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Global cognition and 8-year survival among Japanese community-dwelling older adults

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Objective: We sought to examine the longitudinal relationship between cognitive function and all-cause mortality among Japanese community-dwelling older adults, using an 8-year prospective cohort study design with mortality surveillance.

Methods: A total of 454 men and 386 women, aged 70 years and older, participated in the study. The Mini Mental State Examination (MMSE) was administered to assess global cognition. The total MMSE score and subscale scores were used as independent variables, and age, gender, education level, chronic disease, sensory deficit, depressive symptoms, and instrumental activities of daily living were used as covariates.

Results: During the follow-up period, 191 subjects (139 men and 52 women) died, and 64 subjects (31 men and 33 women) moved to a different region of Japan and were lost to follow-up. Use of the multivariate Cox proportional hazards model, adjusted for potential confounders, showed that global cognition was significantly and independently associated with mortality (hazard ratio [HR] = 1.59, 95% confidence interval [CI]: 1.14–2.23 and HR = 2.81, 95% CI: 1.77–4.36 for the middle [24–27 points] and lowest [0–23 points] categories, respectively). Among the MMSE subscales, *place orientation* (HR = 1.57, 95% CI: 1.09–2.25), *calculation* (HR = 1.67, 95% CI: 1.18–2.35), and *delayed recall* (HR = 1.42, 95% CI: 1.03–1.96), were also significantly and independently associated with mortality.

Conclusions: Our study suggests that among older individuals, those with lower levels of cognitive function are more likely to have a shorter lifespan compared with those with higher cognitive functioning.

Key words: all-cause mortality; cognition; community older adults; Mini Mental State Examination (MMSE)
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Introduction

Cognitive function is an important contributor to health among older adults. A number of recent studies have examined the longitudinal association between cognitive function and mortality among older adults. Among the different domains of cognitive function, episodic memory (Small and Backman, 1997; Portin *et al.*, 2001), executive function (Johnson *et al.*, 2007; Lavery *et al.*, 2009), and information processing speed (Smits *et al.*, 1999; Rosano *et al.*, 2008; Lavery *et al.*, 2009) have been shown to predict mortality among older adults living in a community setting. Global cognition measured by the Mini Mental State Examination (MMSE) (Folstein *et al.*, 1975) also predicts mortality (Kelman *et al.*, 1994; Bruce *et al.*, 1995; Gussekloo *et al.*, 1997; Fredman *et al.*, 1999; Korten *et al.*, 1999; Andersen *et al.*, 2002; Nguyen *et al.*, 2003). The MMSE is the most widely used test for objectively measuring cognitive function, and its validity and reliability have been confirmed (Tombaugh and McIntyre, 1992).

Only a few studies have examined the association between MMSE subscales and mortality. A study (Villarejo *et al.*, 2011) reported a longitudinal association between the three-word delayed recall task of the MMSE and all-cause mortality among non-demented older individuals. However, longitudinal associations between the other MMSE subscales and mortality are unclear. A careful examination of the relationship between MMSE subscales and mortality should help facilitate the prediction of early death among older adults in epidemiological surveys in the community and in clinical settings.

In this study, we examined the longitudinal relationship between cognitive performance, based on the MMSE, and all-cause mortality among Japanese community-dwelling older adults, using an 8-year surveillance of mortality.

Methods

Participants

The data for the present study were acquired from mass health checkups for community-dwelling older adults (*Otasha-Kenshin*) (Iwasa *et al.*, 2007; Suzuki *et al.*, 2008), conducted in 2002 by the Tokyo Metropolitan Institute of Gerontology. The Japanese term *Otasha-Kenshin* translates into "health checkups for accomplishing successful aging." The study was conducted in Itabashi ward in northern Tokyo, Japan, and we were granted access to the municipal resident registration files by the Itabashi ward authorities. Participants took part in a face-to-face interview, to establish the baseline, with trained research assistants. The study was approved by the Ethics Committee of the Tokyo Metropolitan Institute of Gerontology. As of 2002, a sample of 1945 residents (aged 70–84 years) was randomly obtained from the municipal resident registration files. We sent a letter asking them to participate in checkups. Eight hundred forty-seven individuals agreed to participate (43.5% participation rate). There was a lower proportion of women compared with men who participated in the baseline survey (46.2% *vs.* 51.9%, respectively, $p = 0.012$). Participants and non-participants were almost identical in age (76.2 *vs.* 76.4 years, respectively, $p = 0.233$).

Of those who participated in the baseline survey, seven were excluded from the analysis: one subject had missing educational information and six had missing MMSE scores. In total, 840 participants (454 men and 386 women, mean age of 76.2 ± 3.6 years at baseline) with complete data sets were included, and their data F1 were used for the 8-year mortality surveillance (Figure 1).

Mortality follow-up

Because the survey was completed at the end of 2002, we defined January 1, 2003 as the baseline for the follow-up period in the present study. Thus, we carried out an 8-year mortality surveillance, from January 1, 2003 to January 1, 2011.

Current residency in Itabashi ward on January 1, 2011 was determined using the municipal resident registration files for Itabashi ward. The dates on which residents moved away or died were identified from the registration files and used to calculate survival times. The certifications and dates of all decedents and those moving away were obtained from the Itabashi ward authorities.

The dependent variable in the analyses was survival time, calculated as the number of days between the baseline (i.e., January 1, 2003) and the date of death or censoring (including survivors and dropouts due to migration from Itabashi ward). Survivors were censored on January 1, 2011. Dropouts were censored on the date of migration from Itabashi ward.

We used all-cause mortality as the dependent variable because we did not have any data regarding the cause of death among the decedents.

