P- 8

The Effect of Premorbid Disability on Motor Recovery after First-Ever Ischemic Stroke: How and How much

Hyun Haeng Lee, MD., MS.[1], Yuk Doyoung, MD.[1], Min Kyun Sohn, MD., PhD.[2], Jongmin Lee, MD., PhD.[1], Deog Young Kim, MD., PhD.[3], Yong-Il Shin, MD., PhD.[4], Gyung-Jae Oh, MD., PhD.[5], Yang-Soo Lee, MD., PhD.[6], Min Cheol Joo, MD., PhD.[7], So Young Lee, MD., PhD.[8], Min-Keun Song, MD., PhD.[9], Junhee Han, PhD.[10], Jeonghoon Ahn, PhD.[11], Young-Hoon Lee, MD., PhD.[7], Yun-Hee Kim[13] Won Hyuk Chang, MD., PhD.[12,14]

[1]Department of Rehabilitation Medicine, Konkuk University School of Medicine, Seoul, Republic of Korea; [2]Department of Rehabilitation Medicine, College of Medicine, Chungnam National University, Daejeon, Republic of Korea; [3]Department and Research Institute of Rehabilitation Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea; [4]Department of Rehabilitation Medicine, Pusan National University School of Medicine, Pusan National University Yangsan Hospital, Yangsan, Republic of Korea; [5]Department of Preventive Medicine, Wonkwang University, School of Medicine, Iksan, Republic of Korea; [6]Department of Rehabilitation Medicine, Kyungpook National University School of Medicine, Kyungpook National University Hospital, Daegu, Republic of Korea; [7]Department of Rehabilitation Medicine, Wonkwang University School of Medicine, Iksan, Republic of Korea; [8]Department of Rehabilitation Medicine, Jeju National University Hospital, Jeju National University School of Medicine, Jeju City, Republic of Korea; [9]Department of Physical and Rehabilitation Medicine, Chonnam National University Medical School, Gwangju, Republic of Korea; [10]Department of Statistics, Hallym University, Chuncheon, Republic of Korea; [11]Department of Health Convergence, Ewha Womans University, Seoul, Republic of Korea; [12]Department of Physical and Rehabilitation Medicine, Center for Prevention and Rehabilitation, Heart Vascular Stroke Institute, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [13]Department of Physical and Rehabilitation Medicine, Sungkyunkwan University School of Medicine, Suwon, Korea; [14]Department of Health Science and Technology, Department of Medical Device Management and Research, Department of Digital Healthcare, SAIHST, Sungkyunkwan University, Seoul, Republic of Korea

Introduction

Stroke is a leading cause of long-term disability worldwide, and motor function recovery after a stroke is a significant concern for both patients and healthcare providers. Premorbid disability, defined as any functional limitation or restriction before the stroke event, is assumed to affect motor recovery after a stroke. However, there is a lack of supporting evidence in the literature. Understanding the relationship between premorbid disability and motor function recovery is critical for designing effective interventions, consulting with stroke patients and caregivers, and establishing a healthcare policy.

Directed acyclic graphs (DAGs) are a useful tool for understanding causal relationships between variables by specifying the roles of various variables with specific relationships to exposure and outcome variables. DAGs also help identify potential confounders to adjust for in order to obtain unbiased estimates for effect size of exposure variables. In this study, we sought to demonstrate the effect size of premorbid disability on motor function after ischemic stroke by elucidating how premorbid disability affects motor function through the DAG framework.

Methods

We conducted a retrospective analysis of the clinical characteristics of patients enrolled in the Korean Stroke Cohort for Functioning and Rehabilitation (KOSCO) between August 2012 and January 2021. The KOSCO study is a multicenter, prospective cohort study that aims to investigate the functional outcomes and rehabilitation of stroke patients in Korea.

Inclusion criteria for the KOSCO study were: (1) first-ever acute stroke; (2) age ≥19 years at stroke onset; and (3) onset of symptoms within 7 days of inclusion in the study. Exclusion criteria were: (1) transient ischemic attack; (2) a history of stroke; (3) traumatic intracerebral hemorrhage; and (4) non-Korean citizens. Additionally, our study excluded patients with hemorrhagic stroke, poststroke >48h hospital arrival time, bilateral lesions, a history of craniectomy, poststroke >1wk intervention, and death or stroke recurrence up to 6 months after the stroke.

We identified potential confounders and mediators through a rigorous literature review and confirmed the roles of these variables through expert consensus. These variables were then incorporated into the DAG. To examine the association between the modified Rankin scale (mRS) at stroke onset and Fugl-Meyer Assessment of Upper Extremity score (FMAUE) or Fugl-Meyer Assessment of Lower Extremity score (FMALE) at three time points (1 week, 3 months, and 6 months), we conducted longitudinal analyses with repeated measures of FMAUE (or FMALE) using mixed-effects models with random slopes and intercepts.

