Ⅱ．　研究成果の刊行に関する一覧

研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Uemura K, Shimada H, Makizako H, Yoshida D, Doi T, Yamada M, Suzuki T	Factors Associated with Life-Space in Older Adults with Amnestic Mild Cognitive Impairment	Geriatr Gerontol Int	13(1)	161-166	2013
Uemura K, Shimada H, Makizako H, Doi T, Yoshida D	Cognitive function affects trainability for physical performance in exercise intervention among older adults with mild cognitive impairment	Clinical Interventions in Aging	8	97-102	2013
Doi T, Makizako H, Shimada H, Yoshida D, Tsutsumimoto K, Sawa R, Misu S, Suzuki T	Effects of multicomponent exercise on spatial-temporal gait parameters among the elderly with amnestic mild cognitive impairment (aMCI): Preliminary results from a randomized controlled trial (RCT)	Arch Gerontol Geriatr	56(1)	104-108	2013
Doi T, Shimada H, Makizako H, Yoshida D, Shimokata H, Ito K, Washimi Y, Endo H, Suzuki T	Characteristics of cognitive function in early and late stages of amnestic mild cognitive impairment	Geriatr Gerontol Int	13(1)	83-89	2013
Suzuki T, Shimada H, Makizako H, Doi	Effects of multicomponent exercise on cognitive function in older adults	BMC Neurol	12	128	2012

T, Yoshida D, Tsutsumimoto K, Anan Y, Uemura K, Lee S, Park H	with amnestic mild cognitive impairment: a randomized controlled trial				
Uemura K, Doi T, Shimada H, Makizako H, Yoshida D, Tsutsumimoto K, Anan Y, Suzuki T	Effects of Exercise Intervention on Vascular Risk Factors in Older Adults with Mild Cognitive Impairment: a Randomized Controlled Trial	Dement Geriatr Cogn Disord Extra	2(1)	445-455	2012
Doi T, Makizako H, Shimada H, Yoshida D, Ito K, Kato T, Ando H, Suzuki T	Brain Atrophy and Trunk Stability during Dual-task Walking among Older Adults	J Gerontol A Biol Sci Med Sci	67(7)	790-795	2012
島田裕之，堤本広大	運動による現場での効果：とくに認知症予防の視点から	Aging & Health	21(4)	24-27	2013
Shimada H, Ishii K, Ishiwata K, Oda K, Suzukawa M, Makizako H, Doi T, Suzuki T	Gait adaptability and brain activity during unaccustomed treadmill walking in healthy elderly females	Gait Posture	38(2)	203-208	2013
Makizako H, Doi T, Shimada H, Yoshida D, Takayama Y, Suzuki T	Relationship between dual-task performance and neurocognitive measures in older adults with mild cognitive impairment	Geriatr Gerontol Int	13(2)	314-321	2013
Yoshida D, Shimada H, Makizako H, Doi T, Ito K, Kato T, Shimokata H, Washimi Y, Endo	The relationship between atrophy of the medial temporal area and daily activities in older adults with mild cognitive impairment	Aging Clin Exp Res	24(5)	423-429	2013

H, Suzuki T					
Kawashima S, Ito K, Kato T, the SEAD-J Study Group	Inclusion criteria provide heterogeneity in baseline profiles of patients with mild cognitive impairment: comparison of two prospective cohort studies	BMJ Open	2	e000773	2012
李成喆, 西田裕紀子, 金興烈, 幸篤武, 森あさか, 丹下智香子, 安藤富士子, 下方浩史	地域在住高齢者の身体活動と認知機能に関する縦断的研究	日本未病システム学会雑誌	18(3)	123-126	2012
西田裕紀子, 丹下智香子, 富田真紀子, 安藤富士子, 下方浩史	高年者の開放'性が知能の経時変化に及ぼす影響：6年間の縦断的検討	発達心理学研究	23(3)	276-286	2012
西田裕紀子, 丹下智香子, 富田真紀子, 安藤富士子, 下方浩史	高齢者の抑うつはその後の知能低下を引き起こすか：8年間の縦断的検討	老年社会科学	34(3)	370-381	2012
下方浩史, 安藤富士子	認知症の実態と予防の重要性	日本未病システム学会雑誌	18(3)	79-83	2012
Shimokata H, Ando F	Aging-related Genes	Anti-Aging Med	9(6)	185-195	2012
T. Yamane, Y. Ikari, T. Nishio, K. Ishii, K. Ishii, T. Kato, K. Ito, D.H.S. Silverman, M. Senda, T. Asada, H. Arai, M. Sugishita, T. Iwatsubo, and the J-ADNI Study	Visual-Statistical Interpretation of 18F-FDG-PET Images for Characteristic Alzheimer Patterns in a Multicenter Study: Inter-Rater Concordance and Relationship to Automated Quantitative Evaluation	AJNR Am J Neuroradiol	35	244-249	2014

Group					
Takahashi R, Ishii K, Senda M, Ito K, Ishii K, Kato T, Makishi Y, Nishio T, Ikari Y, Iwatsubo T, Japanese Alzheimer's Disease Neuroimaging Initiative	Equal sensitivity of early and late scans after injection of FDG for the detection of Alzheimer pattern: an analysis of 3D PET data from J-ADNI, a multi-center study	Ann Nucl Med	27(5)	452-459	2013
伊藤健吾，加藤隆司，文堂昌彦，中村昭範	アルツハイマー病診断の画像診断，基礎講座：老年精神医学と Brain Imaging	老年精神医学雑誌	24	707-714	2013
伊藤健吾，加藤隆司	形態 MRI，脳血流 SPECT および糖代謝 FDG-PET アルツハイマー病診断のバイオマーカー；最近の進歩	老年精神医学雑誌	24	155-162	2013
Lee SC, Yuki A, Nishita Y, Tange C, Kim HY, Kozakai R, Ando F, Shimokata H	Relationship Between Light Intensity Physical Activity and Cognitive Function in a Community-Dwelling Elderly population - 8 year longitudinal study	J Am Geriat Soc	61(3)	452-453	2013
Suzuki T, Shimada H, Makizako H, Doi T, Yoshida D, Ito K, Shimokata H, Washimi Y, Endo	A randomized controlled trial of multicomponent exercise in older adults with mild cognitive impairment	PLoS One	8(4)	e61483	2013