Measurements of cognitive performance

We used the MMSE (Folstein *et al.*, 1975) to assess cognitive function among older adults. The MMSE is the most widely used test of global cognitive function and has been used in numerous studies (Tombaugh and McIntyre, 1992; Dewey and Saz, 2001; Xu *et al.*, 2002; Inagaki *et al.*, 2009). The MMSE includes 12 test items that objectively assess different cognitive domains: (1) *time orientation* (5 points); (2) *place orientation* (5 points); (3) *registration* of three words (3 points); (4a) *calculation* (mentally subtracting seven iteratively from 100, 5 points); (4b) *reverse spelling* (mentally spelling backwards a word presented auditorily); (5) *delayed recall* of the three words presented earlier (3 points); (6) *naming objects* (2 points); (7) *repeating a sentence* (1 point); (8) *listening and obeying* (following a three-stage mmand, 3 points); (9) *reading and obeying* (following a message printed on a card, 1 point); (10) *writing sentences* (1 point); and (11) *copying figures* (copying figures on a sheet of paper, 1 point). Item scores were summed to give the total MMSE score (ranging between 0 and 30), with higher scores reflecting a higher level of global cognitive performance. Although in the original MMSE procedure (Folstein *et al.* 1975), item 4b, *reverse spelling*, was conducted only if participants refused to perform item 4a, *calculation*, both items were implemented in this study. As previously reported (Holtsberg, *et al.* 1995),

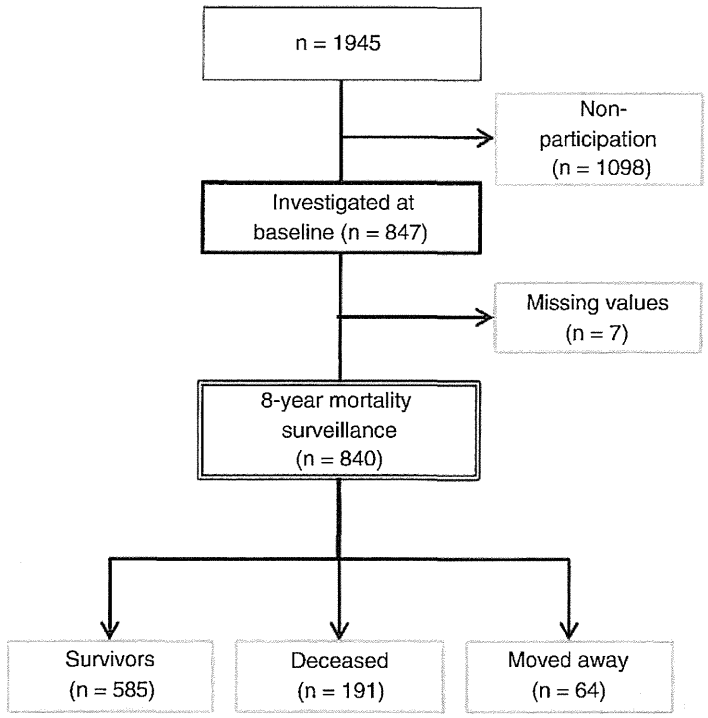

Figure 1 Study sample in the analysis.

Colour online, B&W in print

the higher of the two scores from item 4a, *calculation*, and item 4b, *reverse spelling*, was used for computing the total MMSE score. Thus, in this study, the number of participants for item 4a differed from those of other items because some subjects refused to perform this task ($n=25$).

We divided the MMSE total score into the following three categories: low (0–23 points), middle (24–27points), and high (28–30 points), based on a previous protocol (Gussekloo *et al.*, 1997; Xu *et al.*, 2002). Subjects obtaining 0–23 points were considered to possibly have a cognitive impairment (Tombaugh and McIntyre, 1992).

When analyzing the MMSE subscales, all subscale scores were dichotomized as either completely correct or incorrect according to the score in each subscale. This method was based on a previous protocol (Ishizaki *et al.*, 1998). For example, for the *time orientation* subscale (max = 5 points), participants who scored 5 were considered to have responded correctly and were given 1 point. Those who scored 4 or lower were classified as being incorrect and were given 0 point.

Other measurements

Data for baseline characteristics were used as covariates in the analysis to identify independent associations between cognitive performance and mortality, and to describe the characteristics of the study participants. Data for age, gender, education level, chronic disease, sensory deficit, depressive symptoms (Sheehan, *et al.*, 1998), instrumental activities of daily living (IADL, measured according to the Tokyo Metropolitan Institute of Gerontology Index of Competence [Koyano, *et al.*, 1991]), and self-rated health were included. Chronic disease was self-reported by the participants. Chronic disease was defined as experiencing at least one of the following diseases: history of stroke, heart disease, or diabetes mellitus. Sensory deficit was self-reported by the participants and was defined as experiencing at least one of the following: hearing loss or eyesight problems. To assess IADL, participants were asked to judge whether they were independent with respect to the five daily IADL tasks (e.g., using public transportation and preparing meals) (Koyano *et al.*, 1991). Higher scores reflect a higher level of functioning in IADL. In this study, a cut-off score of 4/5 (meaning that scores of 4 and below were classified as IADL dependent) was used to judge whether participants were dependent with respect to IADL (Ishizaki *et al.*, 2006).

Statistical analysis

We carried out χ^2 tests for categorical variables and analysis of variance for continuous variables to examine differences in baseline characteristics between groups (i.e., survivors *versus* deceased *versus* dropouts). We also carried out χ^2 tests to examine differences in the MMSE subscale scores between the groups. Cox proportional hazards models, controlling for age, gender, education level, chronic disease, sensory deficit, depressive symptoms, and IADL, were used to test the independent relationships between each cognitive performance and all-cause mortality. All statistical procedures were
Q2 performed using SPSS 19.0 for Windows.

Results

During the 8-year follow-up, of the 840 adults, 191 (139 men and 52 women) died and 64 (31 men and 33 women) moved to a different region of Japan and were lost to follow-up.

T1 Table 1 shows the characteristics of the members in the follow-up cohort, collected in 2002, including age, gender, education level, chronic disease, sensory deficit, depressive symptoms, IADL, the distribution of MMSE scores, and mean duration of follow-up. Deceased individuals were more likely to be older ($p < 0.001$), men ($p < 0.001$), and have chronic diseases ($p = 0.012$). They were also more likely to have a lower IADL score ($p < 0.001$), exhibit lower health status ($p = 0.002$), display lower sensory function ($p < 0.001$), and have lower MMSE scores ($p < 0.001$), compared with survivors/dropouts.

