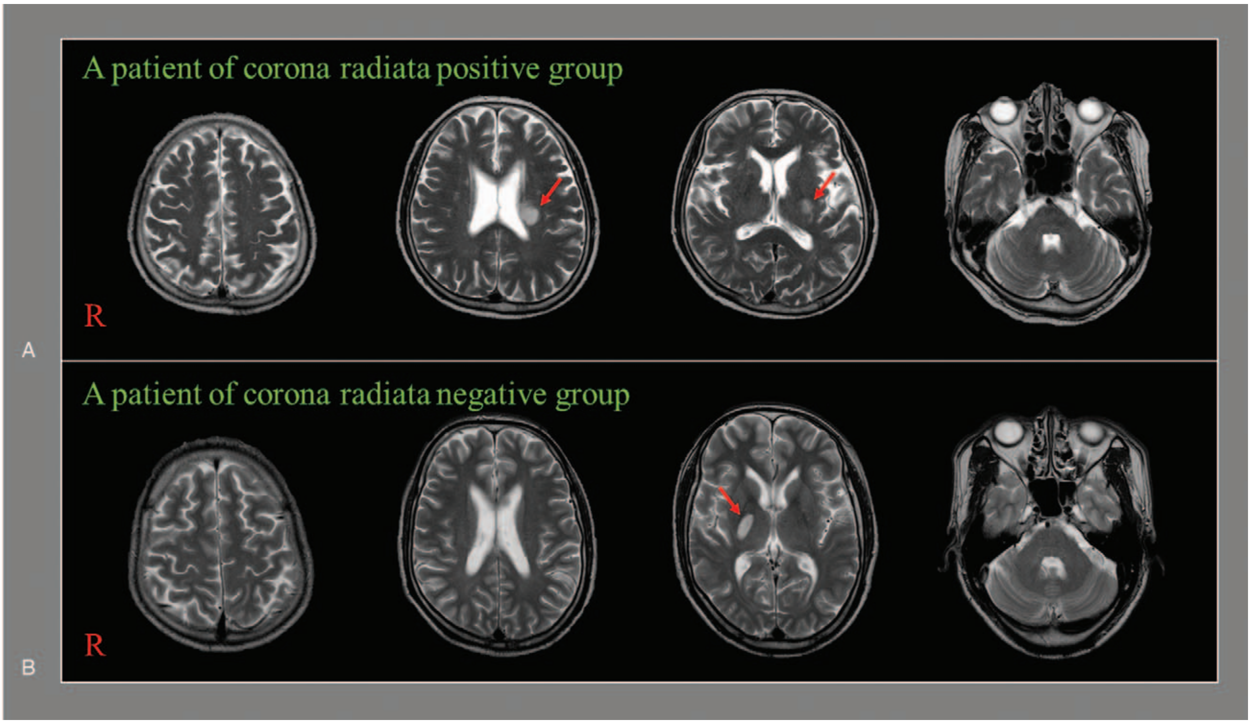

Figure 1. T2-weighted brain magnetic resonance images of a representative patient (42-year-old male) of the corona radiata-positive group who had infarct lesion presence in the corona radiata and the posterior limb of internal capsule (A) and images of a representative patient (49-year-old male) of the corona radiata-negative group who had an infarct lesion in the posterior limb of internal capsule (B).

Changes in motor functions from the first (onset) to second (chronic) evaluations were compared by applying the Wilcoxon signed-rank test. To determine the significance of intergroup differences in MRC and MI scores at the second evaluation, the Mann–Whitney test was employed. Statistical significance was accepted for P values of <.05.

3. Results

Changes in clinical data of the patients from stroke onset to chronic stage are summarized in Table 2. All clinical assessments in terms of MI, MRC, and FAC revealed significant differences between stroke onset and chronic stage evaluations ($P<.05$).

Table 2

Changes in clinical data of the patients from infarct onset (1st evaluation) to chronic stage (2nd evaluation).

	Onset	2nd evaluation	*P* value
MI	4.01 ± 9.81 (median: 0.00)	52.48 ± 11.68 (median: 52.75)	.000*
MRC	0.00 ± 0.00 (median: 0.00)	1.88 ± 1.44 (median: 2.00)	.000*
MBC (score: *n*)	1.00 ± 0.00 (median: 1.00)	3.92 ± 1.60 (1:*1* / 2:*5* / 3:*6* / 4:*3* / 5:*5* / 6:*6*)	.000*
FAC (score: *n*)	0.00 ± 0.00 (median 0.00)	2.98 ± 0.96 (0:*1* / 1:*1* / 2:*5* / 3:*13* / 4:*6* / 5:*0*)	.000*

Values represent mean ± standard deviation.
FAC = functional ambulation category, MI = motricity index, MRC = medical research council score, MBC = modified Brunnstrom classification.
* Significant difference between first and second evaluations, $P<.05$.