H, Kato T					
幸篤武，森あさか，李成喆，安藤富士子，下方浩史	中高年の脳萎縮を抑制する日常歩行量の解明～地域からの無作為抽出者を対象とした大規模縦断研究～	デサントスポーツ科学	34	31-39	2013
Nishita Y, Tange C, Tomida M, Ando F, Shimokata H	Does high educational level protect against intellectual decline in older adults? : a 10-year longitudinal study	Jpn Psycho Res	55	378-389	2013
Shimada H, Makizako H, Doi T, Yoshida D, Tsutsumimoto K, Anan Y, Uemura K, Ito T, Lee S, Park H, Suzuki T	Combined Prevalence of Frailty and Mild Cognitive Impairment in a Population of Elderly Japanese People	JAMDA	14(7)	518-524	2013
Makizako H, Shimada H, Doi T, Hyuntae Park, Yoshida D, Uemura K, Tsutsumimoto K, Liu-Ambrose T, Suzuki T	Poor balance and lower gray matter volume predict falls in older adults with mild cognitive impairment	BMC Neurology	13(1)	102	2013
Makizako H, Shimada H, Doi T, Park H, Yoshida D, Suzuki T	Six-Minute Walking Distance Correlated with Memory and Brain Volume in Older Adults with Mild Cognitive Impairment: A Voxel-Based Morphometry Study	Dement Geriatr Cogn Disord Extra	3	223-232	2013

Makizako H, Shimada H, Park H, Doi T, Yoshida D, Uemura K, Tsutsumimoto K, Suzuki T	Evaluation of multidimensional neurocognitive function using a tablet personal computer: Test–retest reliability and validity in community-dwelling older adults	Geriatr Gerontol Int	13	860-866	2013
Doi T, Shimada H, Makizako H, Lee S, Park H, Tsutsumimoto K, Uemura K, Yoshida D, Anan Y, Suzuki T	Cognitive Activities and Instrumental Activity of Daily Living in Older Adults with Mild Cognitive Impairment	Dement Geriatr Cogn Disord Extra	3	398-406	2013
島田裕之	特集 高齢者における健康増進 Seminar 9. 認知症予防と健康増進	老年医学	51(9)	941-945	2013
島田裕之	認知症の予防	公衆衛生	78(10)	698-702	2014
島田裕之, 土井剛彦	特集／高齢者のフレイル（虚弱）とリハビリテーション MCI 高齢者における運動の意義	Monthly Book Medical Rehabilitation	170	85-93	2014
島田裕之	認知症予防に向けた運動介入とその可能性	認知症の最新医療	4(3)	109-114	2014
島田裕之, 李相侖	認知症予防のためのコミュニティの創出と効果検証	福祉介護テクノプラス 2014年7月号	7(7)	12-18	2014
Shimada H, Makizako H, Doi T, Yoshida D, Tsutsumimoto K, Anan Y, Uemura K, Lee S, Park H, Suzuki T	A large, cross-sectional observational study of serum BDNF, cognitive function, and mild cognitive impairment in the elderly	Frontiers in Aging Neuroscience	6(69)	1-9	2014

Shimada H, Park H, Makizako H, Doi T, Lee S, Suzuki T	Depressive symptoms and cognitive performance in older adults	Journal of Psychiatric Research	57	149-156	2014
Makizako H, Liu-Ambrose T, Shimada H, Doi T, Park H, Tsutsumimoto K, Uemura K, Suzuki T	Moderate-intensity physical activity, hippocampal volume, and memory in older adults with mild cognitive impairment	J Gerontol A Biol Sci Med Sci	70(4)	480-486	2014
Makizako H, Shimada H, Doi T, Park H, Tsutsumimoto K, Uemura K, Lee S, Yoshida D, Anan Y, Ito T, Suzuki T	Moderate-Intensity Physical Activity, Cognition and APOE Genotype in Older Adults with Mild Cognitive Impairment	Ann Gerontol Geriatric Res	1(1)	1002	2014
Doi T, Shimada H, Makizako H, Tsutsumimoto K, Uemura K, Anan Y, Suzuki T	Cognitive function and gait speed under normal and dual-task walking among older adults with mild cognitive impairment	BMC Neurology	14(1)	67	2014
Uemura K, Shimada H, Makizako H, Doi T, Tsutsumimoto K, Yoshida D, Anan Y, Ito T, Lee S, Park H, Suzuki T	Effects of mild and global cognitive impairment on the prevalence of fear of falling in community-dwelling older adults	Maturitas	78(1)	62-66	2014
Doi T, Makizako H, Shimada H, Tsutsumimoto K, Hotta R,	Objectively measured physical activity, brain atrophy, and white matter lesions in older adults with	Experimental Gerontology	62	1-6	2015

Nakakubo S, Park H, Suzuki T	mild cognitive impairment				
Doi T, Shimada H, Makizako H, Tsutsumimoto K, Hotta R, Nakakubo S, Suzuki T	Association of insulin-like growth factor-1 with mild cognitive impairment and slow gait speed	Neurobiol Aging	36	942-947	2015
Hotta R, Doi T, Shimada H, Makizako H, Yoshida D, Anan Y, Tsutsumimoto K, Uemura K, Park H, Suzuki T	Cigarette smoking and cognitive health in elderly Japanese	Am J Health Behav	39(3)	294-300	2015
西田裕紀子、丹下智香子、富田真紀子、安藤富士子、下方浩史	高齢者における知能と抑うつの相互関係：交差遅延効果モデルによる検討	発達心理学研究	25(1)	76-86	2014
Otsuka R, Tange C, Nishita Y, Kato Y, Imai T, Ando F, Shimokata H	Serum docosahexaenoic and eicosapentaenoic acid and risk of cognitive decline over 10 years among elderly Japanese	Eur J Clin Nutr	68	503-509	2014
安藤富士子、西田裕紀子、下方浩史	喫煙が知能・認知機能に及ぼす影響と抗酸化食品の可能性	Geriatric Medicine	52(7)	793-796	2014
下方浩史	地域在住高齢者における要介護化の危険因子	Advances in Aging and Health Research 2013 在宅の高齢者を支える-医療・介護・看取り-		125-135	2014

