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Research Article

Increased Parasympathetic Activity as a Fall Risk Factor Beyond Conventional Factors in Institutionalized Older Adults with Mild Cognitive Impairment

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SUMMARY

Purpose: This study aimed to investigate autonomic nervous function during the orthostatic challenge and its relationship with depression and fall, and to elucidate fall-associated factors, including autonomic function, executive function, and depression among institutionalized older adults with mild cognitive impairment (MCI).

Methods: The study is a cross-sectional descriptive study. Fall experiences in the current institutions were researched. Heart rate variability (HRV) during the orthostatic challenge was measured. Executive function was evaluated using the semantic verbal fluency test and clock drawing test. Depression was assessed using the Geriatric Depression Scale.

Results: Of the 115 older adults, 17 (14.8%) experienced falls in the current institution. None of the HRV indices during the orthostatic challenge showed any significant changes except for the standard deviation of normal RR intervals ($p = .037$) in the institutionalized older adults with MCI. None of the HRV indices was significantly related to the depressive symptoms. Multivariate logistic regression analysis showed that normalized high frequency on lying was independently associated with falls (OR = 1.027, $p = .049$) after adjusting for other conventional fall risk factors although executive function and depressive symptoms were not significant factors for fall.

Conclusion: Institutionalized older adults with MCI were vulnerable to autonomic nervous modulation, especially to sympathetic modulation, during the orthostatic challenge, which was not associated with depressive symptoms. As increased resting parasympathetic activity seemed to play a key role in association with falls, autonomic nervous function assessment should be considered for fall risk evaluation.

Introduction

Falls are one of the major adverse events that lead to negative consequences such as unintentional injuries and death in older adults [1]. Although nurses are making tremendous efforts to prevent falls among institutionalized older adults, 50.2% of institutionalized older adults still suffered from fall for a year, with average 1.3 fall per 1.57 persons [2,3]. As institutionalized older adults are deconditioned with multiple chronic diseases and on various medications, special attention is needed to consider their physiological state for fall risk factors. However, there is a lack of literature considering the underlying physiological conditions in institutionalized older adults.

Mild cognitive impairment (MCI) is a clinical entity characterized by slight cognitive impairment without functional dependence [4], which is associated with 1.53 times higher odds of fall-related injury [5]. Further, older adults with MCI have reported reduced executive function [6]. Executive function—a cognitive subdomain—is an important mediating factor between visual acuity and postural stability, especially in cognitively impaired older adults [7], and is an important factor for daily life activities [8]. Recent studies have shown that executive function is a key cognitive domain involved in gait or postural control [9,10] and is closely related to falls in community-dwelling older adults [11]. As institutionalized older adults with MCI are more likely to have pronounced executive dysfunction, it is necessary to investigate their executive function as a risk factor for falls in institutionalized older adults.

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In addition to cognition, autonomic dysfunction can be considered a risk factor for falls in older adults. With increasing age, the overall ability of cardiac autonomic modulation declines constantly [12]; consequently, blood pressure regulation reduces [13], which, in turn, causes hypotensive episodes and falls [14]. A previous study also reported that autonomic dysfunction is common in patients with MCI [15]. Moreover, as institutionalized older adults with MCI have several chronic diseases and take various medications, including antihypertensives and antidepressants, they may be subject to the exaggerated risk of orthostatic intolerance and fall. Thus, their autonomic nervous function during orthostatic challenge should be assessed and evaluated in association with falls.

Depression has also been suggested as a risk factor for falls in community-dwelling older adults although there are some controversies in institutionalized adults. In a meta-analysis, the authors demonstrated that depressive symptoms were significant predictors of falls [16], whereas Susilowati et al. [17] found no significant relationship between depressive symptoms and falls among institutionalized older adults. Furthermore, considering a recent meta-analysis showing that heart rate variability (HRV) was found to be reduced among depressed older adults [18], HRV may mediate between depressive symptoms and falls. Therefore, it is necessary to examine depressive symptoms and HRV in relation to falls in institutionalized older adults.

This study aimed to investigate the autonomic nervous function during the orthostatic challenge and to explore the involvement of depressive symptoms in autonomic nervous function. This study also aimed to elucidate the associations between autonomic nervous function, cognitive function, including the executive function domain, and depressive symptoms with fall among institutionalized older adults with MCI.