The MI and MRC results for the finger extensors were not significantly different at stroke onset between the CR-positive and CR-negative groups or between the TMS-positive and TMS-negative groups ($P>.05$). Between stroke onset and chronic stage evaluations, significant differences in the MI were observed between the CR-positive (1.91 ± 3.43 and 45.10 ± 7.06, respectively) and CR-negative (5.55 ± 12.54 and 57.90 ± 11.56, respectively) groups ($P<.05$); as well, there were significant differences in the MRC results for the finger extensors for the CR-positive (0.00 ± 0.00 and 0.95 ± 1.01, respectively) and CR-negative (0.00 ± 0.00 and 2.57 ± 1.33, respectively) groups ($P<.05$). In addition, significant differences were observed in the MI in the TMS-positive (3.68 ± 12.21 and 60.37 ± 11.53, respectively) and TMS-negative (4.25 ± 8.07 and 46.70 ± 7.99, respectively) groups as well as in the MRC of the finger extensors (TMS-positive group: 0.00 ± 0.00 and 3.05 ± 0.88; TMS-negative group: 0.00 ± 0.00 and 1.03 ± 1.14, respectively) ($P<.05$). At the second evaluation, the MI results were significantly different between the CR-positive (45.10 ± 7.06) and CR-negative (57.90 ± 11.56) groups, as well as between the TMS-positive (60.37 ± 11.53) and TMS-negative (46.70 ± 7.99) groups ($P<.05$) (Fig. 2). The MRC assessment of the finger extensors also revealed significant differences between CR-positive (0.95 ± 1.01) and CR-negative (2.57 ± 1.33) groups and between TMS-positive (3.05 ± 0.88) and TMS-negative (1.03 ± 1.14) groups ($P<.05$).

Functional hand outcome based on MBC is described in Table 3. Among the patients included in the TMS-positive and CR-negative groups, 9 out of 10 patients (90.0%) belonged to the mild group, and the remainder (10.0%) belonged to the severe group. A higher specificity was observed in the TMS group (0.917) than the CR group (0.667) for prediction of motor

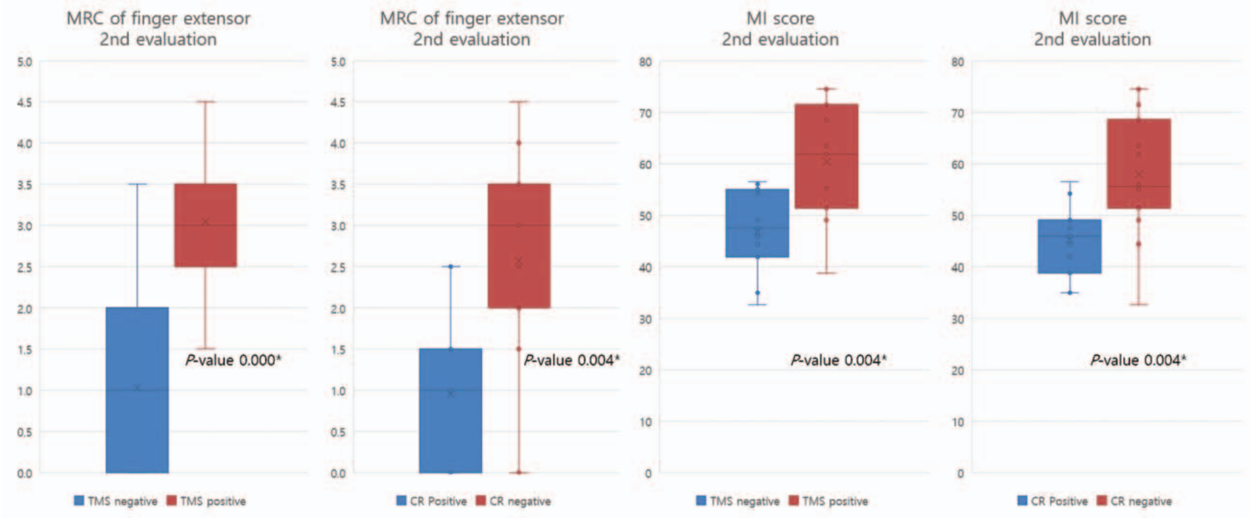

Figure 2. The graphs show that MRC assessment of finger extensors and MI score on second evaluation revealed significant differences between each 2 groups ($P < .05$).

outcome. On the other hand, the involvement of CR showed a higher sensitivity (0.786) than TMS (0.714).

