The official journal of the Japan Atherosclerosis Society and
the Asian Pacific Society of Atherosclerosis and Vascular Diseases

Original Article

J Atheroscler Thromb, 2021; 28: 865-872. http://doi.org/10.5551/jat.58354

Effects of Active Learning Education on Arterial Stiffness of Older Adults with Low Health Literacy: A Randomized Controlled Trial

Kazuki Uemura[1], Minoru Yamada[2], Masafumi Kuzuya[3, 4] and Hiroshi Okamoto[1]

[1] Center for Liberal Arts and Sciences, Faculty of Engineering, Toyama Prefectural University, Imizu, Japan.
[2] Graduate School of Comprehensive Human Sciences, University of Tsukuba, Tokyo, Japan.
[3] Institutes of Innovation for Future Society, Nagoya University, Nagoya, Japan.
[4] Department of Community Healthcare and Geriatrics, Nagoya University Graduate School of Medicine, Nagoya, Japan.

Aim: We examined the effects of active learning education on arterial stiffness and physical activity of community-dwelling older adults with low health literacy.

Methods: This study is a secondary analysis of randomized controlled trial of 60 participants aged 65 and older with low health literacy. The intervention group (n=30) participated in a weekly 90-minute active learning program session for 24 weeks, which addressed health promotion in older age. The control group (n=30) attended a 90-minute health education class in a didactic manner. The outcomes were measured at baseline and in week 24. The degree of arterial stiffness was assessed based on the cardio-ankle vascular index (CAVI) using the VS-1500 device (Fukuda Denshi Co., Ltd., Tokyo, Japan). The shortened version of the self-reported International Physical Activity Questionnaire was used to assess the amount of total physical activity determined by the metabolic equivalent hours per week. We used analysis by intention-to-treat, with multiple imputation for missing data.

Results: Seven participants (11.7%) dropped out prior to the post-intervention assessment. The multiple imputation analysis revealed that the intervention group showed significant improvement in CAVI [between-groups difference (95% confidence interval)=-0.78 (-1.25 to -0.31), Cohen's d=0.82] and physical activity [32.5 (0.3 to 64.7), Cohen's d=0.57] as compared with the control group. The sensitivity analysis for the complete cases showed similar results.

Conclusion: Active learning health education may be effective in improving arterial stiffness and physical activity in older adults with low health literacy.

Key words: Physical activity, Cardiovascular, Preventative health care, Rehabilitation, Behavioral change

Introduction

Arterial stiffness is a major determinant of increased cardiovascular risk[1)]. Pulse wave velocity (PWV) is considered the gold standard for a non-invasive measurement of arterial stiffness, but it has several limitations, including its sensitivity to the blood pressure level and the bias of distance determination[2)]. Recently, the new cardio-ankle vascular index (CAVI) has been used by many research and clinical investigation centres to estimate arterial stiffness independently from blood pressure at the time of measurement[3)]. Several studies have shown CAVI to be a valuable prognostic tool to predict cardiovascular events in different populations[4-7)]. However, there is limited evidence to support the effects of therapeutic intervention on CAVI[2)].

Health literacy is the ability to obtain, understand, appraise, and apply health information[8)]. Low health literacy has been associated with greater healthcare services use[9)], poorer self-management of chronic diseases (e.g. diabetes)[10)], unhealthy lifestyles (e.g. physical inactivity)[11)], a higher mortality rate[12)], and a higher risk of arterial stiffness (CAVI ≥ 9.0) among community-dwelling older adults[13)]. These findings suggest that older adults with low health literacy could

Address for correspondence: Kazuki Uemura, Center for Liberal Arts and Sciences, Faculty of Engineering, Toyama Prefectural University, 5180 Kurokawa, Imizu 939-0398, Japan; E-mail: kuemura@pu-toyama.ac.jp

Received: June 11, 2020 Accepted for publication: September 10, 2020

be at a higher risk of arterial stiffness and related cardiovascular events.