Table 2 shows the MMSE subscale scores. Deceased T2
individuals had lower scores in the seven tasks—*time orientation, place orientation, calculation, reverse spelling, delayed recall, repeated sentences*, and *copying figures*. Because the number who answered items incorrectly in subscales 6 (*naming objects*) and 9 (*reading and obeying*) was so small, we did not conducted any analysis on those subscales.

Figure 2 shows the Kaplan–Meier survival curves F2
corresponding to the relationship between global cognition and mortality. The risk of mortality was significantly higher for lower functioning individuals than for higher functioning individuals (log-rank test: $p < 0.001$).

Table 3 shows the independent association between T3
global cognition and mortality. Following multivariate Cox regression analysis, adjusted for the potential confounders cited earlier, global cognition (hazard ratio [HR] = 1.59, 95% confidence interval [CI] = 1.14 to 2.23 and HR = 2.81, 95% CI = 1.77 to 4.36 for the middle [24–27 points] and lowest [0–23 points] categories, respectively) was significantly and independently associated with mortality.

Table 4 shows the independent associations between T4
MMSE subscale scores and mortality. Following multivariate Cox regression analysis, adjusted for the potential confounders cited earlier, *time orientation* (HR = 1.56, 95% CI: 1.12 to 2.18), *place orientation* (HR = 1.87, 95% CI: 1.37 to 2.56), *calculation* (HR = 1.81, 95% CI: 1.30 to 2.52), *reverse spelling* (HR = 1.42, 95% CI: 1.06 to 1.90), *delayed recall*

Table 1 Distribution of participants' characteristics at baseline ($N = 840$)

	Survivors ($n = 585$)	Deceased ($n = 191$)	Dropouts ($n = 64$)	p-value[b]
Age, mean ± SD (years)	75.6 ± 3.4	77.6 ± 3.8	76.5 ± 4.0	<0.001
Gender (women), *n* (%)	301 (51.5)	52 (27.2)	33 (51.6)	<0.001
Number of years of education, mean ± SD (years)	10.6 ± 2.9	10.9 ± 3.4	10.1 ± 3.7	0.235
Chronic diseases (present), *n* (%)[a]	206 (35.2)	86 (45.0)	31 (48.4)	0.012
Instrumental activities of daily living (dependent), *n* (%)	72 (12.3)	52 (27.2)	9 (14.1)	<0.001
Self-rated health (fair/poor), *n* (%)	108 (18.5)	58 (30.7)	15 (23.4)	0.002
Sensory deficit, *n* (%)	62 (10.6)	42 (22.0)	4 (6.3)	<0.001
Depressive symptoms, *n* (%)	12 (2.1)	7 (3.7)	1 (1.6)	0.404
MMSE, mean ± SD (scores)	28.3 ± 2.1	26.9 ± 3.2	27.9 ± 2.5	<0.001
Duration of follow-up, mean ± SD (years)[c]	8.0	4.7 (2.0)	3.8 (2.2)	–

MMSE, Mini Mental State Examination.
[a]Chronic disease was defined as having at least one of the following diseases: stroke, heart disease, or diabetes mellitus.
[b]χ^2 tests for categorical variables and analysis of variance for continuous variables were used to examine differences in baseline characteristics between groups (survivors *versus* deceased *versus* dropouts).
[c]All survivors were followed up for 8 years (i.e., from January 1, 2003 to January 1, 2011).

Table 2 Number of participants who answered incorrectly on each subscales of the MMSE ($N = 840$)[a]

	Survivors ($n = 585$)	Deceased ($n = 191$)	Dropouts ($n = 64$)	p-value[b]
1. Time orientation, n (%)	81 (13.8)	50 (26.2)	13 (20.3)	<0.001
2. Place orientation, n (%)	103 (17.6)	63 (33.0)	16 (25.0)	<0.001
3. Registration (immediate recall), n (%)	10 (1.7)	7 (3.7)	2 (3.1)	0.256
4a. Calculation, n (%)[c]	330 (57.8)	134 (73.2)	32 (52.5)	<0.001
4b. Reverse spelling, n (%)	205 (35.0)	89 (46.6)	25 (39.1)	0.017
5. Delayed recall, n (%)	257 (43.9)	120 (62.8)	41 (64.1)	<0.001
6. Naming objects, n (%)	3 (0.5)	1 (0.5)	3 (4.7)	–
7. Repeating a sentence, n (%)	40 (6.8)	29 (15.2)	5 (7.8)	0.002
8. Listening and obeying, n (%)	5 (0.9)	5 (2.6)	1 (1.6)	0.174
9. Reading and obeying, n (%)	3 (0.5)	3 (1.6)	1 (1.6)	–
10. Writing sentences, n (%)	32 (5.5)	15 (7.9)	6 (9.4)	0.289
11. Copying figures, n (%)	30 (5.1)	19 (9.9)	6 (9.4)	0.041

MMSE, Mini Mental State Examination.

[a]When analyzing the MMSE subscales, all MMSE subscale scores were dichotomized as either correct or incorrect, according to the score for each subscale.

[b]χ^2 tests were used to examine differences in number (%) of participants who answered MMSE subscale items incorrectly. Because the number who answered items incorrectly in subscales 6 and 9 was so small, we did not conducted any analysis on those subscales.

[c]The number of participants for item 4a (*calculation*) ($n = 815$) differed from those for other items because some subjects refused to perform this task ($n = 25$).