Methods

Study design and participants

This descriptive and cross-sectional study investigated autonomic nervous function during the orthostatic challenge using HRV to explore the involvement of autonomic nervous function in depressive symptoms and analyzed associations of autonomic nervous function, cognitive function, and depressive symptoms with falls. The conceptual models of the study were illustrated in the Figure 1.

A convenience sample of 115 institutionalized older adults aged ≥65 years was recruited from four regional geriatric hospitals in South Korea from July 2017 to February 2020. Older adults with the following characteristics were included: those who complained of decreased memory in answering the question, “Do you feel like your memory is becoming worse?” [19]; who did not have dementia with scores greater than 1.5SD below the mean on the Mini Mental Status Examination for Dementia Screening (MMSE-DS) score regarding age, gender, and education as suggested by a previous study [20]; who could communicate and walk around by themselves or with little assistance from one caregiver; who had been institutionalized for more than 1 week. Older adults with current arrhythmias on the EKG were excluded. The participant selection process was illustrated in the Figure 2.

Based on Long's suggestion for regression model with binary outcomes of at least 10 cases per estimated parameter [21], the minimum number of participants required for the study was 90, with expectation of nine predictors included in the regression model.

Study measures

General characteristics such as years of education, marital status, subjective financial status, smoking, and drinking were obtained via interviews. Clinical information, including age, gender, admission date, and diagnosed disease information, was acquired from medical records.

Fall and fall risk

A fall was defined as an event that resulted in a person coming to rest inadvertently on the ground, floor, or any other such lower level with or without injury [22]. Fall experience in the current institution was assessed with the question, “Have you fallen in the current institution?” Fall situations when the fall occurred in current institutions were also asked. Fall experience and fall situations in the current institutions were verified by caregivers at patients' bedsides to ensure the reliability of patient responses. Further, fall risk was assessed using the Bobath Memorial Hospital Fall Risk Assessment Scale Short Form (BMFRAS-SF) [23]. It has four items: past fall history, level of physical activity, number of fall risk factors, and number of fall risk increasing medications. Each item has a 4-point scale ranging from 0 to 3, with a total score of 12. Individuals with a score greater than 5 are considered to have a high fall risk [23]. It has been shown to have a good sensitivity of 86.7% and a specificity of 67.9% [23].

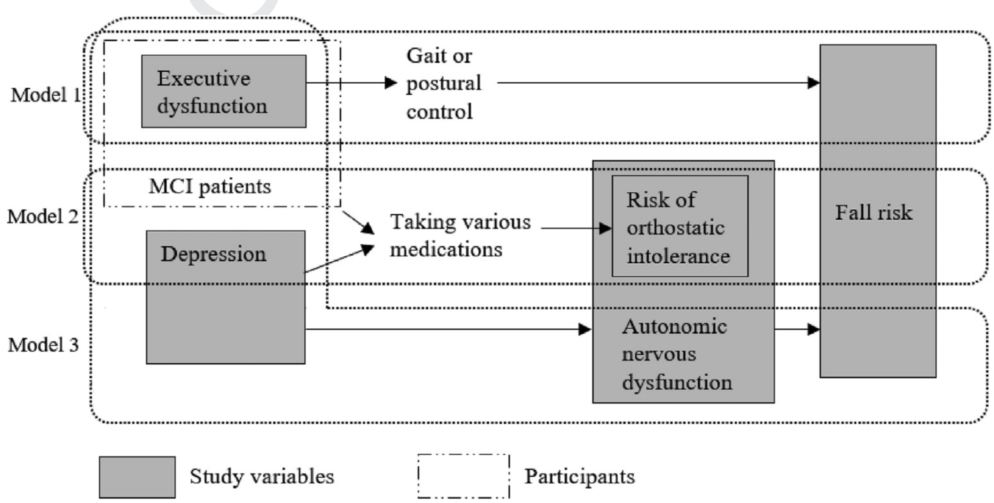

Figure 1. Conceptual model of the study.