Hatano K, Sekimata K, Yamada T, Abe J, Ito K, Ogawa M, Magata Y, Toyohara J, Ishiwata K, Biggio G, Serra M, Laquintana V, Denora N, Latrofa A, Trapani G, Liso G, Suzuki H, Sawada M, Nomura M, Toyama H	Radiosynthesis and in vivo evaluation of two imidazopyridineacetamides, [11C]CB184 and [11C]CB190, as a PET tracer for 18 kDa translocator protein: direct comparison with [11C](R)-PK11195	Ann Nucl Med	29(4)	325-335	2015
Ito K, Fukuyama H, Senda M, Ishii K, Maeda K, Yamamoto Y, Ouchi Y, Ishii K, Okumura A, Fujiwara K, Kato T, Arahata Y, Washimi Y, Mitsuyama Y, Meguro K, Ikeda M, SEAD-J Study Group	Prediction of outcomes in MCI by using 18F-FDG-PET: A multicenter study	J Alzheimers Dis	45	543-552	2015
Ishii K, Ito K, Nakanishi A, Kitamura S, Terashima A	Computer-assisted system for diagnosing degenerative dementia using cerebral blood flow SPECT and 3D-SSP: a multicenter study	Jpn J Radiol	32(7)	383-390	2014

Ⅲ.　研究成果の刊行物・別刷

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ORIGINAL ARTICLE

Factors associated with life-space in older adults with amnestic mild cognitive impairment

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Aim: Restriction of life-space is associated with physical performance and functional decline in older adults. Little is known about the factors associated with life-space in older adults with amnestic mild cognitive impairment (aMCI). The purpose of this study was to identify factors associated with life-space in older adults with aMCI.

Methods: The study participants were 69 older adults (mean age 74.5 years, males 56.5%) who were identified with aMCI. Life-space mobility was measured using a Japanese translation of the life-space assessment (LSA). Age, sex, cognitive function (general function, executive function and processing speed), physical performance, instrumental activities of daily living status (IADL) and fear of falling (FoF) were measured as potential relevant factors.

Results: Univariate analysis showed that the LSA was associated with FoF, sex, physical performance, processing speed and IADL. In the stepwise regression analysis, FoF, processing speed and IADL maintained a significant association with the LSA scores, although sex and physical performance did not reach significance.

Conclusion: The results suggest that the restrictions of life-space in older adults with aMCI were more affected by the FoF, slower processing speed and restricted IADL than sex or physical performance. **Geriatr Gerontol Int 2012; ••: ••–••.**

Keywords: community-dwelling elderly population, fear of falling, information processing, life-space, mild cognitive impairment.

Introduction

Mild cognitive impairment (MCI) is widely regarded as a transitional syndrome between normal cognitive aging and clinical dementia.[1] This is particularly the case for amnestic MCI (aMCI), which is likely to progress to Alzheimer's disease (AD).[2–4] The diagnostic criteria show that people with MCI have "generally" intact activities of daily living (ADL), although investigations of instrumental activities of daily living (IADL) have shown marginal limitations for older adults with MCI.[5–8] Furthermore, older adults with cognitive deficits suggestive of MCI have shown lower mobility, including reduced life-space, driving space and driving frequency, as well as increased driving difficulty compared with cognitively normal individuals.[9]

Life-space is the spatial extent of a person's mobility. It has been conceptualized as a series of concentric zones, ranging from one's bedroom to one's region of the country.[10] Xue *et al.* reported that a slightly constricted life-space (going into the neighbourhood less

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than four times a week) was an important risk factor for the development of frailty, whereas a severely constricted life-space (i.e. never leaving home) indicated a high risk of mortality.[11] A lower fluency of going outdoors (less than once a week) was associated with a limitation in basic ADL and IADL.[12] Thus, an extended life-space seems to play an important role in maintaining health and function in older adults.

Life-space assessment (LSA) was developed to evaluate mobility status by measuring the life-space for elderly individuals living in a community.[13] The LSA may indirectly reflect the physical activity status of older adults because the LSA score is associated with physical performance, ADL and sociodemographic factors.[14] Baker *et al.*[13] suggested that the LSA is sensitive to marginal limitations before older persons experience difficulties in performing ADL or IADL. Older adults with MCI restrict their life-space,[9] and the LSA might be an early marker of functional decline in older adults with MCI. Furthermore, identifying the determinants of life-space is required to identify appropriate therapeutic strategies. According to previous studies among older adults, it has been reported that life-space is larger if they have better physical performance, cognitive function,[15] mental health and IADL functions,[13,16,17] and they are male.[16] However, it is not clear whether factors, such as demographic, physical and cognitive performance, and psychological status, are associated with life-space in older adults with MCI. We focused on aMCI (memory impairment), which is likely to progress to AD.[2–4] The purpose of the present study was to identify the determinants of life-space in older adults with aMCI.

Methods

Participants

The participants were recruited from two volunteer databases ($n = 1543$), which included elderly participants aged 65 years and over who either attended a health check in Obu, Japan, or were selected by stratified random sampling. Figure 1 shows the flowchart of participant recruitment and screening. The strata used in stratified random sampling were age and sex. In the first eligibility assessment for the present study, 528 potential participants who had either a Clinical Dementia Rating of 0.5 or memory complaints were enrolled. A total of 135 participants responded to the second eligibility assessment; 76 participants completed the assessment and met the inclusion criteria. The inclusion criteria required that they live independently in the community, speak Japanese, have adequate hearing and visual acuity, and be able to participate in the examinations, and met the definition of aMCI. In the present study, aMCI was defined according to Peterson's internationally-accepted criteria:[1] having memory complaints and an objective memory impairment,