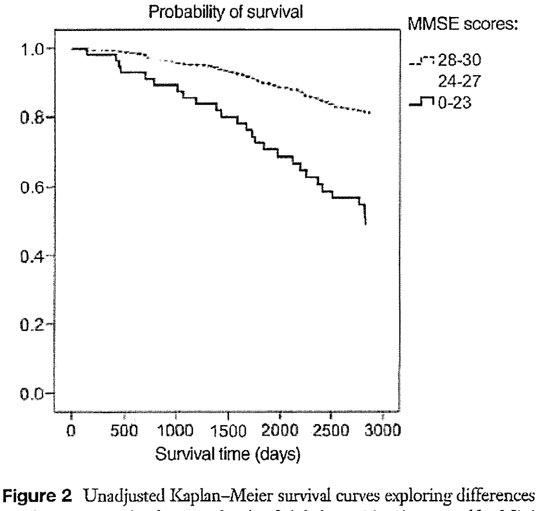

Figure 2 Unadjusted Kaplan–Meier survival curves exploring differences in all-cause mortality between levels of global cognition (measured by Mini Mental State Examination [MMSE]) at baseline over the 8-year follow-up period. Risk of mortality significantly varied according to the level of global cognition (log-rank test: $p < 0.001$). The vertical axis indicates probability of survival. The horizontal axis indicates survival time (days).

(HR = 1.65, 95% CI: 1.22 to 2.25), *repeating a sentence* (HR = 1.53, 95% CI: 1.02 to 2.30), and *copying figures* (HR = 1.95, 95% CI: 1.20 to 3.15) were significantly and independently associated with mortality. Among the subscales, *registration, naming objects, listening and obeying, reading and obeying,* and *writing sentences* were not analyzed because these subscale scores were not associated significantly with mortality in the univariate analyses (Table 3).

To examine whether the relationships between cognitive performance on the MMSE subscales and mortality were affected by cognitive impairment at baseline, we performed the aforementioned analysis excluding possible cases of cognitive impairment based on the MMSE total score. We used a cut-off score of 24, meaning that scores of 23 and below were classified as possible cognitive impairment (Tombaugh and McIntyre 1992) ($n = 57$). The results revealed that, after excluding subjects with a score of 23 or below, the association of *place orientation* (HR = 1.57, 95% CI: 1.09 to 2.25), *calculation* (HR = 1.67, 95% CI: 1.18 to 2.35), and *delayed recall* (HR = 1.42, 95% CI: 1.03 to 1.96) with mortality remained significant.

Table 3 Adjusted hazard ratios of all-cause mortality by MMSE total score ($N = 840$)[a]

MMSE total score	N	Deceased	Hazard ratio (95% confidence interval)	p-value
28–30 (ref.)	588	107	1	
24–27	195	57	1.59 (1.14–2.23)	0.007
0–23	57	27	2.81 (1.79–4.36)	<0.001

MMSE, Mini Mental State Examination.

[a]Adjusted for baseline characteristics (including age, gender, education level, chronic disease, sensory deficit, depressive symptoms, and instrumental activities of daily living).

Table 4 Adjusted hazard ratios of all-cause mortality for each subscale of the MMSE[a,b]

	Total ($n = 840$)				Individuals with no cognitive impairment ($n = 783$)[c]			
	N	Deceased	Hazard ratio (95% confidence interval)	*p*-value	*N*	Deceased	Hazard ratio (95% confidence interval)	*p*-value
1. Time orientation								
Correct (ref.)	696	141	1		679	135	1	
Incorrect	144	50	1.56 (1.12–2.18)	0.009	104	29	1.24 (0.82–1.87)	0.303
2. Place orientation								
Correct (ref.)	658	128	1		637	122	1	
Incorrect	182	63	1.87 (1.37–2.56)	<0.001	146	42	1.57 (1.09–2.25)	0.013
4a. Calculation[d]								
Correct (ref.)	319	49	1		314	47	1	
Incorrect	496	134	1.81 (1.30–2.52)	<0.001	456	111	1.67 (1.18–2.35)	0.004
4b. Reverse spelling								
Correct (ref.)	521	102	1		511	96	1	
Incorrect	319	89	1.42 (1.06–1.90)	0.002	272	68	1.34 (0.97–1.87)	0.079
5. Delayed recall								
Correct (ref.)	422	71	1		417	71	1	
Incorrect	418	120	1.65 (1.22–2.25)	<0.001	366	93	1.42 (1.03–1.96)	0.034
7. Repeating a sentence								
Correct (ref.)	766	162	1		733	145	1	
Incorrect	74	29	1.53 (1.02–2.30)	0.037	50	19	1.44 (0.88–2.38)	0.148
11. Copying figures								
Correct (ref.)	785	172	1		742	154	1	
Incorrect	55	19	1.95 (1.20–3.15)	0.007	41	10	1.31 (0.68–2.50)	0.416

MMSE, Mini Mental State Examination.
[a]Adjusted for baseline characteristics (including age, gender, education level, chronic disease, sensory deficit, depressive symptoms, and instrumental activities of daily living).
[b]All MMSE subscale scores were dichotomized into either completely correct or incorrect, according to the score in each subscale.
[c]Individuals with possible cognitive impairment (MMSE < 24) were excluded.
[d]The number of participants for the item 4a (*calculation*) differed from those for other items because some subjects refused to perform this task. Total sample analysis, $n = 815$; analysis excludes individuals with cognitive impairment ($n = 770$).

Discussion

In this study, we examined the relationship between cognitive performance and all-cause mortality among community-dwelling older people in Japan. Our findings indicate that global cognitive function (measured using the MMSE) predicts mortality after adjusting for potential confounders, such as age, gender, education level, chronic disease, sensory deficit, depressive symptoms, and IADL. In addition, among the MMSE subscales, *place orientation*, *calculation*, and *delayed recall* were significantly and independently associated with mortality. Our study suggests that older individuals with lower levels of cognitive function are more likely to have shorter lives, based on the 8-year follow-up, compared with those with higher cognitive functioning.