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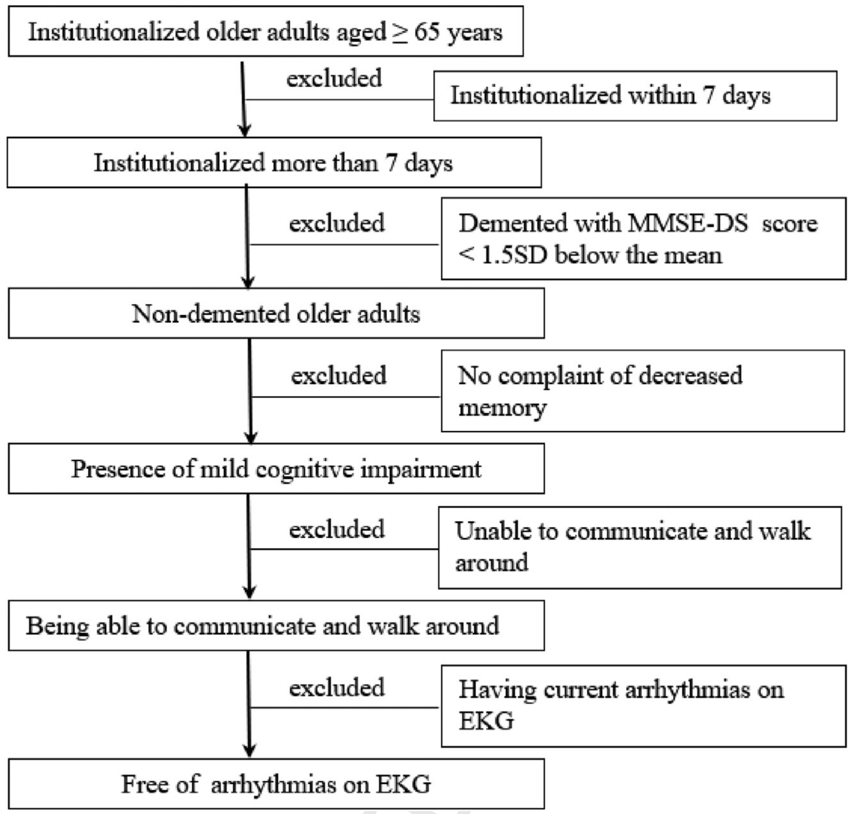

Figure 2. Process of participant selection.

Heart rate variability

For autonomic nervous system function, HRV was measured using Heart Rhythm Scanner 3.0 (Biocom Technologies, Poulsbo, USA) [24] in the participants' room. HRV was measured between 9 a.m. and 11 a.m. to minimize bias from HRV diurnal variation. Caffeine, nicotine, and alcohol intake were restricted from 12 h before the measurement to evaluate HRV accurately. Further, three-channel electrocardiogram electrodes were attached to the inner part of both wrists to measure HRV. It was measured for 5 min in the participant's lying position after 5 min of rest, and for another 5 min in their sitting position after 5 min of resting, as 5 min are believed necessary for adjustment to the posture [25].

The software Heart Rhythm Scanner 5.4.1. version (Biocom Technologies, Poulsbo, USA) was used, developed according to standards and mathematical procedures set forth by the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. HRV was analyzed both in the time domain—the standard deviation of the normal RR intervals (SDNN), root mean square of the differences between adjacent RR intervals (RMSSD)—and the frequency domain—normalized high frequency (nHF), normalized low frequency (nLF), and LF/HF ratio—on each of the two measurements. SDNN is the index of the heart's response to changing workloads and was measured in milliseconds, with higher SDNN indicating better cardiac response to changing workloads [26]. RMSSD is the primary time-domain measure used to estimate vagally mediated changes reflected in HRV, with higher RMSSD indicating greater activity of parasympathetic nervous system [27]. nLF indicates the contribution of the low frequency in the total power, excluding the contribution of very low frequency (VLF), and reflects sympathetic activity dominantly. nHF indicates the contribution of the high frequency in the total power, excluding the contribution of VLF, and is mediated almost entirely by parasympathetic nerve activity. The LF/HF ratio verifies the balance between sympathetic and parasympathetic nervous activities.