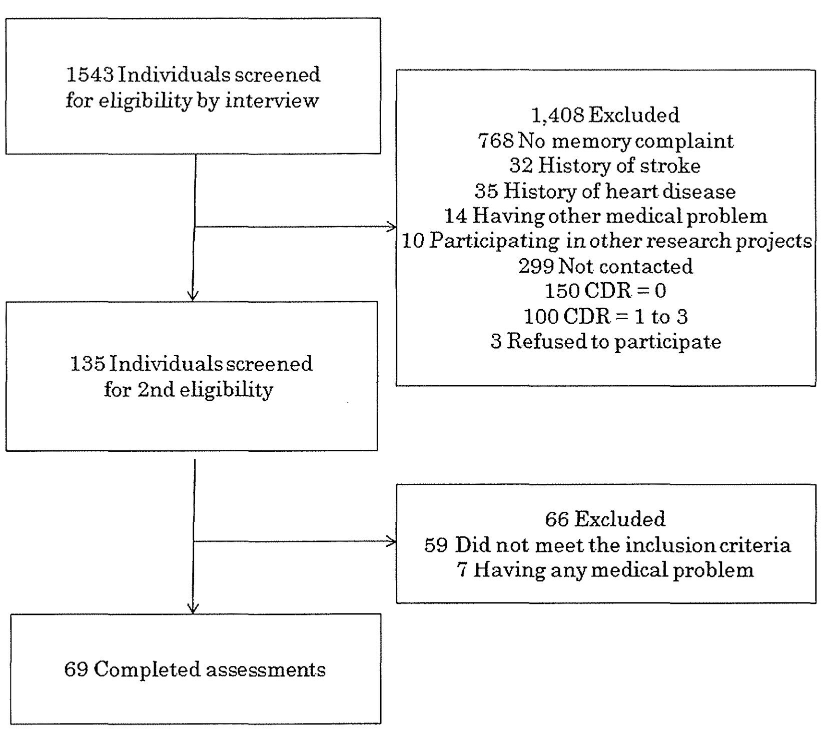

Figure 1 Flow chart of participant recruitment and screening. CDR, Clinical Dementia Rating.

maintaining independent activities of daily living, preserved general cognitive function and no dementia. The objective memory impairment was defined as a lower score on the Wechsler Memory Scale-Revised (WMS-R) Logical Memory II.[18] The cut-off score to define the aMCI was adjusted by educational history (0–9 years: <7 points, 10–15 years: <10 points, more than 16 years: <12 points).[19] In addition, general cognitive function was found to be intact in all the 76 participants whose Mini-Mental State Examination (MMSE) scores were in the range of 24–30.[20] Seven participants were excluded based on the exclusion criteria, specifically a history of major psychiatric illness, other serious neurological or musculoskeletal diagnoses, or depression (Geriatric Depression Scale [GDS] scores greater than or equal to 10[21]). There were 69 older adults in the final analyzed sample ($n = 69$, age $M = 75.4$, proportion of males 56.5%, educational history $M = 11.0$). Written informed consent was obtained from the participants in accordance with the guidelines approved by the National Center for Geriatrics and Gerontology, and the Declaration of Human Rights, Helsinki, 1975.

Measurements

Demographic data were recorded including age, sex and educational history. Life-space mobility was measured using a Japanese translation of the LSA.[13,22] The repeated forward–backward translation procedure was used to produce a Japanese version of the LSA. The translation was carried out by a native English translator and three Japanese translators, and confirmed by Baker *et al.*, a developer of the LSA. The LSA can be used to derive a score based on the reported movement distance for the 4 weeks preceding the assessment. The life-space levels ranged from the room where a person sleeps to beyond the person's town (five life-space levels): (i) "other rooms of your home besides the room where you sleep"; (ii) "an area outside your home, such as your porch, deck, or patio, hallway (of an apartment building) or garage, in your own yard or driveway"; (iii) "places in your neighbourhood other than your own yard or apartment building"; (iv) "places outside your neighbourhood, but within your town"; and (v) "places outside your town." For each life-space level, participants were asked how often they travelled to that area (less than once a week, 1–3 times each week, 4–6 times each week, daily) and whether they required assistance from another person or from an assistive device ("yes" or "no"). The LSA scores ranged from 0 ("totally room-bound") to 120 ("travelled out of town every day without assistance"), with lower scores reflecting lower life-space mobility.

All neuropsychological tests were carried out by well-trained speech therapists, and each score was rechecked by a single therapist blind to the other participant data. General cognitive function was evaluated using the Alzheimer's Disease Assessment Scale (ADAS).[23] The ADAS was designed specifically to evaluate cognitive and behavioural dysfunctions characteristic of AD.

Executive function was assessed using the Trail Making Test forms B (TMT-B).[24] Participants were required to navigate a series of alternating numbers and letters, and connect them in alternating sequential order. The time required to complete each task was recorded, with more time indicating worse performance.

Processing speed was assessed by using a version of the Digit Symbol-Coding (DSC) subtest of the Wechsler Adult Intelligence Scale III.[25] In the test, participants copied symbols that were paired with numbers. Using the key provided at the top of the exercise form, the participant drew the symbol under the corresponding number. The DSC score was the number of correct symbols drawn within 120 s.

The Timed Up & Go Test (TUG) was used to assess physical performance.[26] The TUG involves rising from a chair, walking 3 m, turning around, walking back to the chair and sitting down. Participants were instructed to complete the task at their usual pace. The score represented the time in seconds that the participant required to complete the assessment. Lower times indicate better balancing ability. The recorded TUG score was the lesser of the times measured in the two trials.

IADL were measured by the five-item subscale of Instrumental Self-Maintenance of the Tokyo Metropolitan Institute of Gerontology-Index of Competence (TMIG-IC), which has been shown to be reliable.[27] The IADL subscale of the TMIG-IC consisted of the following items: (i) "Can you use public transportation (bus or train) by yourself?"; (ii) "Are you able to shop for daily necessities?"; (iii) "Are you able to prepare meals by yourself?"; (iv) "Are you able to pay bills?"; and (v) "Can you handle your own banking?" Participants were asked about the competence status of the implementation of each item. The response to each item in the index was designated as "yes" (able to do, 1 point) or "no" (unable to do, 0 point). The total score of the IADL subscale ranges from 0 (limitation of IADL) to 5 (high level of IADL).

Fear of falling (FoF) was measured as a psychological factor causing activity restriction. The FoF refers to the lack of self-confidence that normal activities can be carried out without falling.[28] The FoF was assessed using a closed-ended question: "Are you afraid of falling now?" Participants responded by selecting one item from an ordered set of choices. Participants who responded "somewhat" or "very much" were assigned to the fear group; participants who responded "a little" or "not at all" were assigned to the no-fear group.[29]

Statistical analysis

The relationships between the LSA and the other measurements were examined using Pearson's correlations. Spearman's correlations were used to examine the relationship among ordinal variables; that is, IADL. Unpaired *t*-tests were used to compare the LSA scores for categorical variables; that is, sex and the FoF.