Our findings are similar to the results of previous studies showing a relationship between global cognition (measured using the MMSE) and mortality among community-dwelling older adults (Kelman *et al.*, 1994; Bruce *et al.*, 1995; Gussekloo *et al.*, 1997; Fredman *et al.*, 1999; Korten *et al.*, 1999; Andersen *et al.*, 2002; Nguyen *et al.*, 2003). The findings of these studies and our present report suggest that global cognition is a predictor of mortality among community-dwelling older adults. In addition, the association between global cognition and mortality was significant not only in individuals with possible cognitive impairment (i.e., MMSE total score of 0–23 points) but also in individuals exhibiting a mild deficit in global cognition (i.e., MMSE score of 24–27 points), which is consistent with the previous study (Gussekloo *et al.*, 1997). Previous studies indicate that individuals with cognitive impairment are more likely to have shorter lives, compared with those who are not cognitively impaired (Dewey and Saz, 2001). Our study also confirmed that older individuals who exhibit a mild deficit in global cognition are more likely to have a shorter lifespan, compared with those who are cognitively intact.

We speculate that there are four possible reasons why individuals who exhibited a mild deficit in global cognition (i.e., MMSE score of 24–27 points) were more likely to have shorter lives in this study. The first possible reason is the presence of potential cases of dementia. We divided participants into two groups, using a cut-off score of 24 in the MMSE, and regarded those who had 23 points or lower as having a possible cognitive impairment. A meta-analytic study for the accuracy of the MMSE for the detection of dementia (Mitchell, 2009) reported that the sensitivity and specificity were 79.8% and 81.3% in memory clinic settings, respectively, and that the sensitivity and specificity were 85.1% and 85.5% in non-clinical community settings, respectively. This indicates that the MMSE alone has modest accuracy for dementia diagnosis. As dementia diagnosis was not conducted by a specialist in our study, we cannot exclude the possibility that potential cases of dementia, who generally have poor survival rates (Dewey and Saz, 2001), may have been accidentally included in the group exhibiting a mild deficit in global cognition.

The second possible reason is that individuals who exhibit a mild deficit in global cognition may represent individuals with *mild cognitive impairment* (MCI) (Petersen *et al.*, 2001). Because individuals with MCI are prone to develop dementia (Kluger *et al.*, 1999), they may also be more likely to have a shorter lifespan. In addition, recent studies have demonstrated that individuals with MCI *per se* are more likely to have a shorter lifespan (Guehne *et al.*, 2006).

The third possible reason is physical health status. Cognitive performance among older adults is prone to be affected by physical health status (Tombaugh and McIntyre, 1992), such as functional disability, hearing loss, and chronic disease, which are all closely related to mortality (Korten *et al.*, 1999; Ostbye *et al.*, 1999; Kattainen *et al.*, 2004; Spiers *et al.*, 2005; Takata *et al.*, 2007; Lee *et al.*, 2008). Thus, individuals who exhibited a mild deficit in global cognition (MMSE scores of 24–27) may be likely to have poor physical health, and consequently, they may be more likely to have shorter lives as well. However, because we conducted a multivariate analysis, adjusted for such confounders (including, IADL, sensory function, and chronic disease), to examine the independent associations between cognition and mortality, this possibility is unlikely.

The fourth possible reason may be related to *health literacy*. Individuals who exhibit a mild deficit in global cognition may be less likely in their everyday life to seek appropriate medical care and health information to promote and maintain good health. Thus, they may tend to have a shorter lifespan, especially among older adults. Recent public health studies have focused on health literacy, which are skills that determine the motivation and ability of individuals to gain access to, understand, and use health information (Nutbeam, 1998). Health literacy was reportedly positively associated with cognitive function among older adults (McDougall *et al.*, 2012). In addition, older adults who have low cognitive function were less likely to take part in health surveys (Launer *et al.*, 1994) and checkups (Yoshida *et al.*, 2008) conducted in the community, suggesting that they are less likely to be motivated to keep fit. Therefore, it is possible that because of poor health literacy, individuals who exhibit a mild deficit in global cognition may be more likely to have a shorter lifespan.

The MMSE subscale scores including *time orientation*, *place orientation*, *calculation*, *reverse spelling*, *delayed recall*, *repeating a sentence*, and *copying figures* were significantly and independently associated with mortality, suggesting that these subscales individually can predict early death among older adults. The associations of the MMSE subscales *place orientation*, *calculation*, and *delayed recall* with mortality remained statistically significant after excluding subjects with possible cognitive impairment, defined by a cut-off MMSE score of 23 (Tombaugh and McIntyre, 1992). This finding suggests that these items predict mortality independently of cognitive impairment. In contrast, the associations of the subscales *time orientation*, *reverse spelling*, *repeating a sentence*, and *copying figures* with mortality diminished when subjects who had possible cognitive impairment were excluded from the analyses. These findings suggest that the associations between these four tasks and mortality are significantly affected by cognitive impairment. That is, performance in the four tasks may predict mortality among older adults, but apparently, only in combination with cognitive impairment. As mentioned earlier, because we did not conduct dementia diagnosis at baseline in this study, we cannot completely exclude the influence of possible cases of dementia. Therefore, our preceding interpretations need to be further investigated.

The generalization of our findings may also be limited for two reasons: First, the representativeness of the sample in this study may have been restricted. The participation rate at baseline was relatively low (43.2% participation) because we acquired the data by administering mass health checkups. Therefore, participants in our study may differ in health characteristics from non-participants because of self-selection bias (Iwasa *et al.*, 2007). Second, the relationship between cognitive performance on the MMSE items and mortality found in this study might differ from those in Western countries. Although the validity of the Japanese version of the MMSE has already been confirmed and its mean scores are remarkably similar to those of the Westerners (Ishizaki, *et al.*, 1998), a recent study pointed out differences in performance on subscales of the MMSE between Japanese and a US cohort

(Dodge *et al.*, 2009). We therefore should attend to these previous findings when considering the generalizability of our findings.