Orthostatic hypotension (OH)

OH was defined as a decrease in systolic blood pressure (SBP) of at least 20 mmHg or a decrease in diastolic blood pressure (DBP) of at least 10 mmHg within 3 min of standing from a supine position [25]. To evaluate OH, brachial BP was measured using an electronic sphygmomanometer (HEM-907, Omron, Kyoto, Japan). After the participants rested for 5 min in the lying position, brachial BP was measured. Subsequently, the participants sat on the bed, and brachial BP was measured within 3 min.

General cognitive function and executive function

The Mini Mental Status Examination for Dementia Screening (MMSE-DS) was used to evaluate overall cognitive function [20]. The MMSE-DS comprises 19 items, including tests of orientation, attention, memory, language, and visual-spatial skills. The total score was 30, with higher scores indicating better cognitive function.

Executive function, one of the cognitive domains, is defined as complex cognitive abilities that enable the identification of goals, mental planning, behavior organization, and planning actions to achieve these goals [28]. To evaluate executive function, the semantic verbal fluency (VF) test and clock drawing test (CDT) were used. VF reflects multiple dimensions of executive function of the frontal and temporal lobes, and starts to be damaged from the beginning of Alzheimer disease [29]. For the VF test, participants were asked to speak as many names as possible in an animal category for 1 min; subsequently, the number of correct animal names was counted with higher counts indicating better executive function [30]. The CDT evaluates cognitive abilities, including

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auditory and visual comprehension, concentration, visuospatial abilities, abstract conceptualization, and executive control [31]. For CDT, participants were asked to draw a clock on paper and mark a specific time on it. The Rouleau scoring system was used to calculate the CDT score [32]. The total score ranges from 0 to 10, with higher scores indicating better executive function.

Depressive symptoms

Depressive symptoms were evaluated using the 15-item Geriatric Depression Scale Short Form (GDS-SF) [33]. Each item has a binary response format (yes/no), with scores ranging from 0 to 15. A higher score indicates more severe depressive symptoms. Depression was considered present when the score was equal to or greater than 6. The Korean version of the GDS-SF has been shown to have good validity [34]. The Cronbach's alpha of the GDS-SF was .80 previously [35], and .82 in this study.

Procedures and ethical considerations

Q2 This study was approved by the institutional review board of X University (Approval No. 161XX8-1AR). To recruit participants, the researcher contacted the directors of four regional geriatric hospitals conveniently selected to receive approval for data collection. The directors extracted the names of older adults who met the inclusion criteria and provided the list to the researcher. The researcher then visited the patients to explain the study purpose and procedure and obtain written consent from each participant. The patients were given time to consider participation or discuss it with their family. When necessary, the researcher explained the study to their family via phone call or in person. The older adults who voluntarily decided to participate in the study were included in the study. Subsequently, a research assistant measured HRV and orthostatic BP, and assessed general information and depressive symptoms via one-on-one interviews for approximately 40 min. Clinical information, including diseases diagnosed and medication taken, was collected by reviewing participants' electronic medical records. Participants who completed all procedures were given a small gift as a reward.

Before visiting the participants, three research assistants were educated on data collection protocols over an hour in advance. In addition, they visited four participants together to observe data collection procedures in the beginning and coordinated the details of the protocols through discussion with the others to ensure reliability.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics 25 for Windows (IBM, Armonk, USA). All continuous variables were first assessed for normality using the Shapiro–Wilk test. In descriptive statistics, the mean with standard deviation and median with interquartile range were demonstrated for variables with normal distribution and those without it, respectively. The paired *t*-test and Wilcoxon signed-rank test were used to compare HRV indices during the orthostatic challenge. Because the changes in HRV indices during the orthostatic challenge did not show normal distribution, ranked ANCOVA was used to compare changes in HRV during the orthostatic challenge adjusted for antidepressant medication with presence of depression. For ranked ANCOVA, the residuals of ranked changes in HRV indices during orthostatic challenge adjusted for antidepressants use were calculated, which was analyzed depending on the presence of depression using ANOVA. For univariate analyses for association between study variables and fall experience in the current institutions, chi-square tests, *t*-test, and the Mann-Whitney U test were used. Multiple logistic regression was used to identify the influence of cognitive function, autonomic nervous function, and depression on falls, including age, sex, and other fall risk factors with p value < .10 in the univariate analysis to avoid deleting less significant factors that may have practical and clinical reasoning [36,37]. The level of statistical significance was set at $p < .05$. The Hosmer–Lemeshow goodness-of-fit statistic was used to check the model fit.

