

Arterial Stiffness in Subacute Stroke: Changing Pattern and Relationship with Functional Recovery

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Background: To examine changing patterns in arterial stiffness and functional outcome in patients with subacute stroke, and to determine which parameter shows a strong correlation with the reversal of arterial stiffness, during a 3-month period of comprehensive rehabilitation therapy. **Methods:** This descriptive, observational cohort study enrolled 60 patients (43 male and 17 female; average age, 62.7 years), and all received conventional rehabilitation therapy, during a 3-month period. Brachial-ankle pulse wave velocity (baPWV) was measured as an index of arterial stiffness. Functional assessments included the 6-minute walk test (6MWT), Fugl-Meyer Assessment of hemiparetic upper and lower limbs, the functional ambulatory category, the Berg balance scale, the Korean Mini-Mental Status Examination, and the Korean-Modified Barthel Index. All measurements were conducted at baseline and 1 and 3 months after stroke onset. **Results:** Rehabilitation therapy resulted in a statistically significant improvement in baPWV since 3 months post stroke. Another functional outcome measure showed statistically significant improvements since 1 month after rehabilitation. Multivariable linear regression analysis revealed that a change in baPWV was significantly correlated with changes in the 6MWT. **Conclusions:** Three months of comprehensive rehabilitation therapy led to statistically significant improvements in arterial stiffness and functional outcomes during the subacute phase of stroke. Thus, the comprehensive rehabilitation focused on improving gait endurance would be warranted in subacute stroke patients. **Key Words:** Vascular stiffness—stroke—gait—recovery of function—pulse wave analysis.
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Introduction

Stroke is one of the major causes of death worldwide,¹ and a considerable portion of stroke survivors suffer permanent disabilities² such as gait disturbance, difficulties with activities of daily living (ADL),³ poor physical fitness,⁴ and general deconditioning.⁵

Atherosclerosis is a systemic disease affecting the large- and medium-sized arteries of the entire systemic arterial tree; as such, it plays a significant role in the pathophysiology of cardiovascular (CV)-related diseases such as recurrent stroke, myocardial infarction, and sudden cardiac death. Thus, the risk of atherosclerosis and CV-related morbidity^{6,7} is higher in stroke victims. One independent predictor of atherosclerosis and CV disease⁸ is arterial stiffness, a marker for which is pulse wave velocity (PWV). Carotid-femoral PWV (cfPWV), which is a measure of central artery stiffness, is a predictor of CV-related morbidity and mortality.⁹ To this end, brachial-ankle (ba)PWV, which reflects the stiffness of both the central and peripheral arteries,¹⁰ may not be relevant to CV risk assessment. However, there is a close relationship between baPWV and cfPWV^{9,11} that is independent of gender and race.¹² Indeed, baPWV is related to the thickness of the intima media of the carotid artery and to aortic PWV^{9,11}; a previous study showed that reductions in cfPWV are accompanied by corresponding reductions in baPWV.¹² Moreover, recent studies report a strong association between high baPWV and poor long-term functional outcome and mortality in acute stroke patients.^{13,14} baPWV records brachial and tibial artery waveforms via an automated method that does not require exposure of a femoral site¹⁴; and the procedure is simple and the measuring time is short.¹⁵

However, a majority of studies evaluating arterial stiffness were conducted in a cross-sectional manner; few cohort studies report longitudinal changes in stiffness.^{16,17}

Also, there is little evidence about the effects of comprehensive rehabilitation therapy on arterial stiffness in stroke patients, as measured by baPWV.

Therefore, the aims of the present study were to examine changes in functional outcome and arterial stiffness in patients with subacute stroke during a 3-month period of comprehensive rehabilitation therapy, and to determine which (if any) parameter shows a strong correlation with the reversal of arterial stiffness, as evidenced by short-term functional recovery.

Methods

Participants

The present study was a descriptive, observational cohort study. Eligibility was determined by a rehabilitation doctor (physiatrist). Of 104 screened patients, 71 were eligible for inclusion. Eleven patients dropped out at the 3-month evaluation point; therefore, 60 subacute stroke patients

(43 male and 17 female; average age, 62.7 years) were enrolled between July 2013 and July 2015.

To participate in the study, patients had to have hemiplegia after unilateral ischemic or hemorrhagic stroke. The inclusion criteria were as follows: (1) age 19 years or older at onset of stroke; (2) onset of symptoms within the 7 days prior to admission; (3) first ever stroke involving cortical or subcortical areas, confirmed clinically by computed tomography scans or magnetic resonance imaging; (4) transferred or admitted to the department of rehabilitation medicine for comprehensive rehabilitation therapy; and (5) sufficient cognition to understand the procedures and provide informed consent (Korean version of Mini-Mental Status Examination > 10).

Exclusion criteria were as follows: (1) transient ischemic attack; (2) history of stroke; (3) traumatic intracerebral hemorrhage; (4) musculoskeletal disease involving the lower limbs, including severe painful arthritis, osteoporosis, amputation, or joint contracture; and (5) other concurrent neurological diseases (e.g., Parkinson's disease, multiple sclerosis). The protocol was reviewed and approved by the Institutional Review Board (JNUH 2013-05), and all subjects provided written informed consent prior to the selection procedure.

Measurement of Cardiopulmonary Exercise Capacity

A symptom-limited graded exercise stress test was performed using a motorized calibrated treadmill (T-2100; GE Healthcare Inc., Chalfont St. Giles, UK) or bicycle ergometer (Ergoselect 600K; Ergoline GmbH, Lindenstraße, Germany), and the results were used to prescribe the intensity of aerobic exercise; all stress tests were supervised by a physiatrist and a physical therapist. After the stress test, patients were allowed 15 minutes of seated rest. Cardiorespiratory function was assessed by a 12-lead electrocardiogram (HearTwave II MTWA system; Philips, Morrisville, NC) and by expired-gas analysis (breath-by-breath method) using a portable telemetric system (Cosmed CPET; COSMED Inc., Pavana di Albano, Italy). To determine the target fastest safe walking velocities, subjects began walking on a treadmill at .5 km/h at zero incline; the speed was then gradually increased by .1 km/h increments. Patients performed treadmill walking at the targeted speed at zero incline for 2 minutes, followed by 2 minutes at 4% incline, and a 2% increase in the incline every 2 minutes thereafter.¹⁸ As a safety precaution, patients were provided with gait belt support (minimal handrail support was allowed). All patients were supervised throughout the test.

Patients who could not perform the treadmill stress test underwent a bicycle ergometer test.¹⁹ This test was performed at a rate of 50–60 rpm (revolutions per minute). The workload started at 10 W (watts) for 2 minutes, increasing by 5 W every 2 minutes. Oxygen consumption (VO₂), the respiratory exchange ratio (RER), and heart

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