A multivariate linear regression model was used to examine whether the potential determinants were associated independently with the LSA score. Independent variables included age, sex, the ADAS, DSC, TMT-B, TUG, IADL and FoF scores. Sex and FoF were used as dummy variables (male = 0, female = 1; no fear = 0, fear = 1). Statistical analyses were carried out using the SPSS version 11.0 software package (SPSS, Chicago, IL, USA), with $P < 0.05$ accepted as significant.

Results

Table 1 shows the demographic and clinical characteristics of study participants. In the correlation analysis, the LSA scores had modest correlations with TUG ($r = -0.342$, $P = 0.004$), DSC ($r = 0.365$, $P = 0.002$) and IADL ($r = 0.254$, $P = 0.035$). The LSA was not correlated with age ($r = -0.164$, $P = 0.18$), ADAS ($r = -0.07$, $P = 0.53$) or TMT-B ($r = -0.21$, $P = 0.08$). Males had significantly higher LSA scores than females (males 102.3 ± 19.7, females 88.7 ± 17.8; $P = 0.004$). The no-fear group had significantly higher LSA scores than the fear group (non-fear 104.3 ± 19.7, fear 88.7 ± 17.8; $P < 0.001$).

Table 1 Demographic and clinical characteristics of study participants

	Participants (n = 69)
Age (years)	75.4 ± 6.9 (69–94)
Education (years)	11.0 ± 2.6
Sex (males)	39 (56.5)
MMSE (points)	26.8 ± 1.8
GDS (points)	3.0 ± 2.0
LSA (points)	96.3 ± 19.9
ADAS (points)	6.4 ± 2.2
DSC (points)	45.7 ± 14.7
TMT-B (s)	204.5 ± 109.1
TUG (s)	9.2 ± 2.3
IADL (points)	4.9 ± 0.2
FoF (the fear group)	31 (44.9)

Values are presented as mean ± SD or n (%). ADAS, Alzheimer's Disease Assessment Scale; DSC, Digit Symbol-Coding subtest of the Wechsler Adult Intelligence Scale III; FoF, Fear of Falling; GDS, Geriatric Depression Scale; IADL, Instrumental Activities of Daily Living subscale of TMIG-IC; LSA, Life-Space Assessment; MMSE, Mini-Mental State Examination; TMT-B, Trail Making Test forms B; TUG, Timed Up & Go Test.

Table 2 Factors associated with a larger life-space in stepwise multiple regression

	Factors	β	P	R^2
LSA	FoF	−0.370	0.000	0.37
	DSC	0.278	0.007	
	IADL	0.274	0.008	

DSC, Digit Symbol-Coding subtest of the Wechsler Adult Intelligence Scale III; FoF, Fear of Falling; IADL, Instrumental Activities of Daily Living subscale of TMIG-IC; TUG, Timed Up & Go Test.

Table 2 shows the factors significantly related to LSA scores in the stepwise multiple regression. The stepwise method was used to empirically determine the best combination of the demographic, cognitive, physical and psychological factors to account for the LSA scores. The model explained 37% of the LSA score variance. Factors retained in the final model were the FoF (β = −0.37, $P = 0.001$), DSC (β = 0.278, $P = 0.007$) and IADL (β = 0.274, $P = 0.008$). The excluded variables in the model were age, sex, ADAS, TMT-B and TUG.

Discussion

The present study showed that factors associated with life-space in older adults with aMCI were different from those reported by previous studies investigating older adults without cognitive impairment. The FoF, DSC and IADL maintained a significant association with the LSA scores in the stepwise multiple regression, whereas the TUG and sex did not have a significant association with life-space, unlike in the case of univariate analysis. It is possible that the restrictions of life-space for the aMCI participants were more affected by FoF, slower processing speed and restricted IADL than sex or physical performance.

FOF contributed to multiple aspects (e.g. physical function, cognitive function or psychological status)[30] and led to an unnecessary avoidance of activities for older adults, even though they might have been able to carry out these activities.[31,32] The present findings suggest that the association between FOF and activity restriction might become evident after life-space restriction in older adults with aMCI. Older adults with aMCI might potentially restrict activity accompanied by marginal IADL limitation. It is considered important to reduce FoF by targeting downstream factors, such as increasing physical functioning,[33] or improving medication use[34] and extending life-space activities for older adults with aMCI.

Life-space is a mobility indicator strongly related to cognitive function, particularly processing speed.[15] DSC is the primary measure of mental processing speed, clerical efficiency and visual-motor coordination.[35] The results of the present study suggest that processing speed is one of the factors related to life-space mobility in older adults and specifically suggests that processing speed might perform a more important role for maintaining life-space than other cognitive factors among aMCI individuals. Processing speed is an important domain of cognitive ability and might be useful as a biological marker of cognitive ageing.[36] For example, in terms of the important aspects of life-space, improving processing speed was closely associated with protection against declines in driving mobility[37] and delays in driving cessation[38] in older adults. Driving mobility is more likely to deteriorate in older adults with aMCI than those with healthy cognitive abilities.[9] It is possible that processing speed might be one of several important factors in maintaining not only driving mobility, but also life-space in the older adults, especially in those with aMCI. Furthermore, the assessment of processing speed might have implications for the prediction of decline in the life-space of older adults with aMCI.

A constricted life space is associated with increased risk of AD and cognitive decline among older persons.[39] Findings of the present study might contribute to development of interventions to expand life-space of older adults with aMCI. Specific approaches might be required for older adults with aMCI in order to maintain or expand life-space, such as multicomponent cognitive behavioural group intervention to reduce FoF and associated activity avoidance,[40,41] and speed of processing training.[37,38]

There were several limitations in the present study that need to be mentioned. First, the analyses were based on a cross-sectional design and we were therefore only able to examine the correlates of life-space. Second, the sample size was relatively small. To truly determine the decision factors shaping life-space among aMCI individuals, it is important to compare results between an equal number of participants with and without aMCI. Third, we did not collect data on certain factors that might influence the size of one's life-space, such as sensory function, acute illness or financial strain. These and other factors should be examined in future life-space studies. Finally, we did not compare associated factors in cases of normal older adults, older adults with AD, and older adults with multidomain MCI. Comparative studies on determinants of life-space covering the continuum from normal cognition through MCI to AD should be carried out in the future. Contribution of cognitive factors to life-space might increase with progression of cognitive impairment.