Results

One hundred and fifteen older adults participated in this study. The mean age of the participants was 78.0 years old (SD = 8.20), and 73 (63.5%) were female (Table 1). The median education years was 7 years with the interquartile range of 6, and 34 (29.5%) reported themselves in poor financial status. Most participants did not smoke or drink. The average duration of admission was 302.0 days. The most common disease diagnosed was hypertension (40.1%), followed by musculoskeletal diseases (24.5%) such as arthritis and osteoporosis.

Among the 115 participants, 17 (14.8%) had experienced falls in the current institutions (Table 1). Further, 49 (40.8%) were classified

Table 1 *Descriptive Statistics of Participants Characteristics and Study Variables (n = 115).*

Variables		*n* (%)
Age (years)	Mean (SD)	78.00 (8.20)
Gender	Men	42 (36.5)
	Women	73 (63.5)
Education years	Median (IQR)	7.00 (6.00)
Marital status	Married	45 (39.1)
	Widowed	65 (56.5)
	Single	3 (2.6)
	Divorced	2 (1.7)
Subjective financial status	Good	8 (7.0)
	Average	73 (63.5)
	Poor	34 (29.5)
Smoking	Never	80 (69.6)
	Previous smoker	34 (29.5)
	Current smoker	1 (0.9)
Drinking alcohol	Previous drinker	59 (51.3)
	Never	53 (46.1)
	Sometimes	3 (2.6)
Admission duration (days)	Mean (SD)	302.04 (146.83)
Underlying illness diagnosed[a]	Hypertension	77 (40.1)
	Musculoskeletal disease	47 (24.5)
	Stroke	34 (17.7)
	Cancer	16 (8.3)
	Kidney disease	9 (4.7)
	Parkinson disease	9 (4.7)
Fall experience in current hospitals	Yes	17 (14.8)
	No	98 (85.2)
Fall situation (n = 17)	Losing one's balance	5 (29.4)
	Losing one's footing	4 (23.5)
	Changing position	3 (17.6)
	Walking on stairs	3 (17.6)
	Others	2 (11.8)
Fall risk score	High risk	49 (40.8)
	Low risk	66 (57.4)
Previous fall for 1 year before admission	Yes	41 (35.7)
	No	74 (64.3)
MMSE-DS	median (IQR)	23.00 (8.75)
Verbal fluency	mean (SD)	8.51 (4.07)
Clock drawing test	median (IQR)	8.00 (5.00)
Depressive symptoms	median (IQR)	7.00 (3.00)
	Yes (≥6)	92 (80.0)
	No (<6)	23 (20.0)
Orthostatic hypotension	Yes	14 (12.2)
	No	101 (87.8)

Note. IQR = interquartile range; MMSE-DS = mini-mental status examination for dementia screening; SD = standard deviation.

[a] Multiple diagnoses allowed to secondary diagnosis.

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into the high fall risk group based on the BMFRAS-SF. While the median scores of the MMSE-DS and CDT were 23.0 and 8.0, respectively, the mean score of the VF test was 8.51. Moreover, 92 participants (80.0%) had depression, with a GDS≥6.

For HRV during the orthostatic challenge, SDNN significantly increased from 18.50 millisecond to 20.30 millisecond (p = .037) (Table 2). nHF decreased from 46.9% to 41.6%, while nLF increased from 54.5% to 58.9%, which was not significant. The other HRV indices showed no significant changes during the orthostatic challenge. None of the HRV indices was significantly related to the presence of depression (Table 2).

In univariate analyses, older adults with fall experience in current institutions were significantly younger than those without fall experience (p = .041) (Table 3). The MMSE-DS score (p = .008) and VF score (p = .036) were significantly higher in older adults with fall experience in current institutions than in those without it. However, the CDT score was lower in older adults with fall experience in current institutions although the difference was not significant. Among HRV indices, nHF on lying was significantly higher in older adults with fall experience in current institutions than in those without it (p = .047). There were no significant differences in high fall risk assessed on BMFRAS-SF, presence of OH, and presence of depression between older adults with fall experience in current institutions and those without it.