A randomized controlled trial (RCT) demonstrated that active learning education can effectively enhance one's physical activity, dietary habits, and physical function by improving one's health literacy[14]. We focused on active learning education, involving learners in higher-order thinking (e.g., evaluation, synthesis) and participation in activities (e.g., discussion, presentation, planning) rather than passive listening[15], as an efficient alternative to training-based intervention. If active learning strategies can promote health literacy and physical activity, then it may also improve arterial stiffness. Therefore, in this study, we hypothesised that active learning education is associated with improvements in arterial stiffness. To test this hypothesis, we examined the effects of active learning education on CAVI and physical activity of community-dwelling older adults with low health literacy.

Methods

Study Design

This study is a secondary analysis of a single-blinded RCT, registered with the University Hospital Medical Information Network (UMIN) clinical trials registry (UMIN000023725). Participants were randomly allocated to the intervention group underwent 24- week active learning education (n=30), and the control group attended a didactic health education class (n=30). This study is different from the previous study in terms of the measures analysed. The previous study focused on the improvement of health literacy as primary outcome[16], whereas the present study used arterial stiffness and self-reported physical activity as outcome measures. The local ethics committee (Toyama Prefectural University, approval no. H28-11) approved the study protocol. Outcome assessors were blinded to the group assignment.

Participants

Eligible participants included older adults who obtained a maximum score of 33 out of 50, an indicative of low health literacy, on the shortened version of the European Health Literacy Survey Questionnaire[17]. Individuals meeting the following criteria were excluded: (a) with disability that can affect the execution of basic and instrumental activities of daily living; (b) diagnosed with dementia; (c) with severe cardiac, pulmonary, or musculoskeletal diseases that can limit physical activity; or (d) participating in other research studies. Participants provided signed informed consent before participating in this study, in accordance with the Declaration of Helsinki in 1975.

Intervention

Intervention participants underwent a weekly 90-minute active learning program for 24 weeks. The themes of the program focused on the role of exercise, diet/nutrition, and cognitive activity in health promotion among older adults[14]. This program aimed to promote behavior changes in daily life and self-management in accordance with an individual's health status. Therefore, this weekly class was regarded as an opportunity that older adults can use to learn about and plan strategies to lead a healthy lifestyle. Participants were given a homework for each topic, in which they were instructed to search the assigned topic through books, on the internet, or using any other media. In the subsequent class, participants raised and discussed ideas. An overview of the group work results was provided to the entire class. Using their shared ideas and knowledge, participants planned a behavioral change and implemented healthy behaviors in daily life based on such plans. Additionally, the extent to which the participants were leading a healthy lifestyle was regularly reviewed as a part of the group work. Group work was conducted with small groups of 4 to 5 participants. They self-monitored their physical activity using an accelerometer, then recorded the data on a notebook.

For 24 weeks, control participants attended a 90-minute health education class, which was taught using the didactic teaching method. Although the themes of the program were similar to those in the intervention group, active learning strategies were not used. Control participants received brochures about leading a healthy lifestyle in older adulthood, which delineated the importance of physical activity (e.g. walking, strength training), a balanced diet, and appropriate medical consultation.

Measurements

Arterial Stiffness Measurement

CAVI was determined using a VS-1500 vascular screening system (Fukuda Denshi Co., Ltd., Tokyo, Japan). CAVI is an indicator of arteriosclerosis that reflects vascular stiffness, which is measured by the pulse wave velocity between the heart and the ankle; the Bramwell-Hill equation is used, based on the stiffness parameter β theory[18]. The electrocardiogram, phonocardiogram, and pressures and waveforms of brachial and ankle arteries were measured in the supine position. CAVI was calculated automatically for right and left side and its mean values on both sides were used in the analysis. As peripheral artery disease can affect the accuracy of CAVI, we also ensured and confirmed that none of the participants had this disease, as evidenced by their ankle-brachial indices (ABI) of less than 0.9.