Conclusions

In this study, we examined the relationship between cognitive performance and all-cause mortality among community-dwelling older individuals in Japan. Our findings indicated that global cognition (assessed using the MMSE) predicted mortality after adjusting for potential confounders. Among the MMSE subscales, *place orientation*, *calculation*, and *delayed recall* were significantly and independently associated with mortality. Given that the MMSE is relatively easy to administer, it could be of value during annual health checkups and in primary care settings to detect risk of early death in the community older population. Our results may thus help to facilitate the development of longevity-promoting strategies, and they underscore the importance of early detection and treatment of cognitive decline in older adults. Future research using a longer continuous follow-up survey would be of value to elucidate the relationship between cognition and mortality more clearly, with accompanying data regarding cause of death and professional diagnosis of possible dementia.

Conflicts of interest

None declared.

Author contributions

HI engaged in study conceptualization, data collection, data analysis, and interpretation of results, in addition to writing and editing the manuscript. YY, TS, HK, and HY contributed to data collection, interpretation of results, and discussions on the manuscript. IK contributed to interpretation of results and discussions on the manuscript.

Key points

- This study found the longitudinal relationship between global cognition (measured by the MMSE) and all-cause mortality among community older adults.
- Among the MMSE subscales, *place orientation*, *calculation*, and *delayed recall* were also associated with mortality.

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シート式圧力センサーを用いて計測した歩容左右差による年齢の推定

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ESTIMATION OF AGE FROM THE DIFFERENCE BETWEEN LEFT AND RIGHT WALKING PARAMETERS MEASURED BY A WALK ANALYSIS SYSTEM WITH PLATE SENSORS.

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Abstract

We analyzed walking parameters using by a walk analysis system with plate sensors. The subjects included healthy women from age 21 to 88, who were able to walk without assistance. The results of correlation analysis between age and walk showed that with advancing age, walk ratio was reduced, step length decreased, the difference between left and right walking angle, and stance phase increased. A multivariate analysis was performed for each walking parameter as the objective variable, and age as the explanatory variable. As a result, walk ratio, and the difference between left and right walking angle were significant explanatory variables. Description of the regression rate was 38%.

キーワード: 歩容変数, 左右差, 年齢, 圧力センサー
Key words: *walking parameter, laterality, age, plate sensor*

緒 言

ヒトは二足歩行を獲得したことにより、前肢を利用した多様な生活を送ることが可能となった。二足歩行の開始は約600～700万年前にさかのぼる[1]。人類が二足歩行を獲得したことで、高いところにある果実を摂食し[2]、家族に手で食料を運び[3]、繁殖適応度が高まり[4]、日光への暴露面積を小さくし[5]、日中の活動時間を長くし[6]、捕食者を威嚇する[7]など多くの利点が得られた。個体発生としては、出生後1歳3ヶ月頃から幼児型歩行が始まり、3歳頃に成人型歩行に発達し、歩容の成熟に合わせて生活も多様化していく[8]。

一旦成熟した多くの歩行機能は、加齢に伴い低下することが古くから報告されてきた[9]。歩行速度は、歩幅と歩調の低下に伴い[10] 50歳から徐々に低下し、62歳頃からは急激に低下すると言われている[11]。また、加齢に伴い歩幅の低下[12]、歩隔の増加[13]、1歩行周期中の立脚期割合、両脚支持期割合も増加し[14][15]、足関節[16]、膝関節[15]、股関節[17]の可動域が狭まり、各関節モーメントは低下する[12]。

加齢に関する歩行研究は、予防医学的に広く用いられている。高齢者の疫学研究において、歩行速度の遅い高齢者は、脳血管系疾患リスク[18]やADL低下リスク[19]が増加することが知られており、スクリーニングや、介入の効果検証に歩行速度の評価は重要視されている。

しかし、今まで測定が困難であった左右脚の機能差や左右差の加齢変化については報告が少なく、実用に至っていない。歩幅、立脚時間、遊脚時間の歩容変数は左右対称性が高いという報告[20]や、右脚は推進脚、左脚は支持脚として左右脚には機能差があるとする報告[21]もあるが、被験者の負担が大きいモーションキャプチャを使用して左右差を検出していたため、例数も少なく検証が必要である。

そこで本報告では、計測による心理、身体ストレスが少なく、時間的及び空間的変数を左右別に取得できるシート式圧力センサー[22]を用いて、第一に左右差を含めた歩容変数と年齢の相関性を検討し、第二に左右差を含めた代表的な歩容変数から年齢を推定する式を作成した。

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方　　法

＜全体プロトコール＞

歩容測定会の試験内容は事前に花王株式会社および東京都健康長寿医療研究センターの倫理委員会の承認を得た。試験参加に同意した東京近郊に在住の21歳から88歳までの独立歩行が可能な成人女性353名の自由歩行を圧力シートにより解析し、年齢と歩容変数の相関性を検証した。被験者の平均身長±標準偏差は149.5±7.1cm、平均体重±標準偏差は49.2±8.3kg であった。また、足圧による歩容変数を計測するため、著しい足部・足趾変形を有する方は対象者から除外した。

＜歩容測定＞

10m の歩行路の中央2.4m にシート式圧力センサー型の歩行計測器（ウォーク way：アニマ社製）を設置した。服装はコートやスカートなど歩行を制限する服装は避け、普段使用している服装を着用し、シューズを脱いだ靴下のみの測定条件とした。歩き方は、「いつもどおりに歩いてください」と指示し、自由歩行を測定した。歩容計測回数は、測定場の背景が与える対称性と、歩行の再現性を考慮し、4回計測した。1回の計測で検出されたシート内の歩を全て解析し、4回計測した平均値を代表値として解析した。