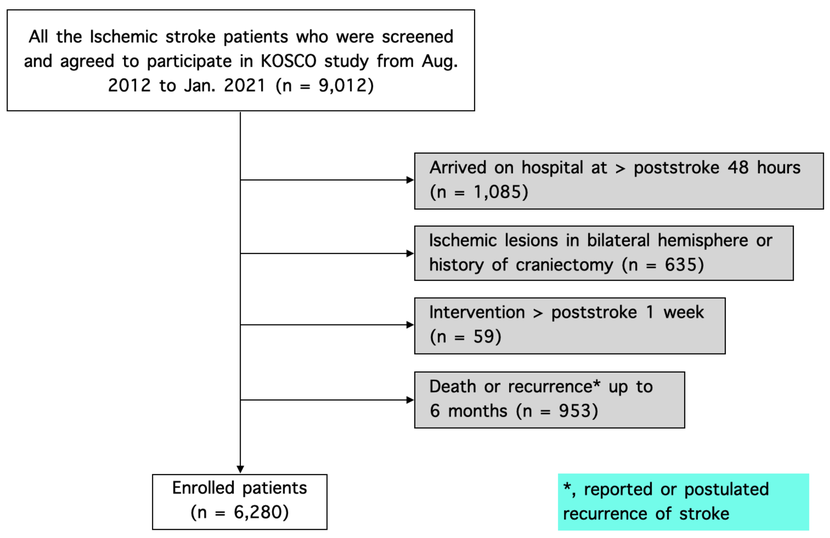

Figure 1. Flow of patient enrollment

Results

A total of 6,282 ischemic stroke patients were enrolled (Fig.1). Our DAG suggested that the minimally sufficient adjustment sets for estimating the total effect of mRS at stroke onset on motor function were age at stroke onset and premorbid conditions such as sex, body mass index, underlying diseases, lifestyle, and family history, which acted as confounders (Fig.2). In the adjusted model as presented in table 1, we found that patients with mRS≥4 (patients with moderately severe disability or severe disability) showed significantly decrease of FMAUE up to post stroke 6 months comparing the patients without premorbid disability (strata, estimates (95% CI); mRS 1, 1.926 (1.219 - 2.633); mRS 2, 2.086 (1.147 - 3.026); mRS 3, 0.564 (-0.813 - 1.940); mRS 4, -4.945 (-6.144 - -3.747); mRS 5, -18.122 (-20.182 - -16.062). We also found that patients with mRS≥4 showed significantly decrease of FMALE up to post stroke 6 months comparing the patients without premorbid disability (strata, estimates (95% CI); mRS 1, 1.019 (0.718 - 1.320); mRS 2, 1.006 (0.606 - 1.406); mRS 3, 0.439 (-0.149 - 1.027); mRS 4, -1.787 (-2.298 - -1.276); mRS 5, -6.361 (-7.245 - -5.478). The results of the adjusted model were similar to those of the unadjusted model.