Physical Activity

The shortened version of the self-reported International Physical Activity Questionnaire (IPAQ)[19] was used to assess physical activity. Participants were asked about the frequency (days/week) and duration (minutes/day) of their physical activities in three levels (walking, moderate- and vigorous-intensity activities). Moderate-intensity activities were defined as those that cause a person to breathe somewhat more heavily than normal, and vigorous activities were defined as those that cause a person to breathe more heavily than normal. They were weighted by their energy requirements as metabolic equivalents (MET), with one MET equating to around one kcal/kg/hour, which approximately corresponds to sitting quietly (3.3 for walking, 4.0 for moderate physical activity, and 8.0 for vigorous physical activity). Therefore, the IPAQ scores were a combined measure of the amount and intensity of physical activity (computed by multiplying the MET score by hours performed within a week) in terms of MET-hour per week (MET-h/week)[20]. Total physical activity, as an outcome measure, was calculated by the sum of the three levels of activity.

Demographic and Clinical Characteristics

Participants' age, sex, educational level, living circumstance, and body mass index were recorded. Their medical conditions (e.g. presence of chronic diseases, the total number of prescribed medications, and smoking status) were assessed. We used the Mini-Mental State Examination (MMSE)[21] and Timed Up & Go Test (TUG)[22] to assess global cognitive function and physical performance. Frailty status was determined according to Fried criteria[23].

Statistical Analysis

The normality of the measured variables was assessed using visual inspection of the data frequency distribution and the Shapiro-Wilk test. Continuous variables are presented as mean ± SD and were compared between the intervention and control groups using independent sample *t* tests. Non-normally distributed data are presented as median (IQR) and were compared using the Mann-Whitney test. Categorical variables are expressed as *n* (%) and were compared using chi-square tests. We compared changes in CAVI and physical activity at 24 weeks from the baseline by group, using independent samples *t* tests. Following the intention-to-treat approach, multiple imputation for missing data on the study outcomes was conducted (based on 20 replications), assuming missing at random. We performed a complete case analysis on participants who underwent post-intervention assessment to test sensitivity. All analyses were conducted using SPSS version 25 (IBM Corp., Chicago). Cohen's *d* values were calculated as measures of effect size.

Results

Fig. 1 presents the trial profile. Thirty participants were allocated to each of the intervention (age= 74.0 ± 4.9; sex = 33.3% male) and control (age= 73.9 ± 4.4; sex = 33.3% male) group. **Table 1** shows baseline demographic characteristics and health-related variables. Seven participants (11.7%) dropped out prior to the post-intervention assessment (intervention group: 2 had medical problems and 2 refused to continue; control group: 1 had medical problems and 2 refused to continue). The median attendance rate in the weekly class of the active learning program was 91.7% (IQR = 87.5–96.9). During the study period, 3 adverse events (i.e., 2 hospitalizations in the intervention group and 1 hip fracture in the control group) were reported, but none of them were attributable to participation in the intervention program.

The primary imputed analysis showed a significantly greater improvement in CAVI [between-groups difference (95% confidence interval) = -0.78 (-1.25 to -0.31), *d* = 0.82] and total physical activity [32.5 (0.3 to 64.7), *d* = 0.57] in intervention group than in control group **(Table 2)**. Results of the complete case analysis showed a significantly greater improvement in CAVI [-0.70 (-1.19 to -0.21), *d* = 0.83] and total physical activity [34.6 (1.2 to 67.9), *d* = 0.51] in intervention group than in control group, which did not differ qualitatively from those in the intention-to-treat dataset.

Discussion

Findings of the RCT showed that a 24-week active learning education improves CAVI and self-reported physical activity among older adults with low health literacy. Some pharmacological (i.e. lipid-lowering and anti-diabetic drugs) and non-pharmacological (i.e. smoking cessation and weight reduction) treatments have been reported to be associated with an improvement in CAVI of patient population[2, 24-26]. This RCT is the first to demonstrate the effectiveness of educational intervention on improving CAVI of older adults with low health literacy. The low attrition rate (≤ 15%)[27] and low risk of adverse events for active