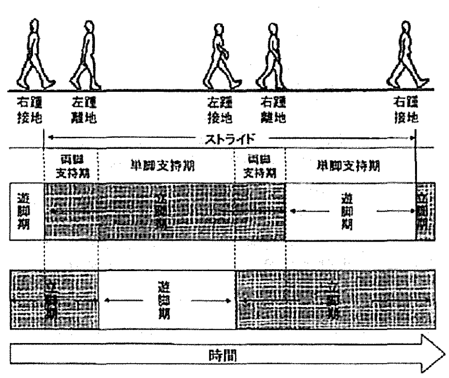

図1　歩容の時間因子（文献21より 引用一部改変）

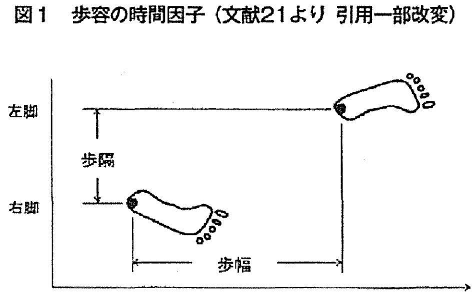

図2　歩容の空間因子における右_歩幅と右_歩隔（文献21より 引用一部改変）

＜歩容解析＞

歩容解析は、幅60cm x 長さ240cm のシートに 1 cm² 間隔に配置された14400個の圧センサーの時系列データから抽出した踵の点を基準点として、時間変数（図1）、空間変数（図2、3）を計算した[22]。表1に歩容変数とした42項目を示した。歩幅と歩隔は身長で除し、立脚期、遊脚期、両脚支持期は1歩行周期で除した相対的変数を用いて詳細を解析した。空間変数は後方の足で左右を決定した（図2，3）。表1の時間左右差と空間左右差は、左右歩容変数の差の絶対値とした。

＜統計処理＞

各項目について年齢との相関係数を求め、有意検定を実施した。左右差は対応のない t 検定を実施した。歩容変数と年齢の散布図を作成し、2次曲線で近似し、近似式と R^2 値を算出した。歩容指標で年齢を説明する式を作成するため、本試験の歩容指標と年齢相関分布図の結果から、各指標で加齢が顕著であった指標を選出した。歩容変数による年齢の推定には、年齢を目的変数、歩行比、相対歩幅、歩行角度差、相対立脚期を独立変数とし、多変量解析の重回帰分析を用いた。全ての解析は有意水準を5％とし、解析には SPSS ver20.0を用いた。

結　　果

1人の被験者に対して1回の測定で解析した歩数は平均が4.26回、標準偏差が0.82、最小歩数は3歩、最大歩数は7歩であった。42項目の歩容変数と身長、体重を加えた44項目の左右差および年齢相関結果を、表2に示した。左右差については、右相対両脚支持期が左に比べて有意に長く、右つま先角度は左に比べて有意に外側を向いていた。

最も年齢と相関の強い項目は相関係数 -0.603の身長

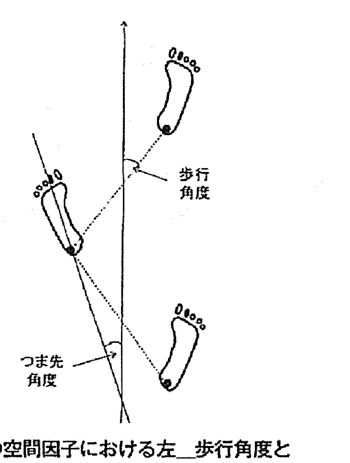

図3　歩容の空間因子における左_歩行角度と左_つま先角度（文献21より 引用一部改変）

表1　歩容解析した42項目と説明

分類	項目	説明
総合	スピード（km/h）	10m通常歩行中の中心2m区間の移動スピード
	ケーデンス（歩/分）	1分間の歩数
	歩行比（m/cpm）	歩幅をケーデンスで除した値。歩行効率を示す
時間	左_歩行周期（sec）	左足が着床してからもう1度着床するまでの時間
	右_歩行周期（sec）	右足が着床してからもう1度着床するまでの時間
	左_立脚期（sec）	左足が着床してから離床するまでの時間
	右_立脚期（sec）	右足が着床してから離床するまでの時間
	左_遊脚期（sec）	左足が離床してから着床するまでの時間
	右_遊脚期（sec）	右足が離床してから着床するまでの時間
	左_両脚支持期（sec）	左足が着床している後半で、右足も着床している時間
	右_両脚支持期（sec）	右足が着床している後半で、左足も着床している時間
	左_相対立脚期（%）	左_歩行周期に対する左_立脚期の割合
	右_相対立脚期（%）	右_歩行周期に対する右_立脚期の割合
	左_相対遊脚期（%）	左_歩行周期に対する左_遊脚期の割合
	右_相対遊脚期（%）	右_歩行周期に対する右_遊脚期の割合
	左_相対両脚支持期（%）	左_歩行周期に対する左_両脚支持期の割合
	右_相対両脚支持期（%）	右_歩行周期に対する右_両脚支持期の割合
空間	左_ストライド（cm）	左足が着床してからもう1度着床するまでの進行方向距離
	右_ストライド（cm）	右足が着床してからもう1度着床するまでの進行方向距離
	左_歩幅（cm）	左足が着床してから右足が着床するまでの進行方向距離
	右_歩幅（cm）	右足が着床してから左足が着床するまでの進行方向距離
	左_歩隔（cm）	左足が着床してから右足が着床するまでの側方方向距離
	右_歩隔（cm）	右足が着床してから左足が着床するまでの側方方向距離
	左_歩行角度（°）	左足が着床してから右足が着床するまでの直線と進行方向の角度
	右_歩行角度（°）	右足が着床してから左足が着床するまでの直線と進行方向の角度
	左_つま先角（°）	左足の傾きと進行方向の角度、内側がマイナス、外側がプラス
	右_つま先角（°）	右足の傾きと進行方向の角度、内側がマイナス、外側がプラス
	左_相対ストライド（%）	左_ストライドを身長で基準化したもの
	右_相対ストライド（%）	右_ストライドを身長で基準化したもの
	左_相対歩幅（%）	左_歩幅を身長で基準化したもの
	右_相対歩幅（%）	右_歩幅を身長で基準化したもの
	左_相対歩隔（%）	左_歩隔を身長で基準化したもの
	右_相対歩隔（%）	右_歩隔を身長で基準化したもの
時間左右差	歩行周期差（sec）	左_歩行周期と右_歩行周期の差
	立脚期差（%）	左_立脚期と右_立脚期の差を1歩行周期で基準化したもの
	遊脚期差（%）	左_遊脚期と右_遊脚期の差を1歩行周期で基準化したもの
	両脚支持期差（%）	左_両脚支持期と右_両脚支持期の差を1歩行周期で基準化したもの
空間左右差	ストライド差（%）	左_ストライドと右_ストライドの差を身長で基準化したもの
	歩幅差（%）	左_歩幅と右_歩幅の差を身長で基準化したもの
	歩隔差（%）	左_歩隔と右_歩隔の差を身長で基準化したもの
	歩行角度差（°）	左_歩行角度と右_歩行角度の差
	つま先角度差（°）	左_つま先角度と右_つま先角度の差