In summary, despite some limitations, this is the first study to explore the determinants of life-space in older adults with aMCI. The presence of FoF, slower processing speed and restricted IADL were more closely related to life-space than physical performance and demographic factors in older adults with aMCI. These findings give new insight into developing effective interventions for preventing life-space restrictions in cognitively frail older adults.

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References

1 Petersen RC, Morris JC. Mild cognitive impairment as a clinical entity and treatment target. *Arch Neurol* 2005; **62**: 1160–1163. discussion 67.

2 Petersen RC, Doody R, Kurz A *et al.* Current concepts in mild cognitive impairment. *Arch Neurol* 2001; **58**: 1985–1992.

3 Winblad B, Palmer K, Kivipelto M *et al.* Mild cognitive impairment – beyond controversies, towards a consensus: report of the International Working Group on Mild Cognitive Impairment. *J Intern Med* 2004; **256**: 240–246.

4 Gauthier S, Reisberg B, Zaudig M *et al.* Mild cognitive impairment. *Lancet* 2006; **367**: 1262–1270.

5 Albert SM, Tabert MH, Dienstag A, Pelton G, Devanand D. The impact of mild cognitive impairment on functional abilities in the elderly. *Curr Psychiatry Rep* 2002; **4**: 64–68.

6 Okonkwo O, Griffith HR, Belue K *et al.* Medical decision-making capacity in patients with mild cognitive impairment. *Neurology* 2007; **69**: 1528–1535.

7 Aretouli E, Brandt J. Everyday functioning in mild cognitive impairment and its relationship with executive cognition. *Int J Geriatr Psychiatry* 2010; **25**: 224–233.

8 Wadley VG, Crowe M, Marsiske M *et al.* Changes in everyday function in individuals with psychometrically defined mild cognitive impairment in the Advanced Cognitive Training for Independent and Vital Elderly Study. *J Am Geriatr Soc* 2007; **55**: 1192–1198.

9 O'Connor ML, Edwards JD, Wadley VG, Crowe M. Changes in mobility among older adults with psychometrically defined mild cognitive impairment. *J Gerontol B Psychol Sci Soc Sci* 2010; **65B**: 306–316.

10 May D, Nayak US, Isaacs B. The life-space diary: a measure of mobility in old people at home. *Int Rehabil Med* 1985; **7**: 182–186.

11 Xue QL, Fried LP, Glass TA, Laffan A, Chaves PH. Life-space constriction, development of frailty, and the competing risk of mortality: the Women's Health And Aging Study I. *Am J Epidemiol* 2008; **167**: 240–248.

12 Shimada H, Ishizaki T, Kato M *et al.* How often and how far do frail elderly people need to go outdoors to maintain

functional capacity? *Arch Gerontol Geriatr* 2010; **50**: 140–146.
13 Baker PS, Bodner EV, Allman RM. Measuring life-space mobility in community-dwelling older adults. *J Am Geriatr Soc* 2003; **51**: 1610–1614.
14 Peel C, Sawyer Baker P, Roth DL, Brown CJ, Brodner EV, Allman RM. Assessing mobility in older adults: the UAB Study of Aging Life-Space Assessment. *Phys Ther* 2005; **85**: 1008–1119.
15 Wood KM, Edwards JD, Clay OJ, Wadley VG, Roenker DL, Ball KK. Sensory and cognitive factors influencing functional ability in older adults. *Gerontology* 2005; **51**: 131–141.
16 Barnes LL, Wilson RS, Bienias JL *et al.* Correlates of life space in a volunteer cohort of older adults. *Exp Aging Res* 2007; **33**: 77–93.
17 Murata C, Kondo T, Tamakoshi K, Yatsuya H, Toyoshima H. Factors associated with life space among community-living rural elders in Japan. *Public Health Nurs* 2006; **23**: 324–331.
18 Wechsler D. *Wechsler Memory Scale-Revised Manual*. San Antonio, TX: The Psychological Corporation, 1987.
19 Aisen PS, Petersen RC, Donohue MC *et al.* Clinical Core of the Alzheimer's Disease Neuroimaging Initiative: progress and plans. *Alzheimers Dement* 2010; **6**: 239–246.
20 Folstein MF, Folstein SE, 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.
21 Yesavage JA. Geriatric depression scale. *Psychopharmacol Bull* 1988; **24**: 709–711.
22 Shimada H, Sawyer P, Harada K *et al.* Predictive validity of the classification schema for functional mobility tests in instrumental activities of daily living decline among older adults. *Arch Phys Med Rehabil* 2010; **91**: 241–246.
23 Rosen WG, Mohs RC, Davis KL. A new rating scale for Alzheimer's disease. *Am J Psychiatry* 1984; **141**: 1356–1364.
24 Kortte KB, Horner MD, Windham WK. The trail making test, part B: cognitive flexibility or ability to maintain set? *Appl Neuropsychol* 2002; **9**: 106–109.
25 Wechsler D. *Wechsler Adult Intelligence Scale – III*. San Antonio, TX: The Psychological Corporation, 1997.
26 Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc* 1991; **39**: 142–148.
27 Koyano W, Shibata H, Nakazato K, Haga H, Suyama Y. Measurement of competence: reliability and validity of the TMIG Index of Competence. *Arch Gerontol Geriatr* 1991; **13**: 103–116.
28 Tinetti ME, Richman D, Powell L. Falls efficacy as a measure of fear of falling. *J Gerontol* 1990; **45**: P239–P243.
29 Maki BE, Holliday PJ, Topper AK. Fear of falling and postural performance in the elderly. *J Gerontol* 1991; **46**: M123–M131.
30 Scheffer AC, Schuurmans MJ, van Dijk N, van der Hooft T, de Rooij SE. Fear of falling: measurement strategy, prevalence, risk factors and consequences among older persons. *Age Ageing* 2008; **37**: 19–24.
31 Howland J, Lachman ME, Peterson EW, Cote J, Kasten L, Jette A. Covariates of fear of falling and associated activity curtailment. *Gerontologist* 1998; **38**: 549–555.
32 Fletcher PC, Hirdes JP. Restriction in activity associated with fear of falling among community-based seniors using home care services. *Age Ageing* 2004; **33**: 273–279.
33 Delbaere K, Crombez G, Vanderstraeten G, Willems T, Cambier D. Fear-related avoidance of activities, falls and physical frailty. A prospective community-based cohort study. *Age Ageing* 2004; **33**: 368–373.
34 Friedman SM, Munoz B, West SK, Rubin GS, Fried LP. Falls and fear of falling: which comes first? A longitudinal prediction model suggests strategies for primary and secondary prevention. *J Am Geriatr Soc* 2002; **50**: 1329–1335.
35 Ryan JJ, Kreiner DS, Bartels JM, Tree HA, Schnakenberg-Ott SD. Thirty-second interval patterns for WAIS-III Digit Symbol and Symbol Search. *Arch Clin Neuropsychol* 2006; **21**: 705–709.
36 Deary IJ, Johnson W, Starr JM. Are processing speed tasks biomarkers of cognitive aging? *Psychol Aging* 2010; **25**: 219–228.
37 Edwards JD, Myers C, Ross LA *et al.* The longitudinal impact of cognitive speed of processing training on driving mobility. *Gerontologist* 2009; **49**: 485–494.
38 Edwards JD, Delahunt PB, Mahncke HW. Cognitive speed of processing training delays driving cessation. *J Gerontol A Biol Sci Med Sci* 2009; **64**: 1262–1267.
39 James BD, Boyle PA, Buchman AS, Barnes LL, Bennett DA. Life space and risk of Alzheimer disease, mild cognitive impairment, and cognitive decline in old age. *Am J Geriatr Psychiatry* 2011; **19**: 961–969.
40 Kempen GI, Wesselink SF, van Haastregt JC, Zijlstra GA. Long-term effect on mortality of a multicomponent cognitive behavioural group intervention to reduce fear of falling in older adults: a randomised controlled trial. *Age Ageing* 2011; **40**: 519–523.
41 Zijlstra GA, van Haastregt JC, Ambergen T *et al.* Effects of a multicomponent cognitive behavioral group intervention on fear of falling and activity avoidance in community-dwelling older adults: results of a randomized controlled trial. *J Am Geriatr Soc* 2009; **57**: 2020–2028.