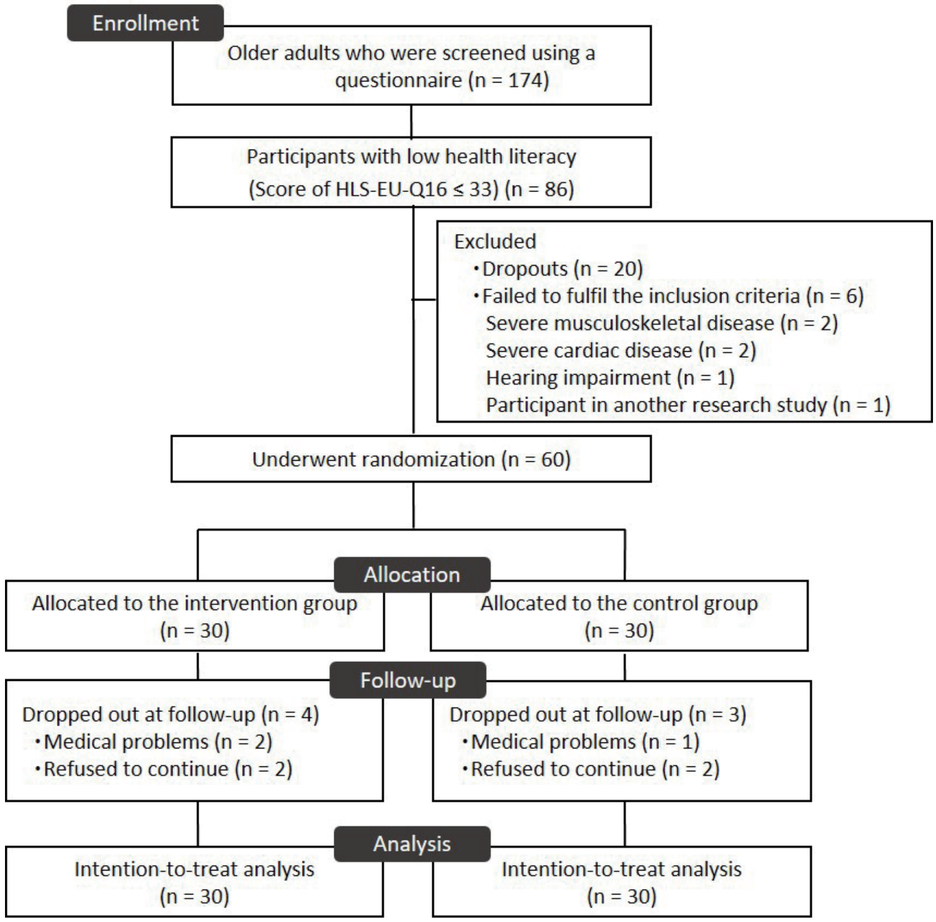

Fig. 1. Study flow diagram

Abbreviations: HLS-EU-Q16 = the 16-item European Health Literacy Survey Questionnaire.

learning education support the applicability to older individuals with low health literacy.

We suppose that increased physical activity mainly contributed to the decrease in CAVI. A longitudinal study showed that adopting a physically active lifestyle is associated with a lower risk of arterial stiffness in older adults[28]. Another study reported that healthy older adults, who underwent an exercise program, including Tai Chi sessions thrice a week, experienced a significant improvement in CAVI after six months of intervention; however, the effects were not maintained after decreasing the frequency to twice a week[29]. Our active learning education aimed to promote not only exercise in the class but also physical activity in daily life, which may contribute to sustainable behavioral changes and improvements in CAVI. Prolonged effects on physical activity improvement were found at 24-week follow-up assessments after intervention cessation[30].

Our active learning program provided the participants the opportunity for improving their abilities of self-management through learning process, including exploration of health promotion, sharing information with other group members, and application for preventive health-care in daily life. The collaborative learning style, which is one of the key elements of active learning[15], may have also enhanced social interaction and boosted the individuals' motivation to increase regular physical activities even among participants with low health literacy, who are less likely to engage in physical activity[11].

