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Original Study

Favorable Effect of Sympathetic Nervous Activity on Rehabilitation Outcomes in Frail Elderly

Koji Shibasaki MD, PhD [a], Sumito Ogawa MD, PhD [a,*], Shizuru Yamada MD [b], Katsuya Iijima MD, PhD [c], Masato Eto MD, PhD [d], Koichi Kozaki MD, PhD [e], Kenji Toba MD, PhD [f], Yasuyoshi Ouchi MD, PhD [g], Masahiro Akishita MD, PhD [a]

[a] *Department of Geriatric Medicine, Graduate School of Medicine, The University of Tokyo, Bunkyo-ku, Tokyo, Japan*
[b] *Komagane-kogen Ladies Clinic, Komagane City, Nagano, Japan*
[c] *Institute of Gerontology, The University of Tokyo, Bunkyo-ku, Tokyo, Japan*
[d] *General Educational Center, The University of Tokyo Hospital, Bunkyo-ku, Tokyo, Japan*
[e] *Department of Geriatric Medicine, Kyorin University School of Medicine, Mitaka City, Tokyo, Japan*
[f] *National Center for Geriatrics and Gerontology, Obu City, Aichi, Japan*
[g] *Federation of National Public Service Personnel Mutual Aid Associations, Toranomon Hospital, Minato-ku, Tokyo, Japan*

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A B S T R A C T

Objectives: Previous studies have suggested the relationship between physical function, mortality, and autonomic nervous activity in frail elderly and that maintaining sympathetic nervous activity might lead to improved physical function and mortality in the elderly population. The aim of this study was to investigate the utility of sympathetic nervous activity measured by heart rate variability in frail elderly patients undergoing inpatient rehabilitation, further focusing the nervous activity on the effect of rehabilitation therapy.
Design: Prospective cohort study.
Participants: Sixty-one subjects aged 75 years or older were recruited after treatment of acute phase illness.
Measurements: Before undergoing rehabilitation, data of 24-hour Holter monitoring and a blood venous sample were obtained. From RR intervals in the electrocardiogram, heart rate and SDs of all NN intervals in all 5-minute segments of the entire recording, power spectral density, low frequency (LF), high frequency (HF), and low frequency/high frequency (LF/HF) were calculated. Functional Independence Measure (FIM) and Barthel index were used to measure physical function.
Results: FIM score and Barthel index were 46.8 ± 25.4 and 32.8 ± 31.7, respectively. Serum total protein, albumin, hemoglobin, and total cholesterol were all significantly related to FIM score and Barthel index before rehabilitation. Heart rate variability indices did not show a significant relationship with physical function, whereas the high LH/HF group showed significant improvement in physical function compared with the low LH/HF group. Moreover, LF/HF frequency was a predictive factor for improvement of physical function after 2 months of rehabilitation.
Conclusion: A favorable effect of preserved LF/HF on rehabilitation outcome was observed in elderly undergoing rehabilitation. Preservation of sympathetic nervous activity may lead to improved physical function in the elderly.

The number of disabled elderly is increasing in Japan, and the number of elderly needing long-term care reached more than 5 million in 2011.[1] It is important for disabled elderly to maintain or improve their physical function. Rehabilitation is a well-established approach to improve physical function after treatment of acute phase illness.[2] In Japan, the underlying causes of physical dysfunction necessitating rehabilitation are cerebrovascular disease, fracture, disuse syndrome, and other diseases that cause physical dysfunction.[3] It is our most urgent task to prevent and treat these diseases, and also to improve physical function after the occurrence of these diseases. Recent studies have indicated a relationship between these underlying diseases and sympathetic nervous activity.[4–8]

With regard to cerebrovascular disease, which is the most frequent cause of elderly becoming frail or needing long-term care, Muslumanoglu et al[4] demonstrated that low sympathetic nervous

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* Address correspondence to Sumito Ogawa, MD, PhD, Department of Geriatric Medicine, Graduate School of Medicine, The University of Tokyo, 7–3–1 Hongo, Bunkyo-ku, Tokyo 113–8655, Japan.
E-mail address: suogawa-tky@umin.ac.jp (S. Ogawa).

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activity measured by skin sympathetic reactivity reflected greater severity of paralysis and severe limited motor function in the chronic phase of ischemic cerebrovascular disease in the elderly. In addition, RR intervals in the electrocardiogram are used to evaluate heart rate variability (HRV),[9] and low frequency/high frequency (LF/HF), which was reported to be a marker of sympathovagal balance or sympathetic modulation, showed a positive correlation with both respiratory and skeletal muscle strength in chronic obstructive pulmonary disease.[5] Moreover, it was reported that low LF/HF value was related to overall mortality in not only frail elderly and elderly in long-term care, but also community-dwelling elderly.[6–8] In addition to these previous reports, we recently showed that elderly in long-term care aged 75 years or older had lower LF/HF than in physically intact elderly controls. Moreover, in only long-term care elderly, the low LF/HF group was significantly associated with high mortality after adjustment for age, sex, cardiovascular risk factors, and physical function. These findings suggest that preserved sympathetic nervous activity might have some favorable effects in long-term care elderly.[8]