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ORIGINAL RESEARCH

Cognitive function affects trainability for physical performance in exercise intervention among older adults with mild cognitive impairment

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Background: Although much evidence supports the hypothesis that cognitive function and physical function are interrelated, it is unclear whether cognitive decline with mild cognitive impairment influences trainability of physical performance in exercise intervention. The purpose of this study was to examine the association between cognitive function at baseline and change in physical performance after exercise intervention in older adults with mild cognitive impairment.

Methods: Forty-four older adults diagnosed with mild cognitive impairment based on the Peterson criteria (mean age 74.8 years) consented to and completed a 6-month twice weekly exercise intervention. The Timed Up and Go (TUG) test was used as a measure of physical performance. The Mini-Mental State Examination (MMSE), Trail Making Test Part B, Geriatric Depression Scale, baseline muscle strength of knee extension, and attendance rate of intervention, were measured as factors for predicting trainability.

Results: In the correlation analysis, the change in TUG showed modest correlations with attendance rate in the exercise program ($r = -0.354$, $P = 0.027$) and MMSE at baseline ($r = -0.321$, $P = 0.034$). A multiple regression analysis revealed that change in TUG was independently associated with attendance rate ($\beta = -0.322$, $P = 0.026$) and MMSE score ($\beta = -0.295$, $P = 0.041$), controlling for age and gender.

Conclusion: General cognitive function was associated with improvements in physical performance after exercise intervention in subjects with mild cognitive impairment. Further research is needed to examine the effects of exercise programs designed to address cognitive obstacles in older adults with mild cognitive impairment.

Keywords: exercise, mobility, rehabilitation, Timed Up and Go test

Introduction

Mild cognitive impairment is widely regarded as a transitional syndrome between normal cognitive ageing and clinical dementia.[1] Deterioration in episodic learning and memory functions constitute the core characteristics of mild cognitive impairment and Alzheimer's disease. Older adults with mild cognitive impairment demonstrate decreased physical performance, which in turn is related to the risk of Alzheimer's disease.[2] Reduced physical function leads to restricted life space mobility,[3] which is associated with increased risk of Alzheimer's disease and cognitive decline among older persons.[4] Improved usual gait speed over a 12-month period predicts a substantial reduction in mortality.[5] Maintaining and improving physical function may be beneficial for preventing conversion to Alzheimer's disease in older adults with mild cognitive impairment.

A better understanding of the modifiable factors independently associated with improved physical performance is needed.[6] This would ensure effective intervention based on a valid theoretical framework for increasing physical performance. Possible modifiable factors include cognitive function, mental status, and physiological function, such as muscular strength. Logsdon et al[7] found that older adults with mild cognitive impairment may benefit significantly from an exercise program specifically designed to address their cognitive needs (ie, memory aids and easy to follow instructions). They suggest that cognitive impairment may prevent successful engagement in exercise. Several studies support the hypothesis that cognitive and physical function are interrelated,[2,8] although it is not clear whether older adults with mild cognitive impairment have decreased trainability for improving physical performance.

The purpose of this study was to examine the association between cognitive function at baseline and trainability of physical performance using a 6-month exercise intervention in older adults with mild cognitive impairment. We used the Timed Up and Go test (TUG) as an assessment of physical performance.[9] This test has frequently been used to assess lower extremity function, mobility, and risk of falls in older adults. Recent research has revealed that TUG is associated with executive function[8] and periventricular leukoaraiosis[10] in older adults with mild cognitive impairment. Changes in TUG before and after intervention were measured as the dependent variable. In the present study, we defined trainability as the ability to be trained and this was expressed by rate of improvement between before and after intervention.[11] By means of correlation and regression analysis, we examined how cognitive function at baseline influenced change in TUG. Other factors including depression, attendance rate, and physiological function (such as muscle strength) were also investigated. Similar to the relationship between physical and cognitive function,[2,8] it is also possible that improvements in physical performance are associated with cognitive function, where cognitive impairment may prevent successful engagement in exercise.