Compared with training-based intervention, active learning education has advantages, including its effectiveness, habituation of physical activity in daily life, and affordability. Active learning education does not need any of the training machines (i.e., bench step, treadmill, and cycle ergometer) and vigorous-intensity exercises (>60% heart rate reserve) that were used in the training programs in previous studies that aimed to decrease arterial stiffness in older adults[31-33]. A meta-analysis that included those studies reported that arterial stiffness measured by PWV was decreased

Table 1. Baseline demographic and study outcomes by group

Characteristic	Intervention group ($n = 30$)	Control group ($n = 30$)	p
Age, years	74.0 ± 4.9	73.9 ± 4.4	0.93[a]
Sex, male	10 (33.3)	10 (33.3)	1.00[b]
Education, years	12.0 (9.0–13.3)	12.0 (11.3–13.3)	0.61[c]
Living alone	6 (20.0)	5 (16.7)	0.74[b]
Body mass index, kg/m^2	22.7 ± 2.5	22.7 ± 3.6	0.97[a]
Mini-Mental State Examination, point (range 0–30)	28.5 (26.0–30.0)	28.0 (26.0–29.0)	0.63[c]
Smoking			0.19[b]
Current	2 (6.7)	0 (0)	
Former	7 (23.3)	4 (13.3)	
Never	21 (70.0)	26 (86.7)	
Frailty status			0.36[b]
Robust	14 (46.7)	15 (50.0)	
Pre-frailty	14 (46.7)	15 (50.0)	
Frailty	2 (6.6)	0 (0)	
Timed Up & Go test (kg)	7.2 (6.7–7.7)	7.2 (6.6–7.9)	0.95[c]
Chronic conditions: n (%)			
Hypertension	12 (40.0)	15 (50.0)	0.51[b]
Diabetes mellitus	3 (10.0)	2 (6.6)	1.00[b]
Hyperlipidemia	8 (26.7)	6 (20.0)	0.54[b]
Heart disease	3 (10.0)	4 (13.3)	1.00[b]
Osteoporosis	3 (10.0)	7 (23.3)	0.17[b]
Number of medications used	1.0 (0–3.0)	2.0 (1.0–3.0)	0.25[c]
Arterial stiffness			
CAVI	9.5 ± 1.1	9.1 ± 1.3	0.14[a]
Increased arterial stiffness (CAVI > 9.0)	21 (70.0)	19 (63.3)	0.58[b]
Physical activity			
Total physical activity (MET-h/week)	31.8 (7.6–73.5)	41.7 (14.7–80.9)	0.39[c]

Note. Values represent mean ± SD or median (IQR) or n (%).
Abbreviations: CAVI = cardio-ankle vascular index; MET = metabolic equivalent.
[a]Calculated using the independent samples t test.
[b]Calculated using the chi-square test.
[c]Calculated using the Mann-Whitney test.

Table 2. Within- and between-groups differences in outcome measures among older adults between baseline and week 24

	Changes between baseline and week 24				
	Intervention group	Control group	Between-group		
	Within-group differences (95 % CI)	Within-group differences (95 % CI)	Between-groups differences (95 % CI)	p	Effect size (Cohen's d)
Multiple imputation analysis					
CAVI*	-0.44 (-0.77 to -0.10)	0.34 (-0.003 to 0.69)	-0.78 (-1.25 to -0.31)	0.001	0.82
Total physical activity (MET-h/week)§	34.8 (11.9 to 57.7)	2.3 (-20.0 to 24.7)	32.5 (0.3 to 64.7)	0.048	0.57
Complete case analysis					
CAVI*	-0.42 (-0.76 to -0.08)	0.28 (-0.07 to 0.64)	-0.70 (-1.19 to -0.21)	0.006	0.83
Total physical activity (MET-h/week)§	34.8 (10.9 to 58.6)	0.2 (-23.2 to 23.6)	34.6 (1.2 to 67.9)	0.043	0.51