In the multivariate logistic regression analysis, age, sex, and factors with p values less than .10 were included. Only nHF on lying was independently associated with falls (OR = 1.03, p = .049) (Table 3). The Hosmer–Lemeshow goodness of fit was not significant (χ^2 = 9.019, p = .341), indicating adequate model fit.

Discussion

This study was conducted to investigate the autonomic nervous function during the orthostatic challenge using HRV measurement, explore the involvement of autonomic nervous function in depressive symptoms, and elucidate the association of cognitive function, including executive function, autonomic nervous function, and depressive symptoms, with falls.

In the study, surprisingly, older adults who experienced falls in current institutions were the ones with higher MMSE-DS scores, better VF, and younger age. This result contradicts the prior finding that cognitive impairment and older age have also been shown to be intrinsic risk factors for falls [38]. The first thing to be considered is that the participants have received general fall preventive care in current institutions; the healthcare personnel have already taken care of those with lower cognition and older age. Second, older adults with older age and lower cognitive functions may have refrained from walking around to have a lower chance of falling. Mendes da Costa et al. [39] pointed out that older adults with older age restricted their activity more than those with younger age owing to fear of falling. Lastly, older age and lower general cognitive ability may not increase risk of falls in institutionalized older adults with MCI. A recent meta-analysis study by Hopkins et al. [40] showed that fall-related factors were physical performances such as gait and dual-tasking ability, rather than age or general cognitive function, in older adults with MCI, consistent with the finding that the association of age and cognitive ability with falls disappeared in the multivariate analysis. Furthermore, they addressed that there were no effective fall intervention programs to reduce fall for MCI patients in previous studies. Therefore, another strategy focusing on physical performance training and cognitive training targeting for dual-task ability or working memory are needed for healthcare personnel to prevent further falls among institutionalized MCI older adults with relatively higher cognitive function and younger age.

All of the participants had significantly increased SDNN upon sitting, which is an appropriate transition to increased cardiac reactivity. However, the increase in nLF and decreased nHF during the orthostatic challenge did not reach a significant level, indicating attenuated sympathetic/parasympathetic modulation. This is consistent with a previous study [41], which addressed autonomic dysfunction in both sympathetic and parasympathetic modulation among community-dwelling older adults with MCI. Although sympathetic modulation is believed to play an important role in postural control [42] and maintained in some healthy older adults [43], notably, a smaller increase in nLF was prominent among the institutionalized older adults with MCI in the study. Thus, it seems that the institutionalized older adults with MCI were vulnerable to sympathetic modulation with a reduced capacity to accelerate cardiac function during the orthostatic challenge. Failing to redistribute autonomic balance during the orthostatic challenge has also given rise to diminished quality of life [44]. Therefore, more attention should be paid to autonomic dysfunction in institutionalized older adults with MCI.

When exploring HRV in relation to fall, however, it was nHF on lying that was significantly higher in older adults with fall experience in current institutions than in those without fall experience although its significant level was somewhat marginal. In addition, its influence outweighed that of cognitive function and others on fall experience in current institutions. This is somewhat different from the study of Razjouyan et al. [45] who suggested that nHF was low in patients with a high fall risk. This discrepancy may be due to

Table 2 *Changes of Heart Rate Variability During Orthostatic Challenge and its Relation With Depression.*

HRV during orthostatic challenge		median (IQR)	Z[a]	p	Residuals of changes in HRV during orthostatic challenge[c] mean (SD)	Depression		Z	p
						Yes (n = 92)	No (n = 23)		
SDNN (millisecond)	Lying	18.50 (19.10)	−2.09	.037	△ in SDNN	−1.82 (26.52)	7.30 (24.96)	1.616	.286
	Sitting	20.30 (23.95)							
RMSSD (millisecond)	Lying	12.60 (26.10)	−0.49	.628	△ in RMSSD	−0.32 (26.77)	1.29 (28.51)	0.034	.855
	Sitting	12.70 (24.90)							
nHF (%), mean (SD)	Lying	46.9 (23.83)	1.99[b]	.050	△ in nHF	0.96 (26.77)	−3.77 (26.48)	0.762	.386
	Sitting	41.6 (22.97)							
nLF (%), mean (SD)	Lying	54.5 (23.76)	−1.59[b]	.114	△ in nLF	1.53 (26.65)	−5.98 (26.34)	0.301	.586
	Sitting	58.9 (22.65)							
LF/HF (a.u)	Lying	1.20 (2.10)	−0.66	.510	△ in LF/HF	2.36 (25.83)	−9.44 (34.58)	1.742	.192
	Sitting	1.40 (2.60)							