Dementia is known to be a limiting factor in rehabilitation.[10–12] Patients with Lewy body dementia and Parkinson disease dementia show low sympathetic activity.[13,14] The same relationship is observed in fractures. β-blockers are widely accepted for the treatment of hypertension and chronic heart failure through reducing sympathetic nervous activity in middle age.[15,16] However, most studies concerning the benefit of β-blockers targeted only middle age, and there have been few studies of elderly aged 75 years or older.[17] In contrast to the benefit of β-blockers in middle age, they were found to have a relationship with incident fracture in elderly people aged 80 years or older.[18]

These findings suggest that it might be necessary to maintain sympathetic nervous activity in very elderly people, especially in frail or long-term care elderly. However, few studies have examined the relationship between sympathetic nervous activity and the effect of rehabilitation therapy in very elderly people. Therefore, we investigated whether sympathetic nervous activity affects physical function increment in elderly aged 75 years or older undergoing rehabilitation therapy. The aim of this study was to determine whether the high sympathetic nervous activity group would show greater improvement in physical function, and whether sympathetic nervous activity could predict the effect of rehabilitation.

Methods

Setting and Participants

This observational study analyzed 61 consecutive elderly persons aged 75 years or older who were admitted to a rehabilitation unit. The hospital was located in Nagano prefecture, Japan. Inclusion criteria were elderly aged 75 years or older undergoing rehabilitation. Exclusion criteria were treatment of acute phase disease within the last 2 weeks, arrhythmia, administration of anti-arrhythmia drugs or β-blockers, malignancy, and neurodegenerative disease.[9] Medical records were reviewed to obtain information on history of cardiovascular disease, such as hypertension, diabetes mellitus, hyperlipidemia, chronic heart failure, or ischemic heart disease, which was confirmed by the patient or family. This study protocol was approved by the institutional review board of the Keijinkai Kikyougahara Hospital. Written informed consent was obtained from all participants or their families.

Heart Rate Variability

Ambulatory Holter recording was performed for 24 hours using QR2100 (Fukuda ME, Kogyo, Tokyo, Japan) and processed with HS1000VL (Fukuda ME Kogyo). For time domain analysis, the SDs of all NN intervals in all 5-minute segments of the entire recording (SDANN) were calculated, and frequent domain analysis was performed with fast Fourier transform. From the power spectral density, LF (0.04 ~ 0.15 Hz), HF (0.15 ~ 0.40 Hz), and LF/HF were determined.

Anthropometric, Physical Function, and Hematologic Measures

Height, weight, and body mass index (BMI) were measured before Holter monitoring. FIM score[19] and Barthel index[20] were determined to assess physical function. Venous blood samples were obtained from individuals in the morning after an overnight fast. Blood cell counts and serum levels of chemical parameters were determined by a commercial laboratory (Health Science Research Institute, Yokohama, Japan).

Statistical Analysis

Data were analyzed using SPSS software (Ver.11.0.1J; SPSS Japan Inc., Tokyo, Japan). Pearson correlation coefficient was calculated to determine the relationship between physical function and blood nutritional data and HRV indices. Standardized multiple regression analysis of FIM and Barthel index was performed with age, sex, and the disease necessitating rehabilitation as covariates. One-way analysis of variance was used for the effect of 2 months of rehabilitation on each HRV index. Age, sex, BMI, the disease necessitating rehabilitation, FIM before undergoing rehabilitation (pre-FIM), blood nutritional data, and HRV indices, including heart rate, SDANN, LF, HF, and LF/HF were used as covariates in stepwise regression analysis to determine independent predictors of increment of FIM after 2 months of rehabilitation (ΔFIM). For selected predictive factors, the standardized regression coefficient (β) was calculated by multiple regression analysis.

Results

We registered 61 elderly people who received rehabilitation, and assessed physical function and HRV from 24-hour Holter monitoring. The background data of this study are shown in Table 1.

The underlying diseases necessitating rehabilitation were cerebrovascular disease (n = 37, 60.7%), disuse syndrome (n = 14, 23.0%), and fracture (n = 10, 16.3%). Mean age was 86 ± 5 years, blood nutritional data including total protein, albumin, total cholesterol,

Table 1
Characteristics of Elderly Individuals

Category	Measurement Items	Results
Background data	Number	61
	Age	86 ± 6 (75–100)
	Sex, male (%)	20 (32.8)
	BMI, kg/m^2	19.7 ± 3.2
Type of disease, n (%)	Cerebrovascular disease	37 (60.7)
	Disuse syndrome	14 (23.0)
	Fracture	10 (16.3)
Blood nutritional data	Total protein, g/dL	6.4 ± 0.7
	Albumin, g/dL	3.4 ± 0.5
	Hemoglobin, g/dL	12.1 ± 1.7
	Total cholesterol, mg/dL	177 ± 44
Physical function	FIM	46.8 ± 25.4
	Barthel index	32.8 ± 31.7
HRV indices	Heart rate (beats per minute)	74.8 ± 12.8
	SDANN, ms	85.7 ± 35.5
	LF, ms^2	35.8 ± 27.5
	HF, ms^2	63.8 ± 57.8
	LF/HF	0.70 ± 0.26

Values are mean ± SD.