Notes. *A negative difference between the means of the two groups indicates that improvements are greater in the intervention group than in the control group.
§A positive difference between the means of the two groups indicates that improvements are greater in the intervention group than in the control group.
Abbreviations: CAVI = cardio-ankle vascular index; MET = metabolic equivalent.

in aerobic trained groups as compared with controls, and the standardized mean difference was 0.44 in the older age subgroup (mean age ≥ 52.5 y)[34]. According to the Cohen guidelines[35], this effect is considered small to medium. Meanwhile, our education program showed a large effect size (Cohen's $d=0.82$) without both special equipment and exercise prescription by professionals. It was much larger even when compared with the effects size of the exercise intervention study that used CAVI as the outcome (Cohen's $d=0.26$)[29]. Although our program is based on education and supposed to require lower physical burden than training-based intervention, the characteristics to promote self-reliant efforts in daily life other than the weekly classes may contribute to the larger effect sizes. According to the above-mentioned advantages, active learning education can be considered as the suitable intervention to improve arterial stiffness and physical activity in terms of both effectiveness and feasibility in the community.

CAVI has been used in clinical settings and recognized as a strong predictor of cardiovascular events[36]. Otsuka and colleagues[5] investigated changes in CAVI after management of atherosclerotic risk factors and whether these changes influenced the incidence of future cardiovascular events in patients with coronary artery disease (mean age 65 years). The results showed that the subjects with improvement in CAVI 6 months later had a lower risk of cardiovascular events during follow-up (2.9 years) than those without improvement. Taniguchi and colleagues[37] identified four trajectory patterns with advancing age for brachial-ankle PWV among community-dwelling older adults and demonstrated that individuals with very high PWV had a higher risk of all-cause mortality. Thus, it seems to be important for lowering the risk of the negative consequences to improve arterial stiffness, which progressively increases with aging, through therapeutic interventions, including the promotion of healthy lifestyles.

This study was limited by a small sample size and its failure to conduct follow-up assessments. A follow-up study must determine whether the beneficial effects of active learning education on arterial stiffness can be maintained beyond intervention cessation. Additionally, the mechanism of improvement in arterial stiffness has not been completely clarified. Not only expected mediating factors (e.g. healthy lifestyles), but also some unexpected confounding factors might affect the effects of active learning education.

Conclusion

We demonstrated the beneficial effects of active learning education on arterial stiffness, based on improvements in CAVI and the self-reported physical activity of older adults with low health literacy. According to its advantages, including the large effect size and affordability, active learning education in a community-based prevention program may favorably contribute to the improvements of arterial stiffness and physical activity.

Funding

This work was supported by the Grant-in-Aid for Young Scientists of the Japan Society for the Promotion of Science [18K17926].

Acknowledgements

We wish to thank the Imizu City office for assisting with participant recruitment.

Conflict of Interest

None.

References

1) Mattace-Raso FU, van der Cammen TJ, Hofman A, van Popele NM, Bos ML, Schalekamp MA, Asmar R, Reneman RS, Hoeks AP, Breteler MM and Witteman JC: Arterial stiffness and risk of coronary heart disease and stroke: the Rotterdam Study. Circulation, 2006; 113: 657-663
2) Asmar R: Principles and usefulness of the cardio-ankle vascular index (CAVI): a new global arterial stiffness index. European Heart Journal Supplements, 2017; 19: B4-B10
3) Shirai K: Further Role of Blood Pressure-Independent CAVI in Addition to a Predictor of Cardiovascular Events. J Atheroscler Thromb, 2020; 27: 639-640
4) Satoh-Asahara N, Kotani K, Yamakage H, Yamada T, Araki R, Okajima T, Adachi M, Oishi M, Shimatsu A, Japan O and Metabolic Syndrome Study G: Cardio-ankle vascular index predicts for the incidence of cardiovascular events in obese patients: a multicenter prospective cohort study (Japan Obesity and Metabolic Syndrome Study: JOMS). Atherosclerosis, 2015; 242: 461-468
5) Otsuka K, Fukuda S, Shimada K, Suzuki K, Nakanishi K, Yoshiyama M and Yoshikawa J: Serial assessment of arterial stiffness by cardio-ankle vascular index for prediction of future cardiovascular events in patients with coronary artery disease. Hypertens Res, 2014; 37: 1014-1020
6) Gohbara M, Iwahashi N, Sano Y, Akiyama E, Maejima N, Tsukahara K, Hibi K, Kosuge M, Ebina T, Umemura S and Kimura K: Clinical Impact of the Cardio-Ankle Vascular Index for Predicting Cardiovascular Events After Acute Coronary Syndrome. Circ J, 2016; 80: 1420-1426
7) Kirigaya J, Iwahashi N, Tahakashi H, Minamimoto Y, Gohbara M, Abe T, Akiyama E, Okada K, Matsuzawa Y,