Note. HRV = heart rate variability; IQR = interquartile range; nHF = normalized high frequency; nLF = normalized low frequency; RMSSD = root mean square of the successive differences; SD = standard deviation; SDNN = standard deviation of normal RR intervals.
[a] Wilcoxon signed rank test.
[b] *t*-test.
[c] Adjusted for taking antidepressants.

Table 3 *Associated Factors of Fall Experience in Current Hospitals (n = 115).*

Variables		Univariate analysis				Multivariate analysis		
		Fall experience in current hospitals, *n* (%)		Mann-Whitney's U or χ^2	*p*	Fall experience in current hospitals, Yes		
		Yes (*n* = 17)	No (*n* = 98)			Exp(B)	CI	*p*
Age, mean (SD)		74.29 (7.16)	78.62 (8.23)	2.04[a]	.044	0.98	0.896–1.080	.735
Gender	Men	6 (35.3)	36 (36.7)	0.01	.915	–	–	–
	Women	11 (64.7)	62 (63.3)			1.29	0.324–5.091	.721
Education years, median (IQR)		9.00 (6.00)	9.00 (6.00)	812.00	.765	–	–	–
Admission duration		792.50 (1180.75)	311.00 (896.00)	22.00	.282	–	–	–
Previous fall before admission	Yes	8 (47.1)	33 (33.3)	1.20	.274	–	–	–
	No	9 (52.9)	65 (66.7)			–	–	–
Fall risk	High risk	13 (76.5)	52 (53.1)	3.23	.060[b]	5.23	0.992–27.542	.051
	Low risk	4 (23.5)	46 (46.9)			–	–	–
MMSE-DS, median (IQR)		26.50 (4.75)	22.00 (15.00)	504.00	.008	1.10	0.919–1.321	.293
Verbal fluency, mean (SD)		10.41 (4.00)	8.19 (4.01)	−2.12[a]	.036	1.04	0.816–1.329	.744
Clock drawing test, median (IQR)		7.50 (4.00)	8.00 (9.00)	624.00	.424	–	–	–
Depressive symptoms	Yes	13 (76.5)	79 (80.2)	0.13	.748	–	–	–
	No	4 (23.5)	19 (19.8)			–	–	–
Orthostatic hypotension	Yes	1 (5.9)	13 (13.1)	0.72	.689[b]	–	–	–
	No	16 (94.1)	85 (86.9)			–	–	–
Heart rate variability								
SDNN (millisecond) median (IQR)	Lying	18.00 (27.40)	20.30 (19.00)	609.50	.956	–	–	–
	Sitting	21.60 (34.03)	20.70 (25.05)	548.50	.552	–	–	–
RMSSD (millisecond) median (IQR)	Lying	12.00 (34.90)	12.60 (23.30)	597.50	.861	–	–	–
	Sitting	13.90 (38.48)	12.80 (20.55)	450.00	.112	–	–	–
nHF (%), mean (SD)	Lying	58.69 (22.07)	44.92 (23.89)	−2.01[a]	.047	1.03	1.000–1.055	.049
	Sitting	39.96 (25.35)	41.82 (22.37)	0.29[a]	.774	–	–	–
nLF (%), mean (SD)	Lying	48.31 (24.92)	55.67 (23.76)	1.09[a]	.277	–	–	–
	Sitting	60.03 (25.37)	58.77 (22.14)	−0.20[a]	.843	–	–	–
LF/HF (a.u), median (IQR)	Lying	1.00 (2.20)	1.30 (2.10)	552.00	.529	–	–	–
	Sitting	1.15 (2.20)	1.80 (2.80)	553.50	.586	–	–	–
Constant		–	–	–	–	0.00		.208