We hypothesized that reduced cognitive functioning affects trainability of physical performance by exercise intervention in older adults with mild cognitive impairment. This investigation is critical for the exploration of the modifiable factors associated with trainability in order to plan future rehabilitation programs that prevent deterioration of physical and cognitive function.

Materials and methods

Subjects

The participants were recruited from two volunteer databases (n = 1543), which included elderly participants aged 65 years and over who either attended a health check in Obu, Japan, or were selected by stratified random sampling. The strata used in our stratified random sampling were age and gender. Criteria for inclusion in this intervention study required that participants were 65 years or older, living independently in the community (ie, no impairment of activities of daily living), and Japanese-speaking, with sufficient hearing and visual acuity to participate in the examinations. In the first eligibility assessment for this study, 528 potential participants who had either a Clinical Dementia Rating of 0.5 or subjective memory complaints were screened. One hundred and thirty-five participants met the criteria for the second eligibility assessment. They also needed to meet the Peterson criteria for a diagnosis of mild cognitive impairment.[1] The final sample consisted of 44 older adults (mean age 74.8 years; 20 males; mean years of education, 11.1 years). These participants were exposed to an exercise intervention and they completed a randomized controlled trial that aimed to examine the effect of multicomponent exercise on cognitive function. The design and the primary results of the study have been reported elsewhere.[12]

Exclusion criteria included a history of major psychiatric illness (eg, schizophrenia or bipolar disorder) and other serious neurological or musculoskeletal diagnoses. This study was approved by the ethics committee of National Center for Geriatrics and Gerontology, Japan. Appropriate written informed consent was obtained for all participants.

Procedures

The 6-month exercise program involved biweekly 90-minute sessions with a combination of aerobic exercise, muscle strength training, and postural balance retraining. In addition, the exercise program focused on promoting exercise and behavior change. Two trained physiotherapists involved in geriatric rehabilitation conducted the interventions. Each supervised session began with a 10-minute warmup period and stretching exercise, followed by 20 minutes of muscle strength exercise. The participants then practiced aerobic exercise, postural balance retraining, and a combination of both activities over a period of 60 minutes.

Before and after each session of the program, physiotherapists conducted a health check of each participant. The physiotherapists and a well trained instructor implemented risk management for adverse events during the program. In the aerobic exercise, participants performed stair stepping and endurance walking. The intensity of the aerobic exercise was prescribed at approximately 40% of maximum heart rate during weeks 1–8. The intensity was then increased to 60% of maximum heart rate from week 9. Heart rate was measured before and after exercise at every training session for risk management and estimation of the strength of training. The strength of aerobic exercise was adjusted by the height of the stair in stair stepping, walking speed, or weights put on participants' feet in endurance walking. Eleven of the 40 classes during the 6-month intervention period included approximately 20–30 minutes of consecutive outdoor walking. Muscle strength training was mainly performed using subjects' own weight; training equipment was not used (eg, knee extension, calf raise, squat). Postural balance exercise (such as tandem walking and side walking on balance boards) was also included in the program. There were five different widths of balance boards (4, 6, 8, 10 and 12 cm), which were narrowed progressively. Further, participants performed a combination of exercises (eg, circuit training including stair-stepping, endurance walking, and walking on balance boards). They also performed concurrent cognitive tasks during exercise (eg, walking while inventing a poem) because effects of dual tasks on brain activation have been reported.[13] Between individual training sessions, participants were invited to sit and rest for about 5 minutes. Participants were required to perform daily home-based muscle strength exercises and walking. These were self-monitored using a booklet and pedometer based on the concept of promoting exercise and behavior change.

Physical performance test to assess trainability

The TUG was used to assess physical performance.[9] The TUG involves rising from a chair, walking 3 meters, turning around, walking back to the chair, and sitting down. Participants were instructed to complete the task at their usual walking pace. The score for this test represents the time (in seconds) that the participant needed to complete the assessment. Lower times indicate better physical performance. The recorded TUG score was the lesser of the times measured in the two trials in order to exclude immediate change by learning effects from the measured value.[14] Licensed and well-trained physical therapists assessed the physical performance tests. Interrater reliability of TUG is very high in community-dwelling older adults (intraclass coefficient of 0.98).[15] Changes in TUG were calculated as trainability using the following formula:

(Post score – pre score)/pre score.[11]

Thus, a higher negative value represents greater improvement by exercise intervention.

Potential correlates

All measurements were performed before the intervention commenced. Demographic data were recorded, including age, gender, number of medications, and educational history. Depressive symptoms were measured using the 15-item Geriatric Depression Scale (GDS).[16]

All neuropsychological testing was conducted by well trained speech therapists. Each score was rechecked by one therapist who was blinded to all other participant data. General cognitive function was assessed with the Japanese version of 30-item Mini-Mental State Examination (MMSE),[17] the most frequently used cognitive screening measure in cognitive aging research, with good test-retest reliability (intraclass coefficient = 0.827).[18,19] Executive function was assessed using the Trail Making Test Part B (TMT-B).[20] For this task, participants were required to navigate a series of alternating numbers and letters, and connect them in alternating sequential order. In the Japanese version of the TMT-B, letters from the Roman alphabet are exchanged for Kana characters.[21] The time required to complete each task was recorded, where a higher time indicates a poorer performance. The TMT-B has demonstrated adequate test-retest reliability for use in longitudinal studies.[21]

The participants' muscle strength of knee extension was measured twice using a dynamometer (MDKKS, Molten Co, Ltd, Tokyo, Japan). The recorded strength score was the higher of the strength measurements (Nm/kg) in the two trials.[22]

Statistical analysis

The data were analyzed using the Statistical Package for Social Sciences version 19.0 for Windows (SPSS Inc, Chicago, IL). A probability level of $P < 0.05$ was considered to be statistically significant. Data were expressed as mean values and standard deviations. TUG scores were compared before and after intervention using the paired Student's *t*-test. The relationships between change in TUG score and potential correlates (measurements at baseline and attendance rate for exercise intervention) were investigated using Pearson's correlation. A stepwise multivariate linear regression model was used to examine whether potential predictors were independently associated with the change in TUG. Age, gender, and other variables that were significantly correlated with change in TUG were entered as independent variables.

Results

Table 1 shows the demographic and baseline clinical characteristics and attendance rate of the study participants. Mean adherence to the exercise program was 88.2%. TUG showed significant ($P < 0.001$) improvement between before