Maejima N, Hibi K, Kosuge M, Ebina T, Tamura K and Kimura K: Impact of Cardio-Ankle Vascular Index on Long-Term Outcome in Patients with Acute Coronary Syndrome. J Atheroscler Thromb, 2020; 27: 657-668
8) Sorensen K, Van den Broucke S, Fullam J, Doyle G, Pelikan J, Slonska Z, Brand H and Consortium Health Literacy Project E: Health literacy and public health: a systematic review and integration of definitions and models. BMC public health, 2012; 12: 80
9) Vandenbosch J, Van den Broucke S, Vancorenland S, Avalosse H, Verniest R and Callens M: Health literacy and the use of healthcare services in Belgium. Journal of epidemiology and community health, 2016; 70: 1032-1038
10) Marciano L, Camerini AL and Schulz PJ: The Role of Health Literacy in Diabetes Knowledge, Self-Care, and Glycemic Control: a Meta-analysis. Journal of general internal medicine, 2019; 34: 1007-1017
11) Aaby A, Friis K, Christensen B, Rowlands G and Maindal HT: Health literacy is associated with health behaviour and self-reported health: A large population-based study in individuals with cardiovascular disease. Eur J Prev Cardiol, 2017; 24: 1880-1888
12) Berkman ND, Sheridan SL, Donahue KE, Halpern DJ and Crotty K: Low health literacy and health outcomes: an updated systematic review. Ann Intern Med, 2011; 155: 97-107
13) Uemura K, Yamada M, Kuzuya M and Okamoto H: [The association of limited health literacy and risk of arterial stiffness in community-dwelling older adults]. Nihon Ronen Igakkai Zasshi, 2018; 55: 605-611
14) Uemura K, Yamada M and Okamoto H: Effects of Active Learning on Health Literacy and Behavior in Older Adults: A Randomized Controlled Trial. J Am Geriatr Soc, 2018; 66: 1721-1729
15) Bonwell CC and Eison JA: Active Learning: Creating Excitement in the Classroom. ASHE-ERIC Higher Education Report No. 1, Washington, DC., 1991
16) Uemura K, Yamada M and Okamoto H: The effectiveness of an active learning program in promoting a healthy lifestyle among older adults with low health literacy: a randomized controlled trial. Gerontology, 2021; 67:25-35
17) Nakayama K, Osaka W, Togari T, Ishikawa H, Yonekura Y, Sekido A and Matsumoto M: Comprehensive health literacy in Japan is lower than in Europe: a validated Japanese-language assessment of health literacy. BMC public health, 2015; 15: 505
18) Kawasaki T, Sasayama S, Yagi S, Asakawa T and Hirai T: Non-invasive assessment of the age related changes in stiffness of major branches of the human arteries. Cardiovasc Res, 1987; 21: 678-687
19) Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF and Oja P: International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc, 2003; 35: 1381-1395
20) Moore SC, Gunter MJ, Daniel CR, Reddy KS, George PS, Yurgalevitch S, Devasenapathy N, Ramakrishnan L, Chatterjee N, Chanock SJ, Berndt SI, Mathew A, Prabhakaran D and Sinha R: Common genetic variants and central adiposity among Asian-Indians. Obesity (Silver Spring), 2012; 20: 1902-1908
21) Folstein MF, Folstein SE and McHugh PR: “Mini-mental state”. A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res, 1975; 12: 189-198
22) Podsiadlo D and Richardson S: The timed “Up & Go”: a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc, 1991; 39: 142-148
23) Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA and Cardiovascular Health Study Collaborative Research G: Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci, 2001; 56: M146-156
24) Ichihara A, Hayashi M, Koura Y, Tada Y, Kaneshiro Y and Saruta T: Long-term effects of statins on arterial pressure and stiffness of hypertensives. J Hum Hypertens, 2005; 19: 103-109
25) Nagayama D, Saiki A, Endo K, Yamaguchi T, Ban N, Kawana H, Ohira M, Oyama T, Miyashita Y and Shirai K: Improvement of cardio-ankle vascular index by glimepiride in type 2 diabetic patients. Int J Clin Pract, 2010; 64: 1796-1801
26) Hayashi K, Yamamoto T, Takahara A and Shirai K: Clinical assessment of arterial stiffness with cardio-ankle vascular index: theory and applications. J Hypertens, 2015; 33: 1742-1757; discussion 1757
27) de Morton NA: The PEDro scale is a valid measure of the methodological quality of clinical trials: a demographic study. Australian Journal of Physiotherapy, 2009; 55: 129-133
28) Endes S, Schaffner E, Caviezel S, Dratva J, Autenrieth CS, Wanner M, Martin B, Stolz D, Pons M, Turk A, Bettschart R, Schindler C, Kunzli N, Probst-Hensch N and Schmidt-Trucksass A: Long-term physical activity is associated with reduced arterial stiffness in older adults: longitudinal results of the SAPALDIA cohort study. Age Ageing, 2016; 45: 110-115
29) Mori K, Nomura T, Akezaki Y, Yamamoto R and Iwakura H: Impact of Tai Chi Yuttari-exercise on arteriosclerosis and physical function in older people. Arch Gerontol Geriatr, 2020; 87: 104011
30) Uemura K, Kamitani T, Yamada M and Okamoto H: Longitudinal Effects of Active Learning Education on Lifestyle Behavior and Physical Function in Older Adults. J Am Med Dir Assoc, 2020;
31) Madden KM, Lockhart C, Cuff D, Potter TF and Meneilly GS: Aerobic training-induced improvements in arterial stiffness are not sustained in older adults with multiple cardiovascular risk factors. J Hum Hypertens, 2013; 27: 335-339
32) Madden KM, Lockhart C, Cuff D, Potter TF and Meneilly GS: Short-term aerobic exercise reduces arterial stiffness in older adults with type 2 diabetes, hypertension, and hypercholesterolemia. Diabetes Care, 2009; 32: 1531-1535
33) Ohta M, Hirao N, Mori Y, Takigami C, Eguchi M, Tanaka H, Ikeda M and Yamato H: Effects of bench step exercise on arterial stiffness in post-menopausal women: contribution of IGF-1 bioactivity and nitric oxide production. Growth hormone & IGF research: official jour-

nal of the Growth Hormone Research Society and the International IGF Research Society, 2012; 22: 36-41
34) Montero D, Vinet A and Roberts CK: Effect of combined aerobic and resistance training versus aerobic training on arterial stiffness. International journal of cardiology, 2015; 178: 69-76
35) Cohen J: Statistical Power Analysis for the Behavioral Sciences, Routledge, New York, 1988
36) Saiki A, Ohira M, Yamaguchi T, Nagayama D, Shimizu N, Shirai K and Tatsuno I: New Horizons of Arterial Stiffness Developed Using Cardio-Ankle Vascular Index (CAVI). J Atheroscler Thromb, 2020; 27: 732-748
37) Taniguchi Y, Kitamura A, Shinozaki T, Seino S, Yokoyama Y, Narita M, Amano H, Matsuyama Y, Fujiwara Y and Shinkai S: Trajectories of arterial stiffness and all-cause mortality among community-dwelling older Japanese. Geriatr Gerontol Int, 2018; 18: 1108-1113