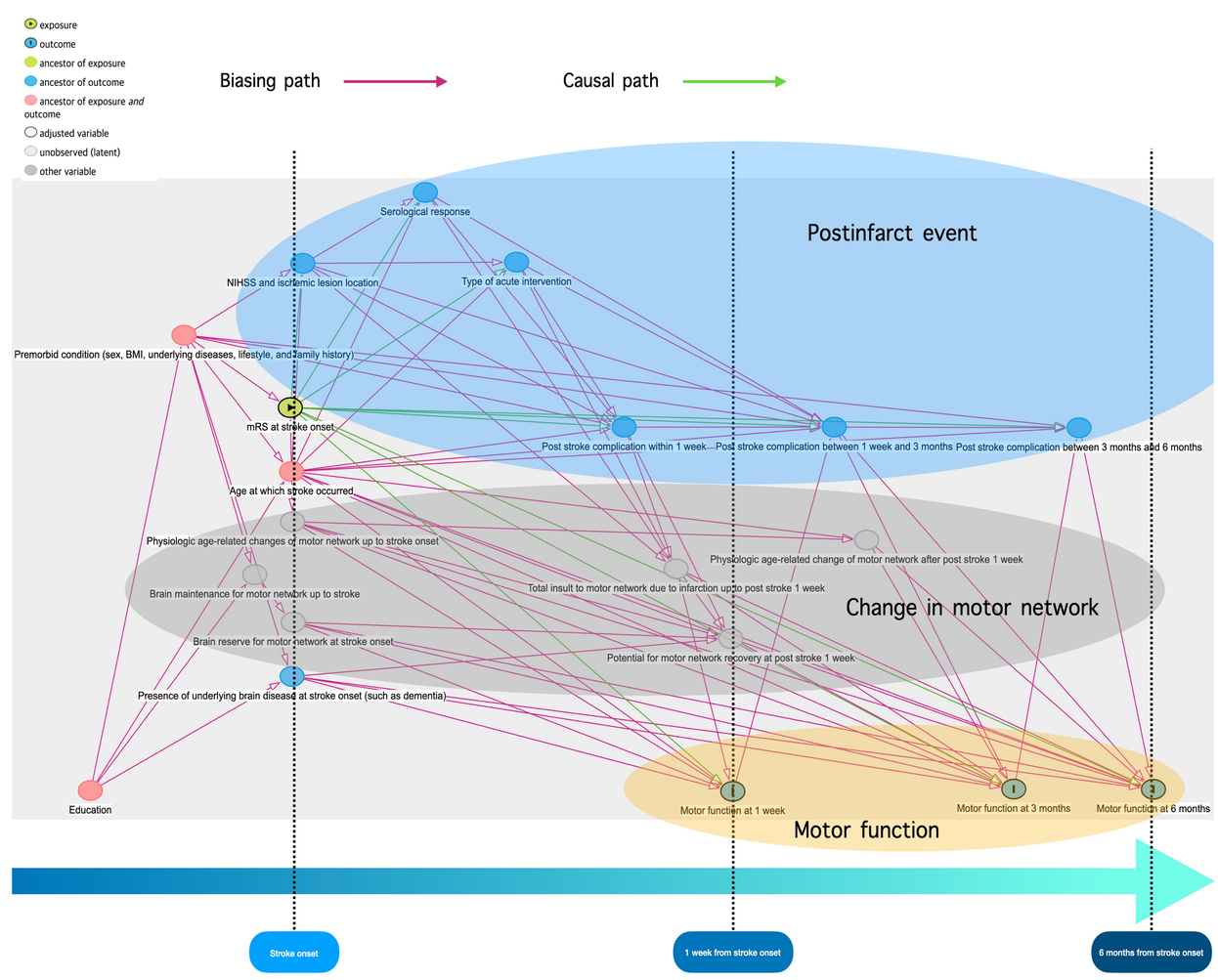

Figure 2. Directed acyclic graph related to premorbid disability and motor function after ischemic stroke

Table 1. Estimated difference of the upper and lower extremity Fugl-Meyer Assessment score up to post stroke 6 months according to the premorbid functional status[a]

Strata of premorbid functional status	Average difference of FMAUE and FMALE (95% CI)	
	Model 1 (No covariates)	Model 2
FMAUE up to post stroke 6 months		
mRS 0	1 [Reference]	1 [Reference]
mRS 1	1.344 (0.625 – 2.062)	1.926 (1.219 – 2.633)
mRS 2	1.027 (0.076 – 1.978)	2.086 (1.147 – 3.026)
mRS 3	-0.733 (-2.138 – 0.673)	0.563 (-0.813 – 1.940)
mRS 4	-5.936 (-7.149 – -4.722)	-4.945 (-6.144 – -3.747)
mRS 5	-20.142 (-22.266 – -18.019)	-18.122 (-20.182 – -16.062)
FMALE up to post stroke 6 months		
mRS 0	1 [Reference]	1 [Reference]
mRS 1	0.750 (0.440 – 1.060)	1.019 (0.718 – 1.320)
mRS 2	0.393 (-0.018 – 0.804)	1.006 (0.606 – 1.406)
mRS 3	-0.253 (-0.864 – 0.357)	0.439 (-0.149 – 1.027)
mRS 4	-2.273 (-2.799 – -1.748)	-1.787 (-2.298 – -1.276)
mRS 5	-7.277 (-8.201 – -6.352)	-6.361 (-7.245 – -5.478)

FMAUE, Fugl–Meyer Assessment of Upper Extremity score; FMALE, Fugl–Meyer Assessment of Lower Extremity score; CI, confidence interval; mRS, modified Rankin Scale

[a] Results from mixed-effects linear regression analysis demonstrating the association between premorbid functional status and FMAUE (or FMALE) at 3 time points (1 week, 3 months, and 6 months).

[b] Model 1 has no covariate, in which we analyzed 5,589 individuals for FMAUE and 5,602 individuals for FMALE up to post stroke 6 months.

[c] Model 2 adjusted for minimally sufficient adjustment set obtained from DAG analysis, including age at stroke onset, sex, body mass index, risk factors for stroke, comorbidities, smoking, alcohol consumption, and family history. The model analyzed 5,370 individuals for FMAUE and 5,380 individuals for FMALE up to post stroke 6 months.

Conclusion

The results of our investigation provide compelling evidence for a causal link between pre-existing functional status and motor deficits in individuals suffering from stroke. Consequently, mitigating premorbid disability may serve as a crucial approach to enhance motor performance following a stroke event, which have important implications for health policymaking.

Acknowledgement

This work was supported by the Research Program funded by Korea Disease Control and Prevention Agency (3300-3334-300-260-00, 2013-E33017-00, 2013E-33017-01, 2013E-33017-02, 2016-E33003-00, 2016-E33003-01, 2016-E33003-02, 2019-E3202-00, 2019-E3202-01, 2019-E3202-02, 2022-11-006).