4. Discussion

In the current study, we investigated the prognosis prediction for hemiparesis in patients with severe hemiparesis due to infarction in the AChA region and obtained the following results. First, the patients without a CR infarction showed better motor outcome than the patients with a CR infarction in terms of total motor (MI) and hand motor (MRC) functions. Second, the patients with a positive hand muscle MEP response had better motor outcomes than patients with a negative hand muscle MEP response in both total motor (MI) and hand motor (MRC) functions. Third, with regard to the patients' functional outcomes at the second evaluation, 14 (53.85%) of 26 patients recovered to exhibit a functional hand outcome (MBC score ≥5) which indicates the ability of fine motor activity and 19 (73.07%) of 26 patients recovered sufficiently to have an independent gait (FAC score ≥3).

The results showing that patients without a CR lesion but with a positive MEP response had better motor outcomes appear to indicate the importance of preservation of the lateral CST. Because the posterior portion of the CR, as well as the PLIC, are the descending pathways of the lateral CST, the patients with lesions in the CR and the PLIC had the possibility of a more severe lateral CST injury than those patients without a CR lesion.[20–22] Regarding the TMS results, because a positive MEP response indicates preservation of the integrity of the lateral CST, the patients with the positive MEP response appeared to show better motor outcomes than the patients with negative MEP responses.[26–28] Consequently, our results suggest that preservation of the lateral CST may be an important prognostic factor for motor outcome in patients with AChA infarction. Therefore, the presence of a MEP response on TMS and involvement of a CR lesion appear to be useful predictive factors when assessing motor outcome in the patients with infarction in the AChA region.

In this study, we observed relatively poor functional outcomes as only approximately half of the patients showed functional hand recovery and approximately two-thirds of the patients

Table 3

Proportion of functional hand outcome based on modified brunnstrom classification.

Group	Number	MBC Mild, n (%)	MBC Severe, n (%)	Sensitivity	Specificity	Odds ratio	*P* value (Fisher's exact test)
TMS group				0.714	0.917	27.500	.002
TMS-positive	11	10 (90.9)	1 (9.1)				
TMS-negative	15	4 (26.7)	11 (73.3)				
CR group				0.786	0.667	7.333	.045
CR-positive	11	3 (27.3)	8 (72.7)				
CR-negative	15	11 (73.3)	4 (26.7)				
TMS & CR groups							
TMS-positive & CR-negative	10	9 (90.0)	1 (10.0)				
TMS-positive & CR-positive	1	1 (100.0)	0 (0.0)				
TMS-negative & CR-negative	5	2 (40.0)	3 (60.0)				
TMS-negative & CR-positive	10	2 (20.0)	8 (80.0)				

CR = corona radiate, MBC = modified Brunnstrom classification, TMS = transcranial magnetic stimulation.

recovered to walk independently, results that appear to be related to the involvement of the lateral CST in the AChA region even though the AChA region is relatively narrow compared to other arterial regions. The patients' relatively poor functional outcomes appear to support the results reported by Shenton & Reding showing a poor functional outcome of the affected hand.[12] The functional outcomes reported in this study are worse than those presented in previous studies that involved patients with CR and pontine infarctions.[43,44]

As we described in the introduction, a few studies reporting on prognosis prediction of motor outcome have attempted to demonstrate predictors of motor outcome in patients with AChA infarction by assessing clinical observations, radiologic findings, and DTI results.[12,14,17] As a result, to our best knowledge, the present study is the first to demonstrate the usefulness of TMS for prognosis prediction in patients with AChA infarction. However, some limitations of this study should be considered when interpreting the results. First, this study included a relatively small number of patients and was conducted retrospectively. Therefore, further prospective studies including a larger number of patients should be encouraged. Second, we did not employ DTI, which can be used to determine the CST state by analyzing the imaging parameters.[43,44] Furthermore, diffusion tensor tractography (DTT), which is derived from DTI data, would have allowed a three-dimensional reconstruction of the CST.[43,44] In some recent studies, DTT has been used for prognosis prediction of motor outcome in stroke patients.[14,29,45] Therefore, further studies using DTI or a combination of TMS and DTI/DTT to elucidate prognosis prediction of motor outcome in stroke patients should be undertaken.

5. Conclusion

In conclusion, we found that the co-presence of CR and PLIC lesions and a negative MEP response on TMS were related to a poor motor outcome in patients with AChA infarction. Consequently, a combination of radiologic and TMS assessments can be considered for prognosis prediction of motor outcome in AChA infarction patients.

Author contribution

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