Note. IQR: interquartile range; MMSE-DS: mini-mental status examination for dementia screening; nHF: normalized high frequency; nLF: normalized low frequency; RMSSD: root mean square of the successive differences; SD: standard deviation; SDNN: standard deviation of normal RR intervals.
[a] *t*-test.
[b] Fisher's exact test.

the fact that most participants in the previous study were adults and young older adults. As parasympathetic modulation appeared to be maintained during the aging process, whereas other HRV indices were reduced [46], parasympathetic modulation in older adults might be preserved more than sympathetic modulation, which contributes to fall occurrence. Indeed, LF/HF in the prior study was approximately 3.8, which is much greater than 1.3 in the study. Moreover, institutionalized older adults may be on medications that reinforce parasympathetic activity and weaken sympathetic activity, such as antidepressants and various antihypertensives. Thus, increased parasympathetic activity during lying likely plays a key role in the occurrence of falls in institutionalized older adults. On the other hand, there was no significant difference in the presence of OH between older adults with fall experience in current institutions and those without it. There have been controversies regarding OH as a significant risk factor for falls [47]. A recent meta-analysis reported that OH was associated with time to fall incidence, not with fall occurrence itself [48], in line with the findings of the study. Considered together, autonomic nervous function assessment based on HRV is likely more sensitive than OH assessment for evaluating fall risk in institutionalized older adults with MCI.

In the study, depressive symptoms were not associated with falls. This is contrary to a prior result that depression increased the risk of falls in community-dwelling older adults [49]. This may be because of the severity of the depressive symptoms. The participants in the prior study were relatively low depressed, with a prevalence of depression of only 10% and free-living in community settings. However, in the study, 86.4% of older adults were depressed, with a GDS >5. Further, Kamińska, Brodowski, and Karakiewicz [50] suggested there was no difference in depressive symptoms between fallers and nonfallers, but depressive symptoms were involved in the number of falls. Therefore, depressive symptoms seem to have little relevance to fall occurrence in institutionalized older adults with severe depression.

In addition, depressive symptoms were not related to changes of HRV during orthostatic challenge in the study, whereas Luo et al. [51] addressed reduced HRV function in older adults with depression. This difference might come from the type of antidepressant medications that were taken by some depressive older adults. Some of prior studies addressed antidepressant agents from different classes may differentially impact HRV, addressing tricyclic antidepressants decrease HRV and selective serotonin reuptake inhibitors do not or do so to a lesser extent [52,53]. In the study, taking antidepressants was adjusted but type of antidepressants was not, which may lead to the inconsistency. Because the involvement of antidepressants in HRV alterations in depressive patients is still somewhat debatable, further research is needed to investigate the different effect of antidepressants on HRV in older adults with depression.

This study has certain limitations. First, fall occurrence was retrospectively investigated in a small number of older adults who experienced falls. Prospective research with larger sample sizes is needed to follow up fall occurrence to identify contributing factors to falls in the future. Second, the measurement of HRV was as short as 5 min and performed only once. However, as HRV measurement for 5 min was reported to be stable compared to that for 24 h [54] and performed in a relatively consistent time frame, it would be worthy of being accepted. Third, the effects of medications could not be controlled for HRV although those were controlled for falls. Further research is needed to determine the types of antidepressants, antihypertensives, and other cardiac medications that affect autonomic nervous activity. Finally, we cannot help pointing out missing variable bias because only seven predictors were included in the final logistic regression model, which may lead to no predictor except for the one marginally significant factor, nHF on lying.

Conclusion

In the study, fall experience in current institutions was significantly associated with younger age and better cognitive function. Therefore, another strategy is needed for healthcare personnel to prevent further falls among MCI older adults with younger age and higher general cognitive function. Further, institutionalized older adults with MCI had attenuated sympathetic/parasympathetic modulation, and higher nHF on lying was independently associated with fall experience in current institutions. Thus, parasympathetic function based on HRV assessment should be considered as a significant factor for evaluating fall risk. Depression was not significantly associated with HRV or falls. In the future, studies with prospective fall follow-up in a large population considering medications, and their effects on a relationship between depression and HRV are needed.

Conflict of interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.anr.2023.05.001.

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