および歩行比であり、次いで相関係数-0.546の左_歩幅であった。44項目中36項目は年齢と有意に相関し、左右立脚期、左右歩隔、左つま先角度、立脚期差、遊脚期差、両脚支持期差の8項目は有意な相関が認められなかった。以降左右差の認められた両脚支持期とつま先角度以外の歩容変数は左右平均値を用いて解析した。

初めに身体情報を示した。身長は加齢に伴い低下を示し（図4A）、体重は50代にピークを持つ一時的な増加を認めたが、60代以降では減少した（図4B）。

次に、年齢と相関係数の高かった総合指標である歩行比と、歩行比の構成要素である平均歩幅とケーデンスを示した（図5）。歩行比は、加齢に伴い低下を示した（図5A）。平均歩幅は、40代にピークを持つ一時的な伸張を認めたが、50代以降は短縮した（図5B）。ケーデンスは加齢とともに増加を示した（図5C）。

空間指標の結果を示した。平均相対歩幅、平均相対歩隔および平均歩行角度と左右つま先角度の年齢の相関分布図を示した（図6）。平均相対歩幅は年齢があがるにつれて短縮を示し（図6A）、相対歩隔は50代にピークを持つ一時的な短縮を認めたが、その後は拡大した（図6B）。歩行角度は60代以降で拡大した（図6C）。また、つま先角度は右が左より外向きである傾向は確認されたが、顕著な加齢変化は認められな

表2　歩容の左右差と年齢相関

項目	平均±標準偏差	左右差（p）		年齢相関（r,p）		
身長（cm）	149.5 ± 7.1			-0.603	<0.001	***
体重（kg）	49.2 ± 8.3			-0.165	0.002	**
スピード（km/h）	4.10 ± 0.81			-0.418	<0.001	***
ケーデンス（歩/分）	122 ± 11.0			0.194	<0.001	***
歩行比（m/cpm）	0.0046 ± 0.0008			-0.603	<0.001	***
左＿歩行周期（sec）	0.991 ± 0.097	0.894	n.s.	-0.204	<0.001	***
右＿歩行周期（sec）	0.992 ± 0.101			-0.217	<0.001	***
左＿立脚期（sec）	0.60 ± 0.07	0.772	n.s.	-0.090	0.093	n.s.
右＿立脚期（sec）	0.60 ± 0.07			-0.061	0.255	n.s.
左＿遊脚期（sec）	0.39 ± 0.04	0.406	n.s.	-0.360	<0.001	***
右＿遊脚期（sec）	0.39 ± 0.04			-0.381	<0.001	***
左＿両脚支持期（sec）	0.11 ± 0.03	0.127	n.s.	0.150	0.005	**
右＿両脚支持期（sec）	0.11 ± 0.02			0.184	<0.001	***
左＿相対立脚期（%）	60.7 ± 2.2	0.431	n.s.	0.276	<0.001	***
右＿相対立脚期（%）	60.8 ± 2.3			0.398	<0.001	***
左＿相対遊脚期（%）	39.3 ± 2.2	0.064	n.s.	-0.276	<0.001	***
右＿相対遊脚期（%）	39.0 ± 2.2			-0.321	<0.001	***
左＿相対両脚支持期（%）	10.7 ± 1.9	0.040	*	0.316	<0.001	***
右＿相対両脚支持期（%）	10.9 ± 1.9			0.376	<0.001	***
左＿ストライド（cm）	110.4 ± 18.4	0.763	n.s.	-0.531	<0.001	***
右＿ストライド（cm）	110.8 ± 18.5			-0.521	<0.001	***
左＿歩幅（cm）	55.7 ± 9.2	0.567	n.s.	-0.546	<0.001	***
右＿歩幅（cm）	55.3 ± 9.6			-0.518	<0.001	***
左＿歩隔（cm）	8.0 ± 2.8	0.648	n.s.	0.096	0.072	n.s.
右＿歩隔（cm）	7.9 ± 2.7			0.099	0.062	n.s.
左＿歩高角度（°）	8.5 ± 3.7	0.908	n.s.	0.286	<0.001	***
右＿歩高角度（°）	8.6 ± 3.9			0.281	<0.001	***
左＿つま先角度（°）	0.8 ± 5.4	<0.001	***	0.094	0.079	n.s.
右＿つま先角度（°）	6.8 ± 6.6			0.157	0.003	**
左相対ストライド（%）	73.7 ± 10.8	0.736	n.s.	-0.398	<0.001	***
右相対ストライド（%）	74.0 ± 10.9			-0.388	<0.001	***
左相対歩幅（%）	37.2 ± 5.4	0.516	n.s.	-0.416	<0.001	***
右相対歩幅（%）	36.9 ± 5.7			-0.389	<0.001	***
左相対歩隔（%）	5.4 ± 2.0	0.668	n.s.	0.169	0.001	**
右相対歩隔（%）	5.3 ± 1.9			0.177	<0.001	***
歩行周期差（sec）	0.015 ± 0.25			-0.224	<0.001	***
立脚期差（%）	1.44 ± 1.8			-0.007	0.889	n.s.
遊脚期差（%）	1.44 ± 1.68			0.081	0.131	n.s.
両脚支持期差（%）	1.00 ± 0.85			0.094	0.078	n.s.
ストライド差（%）	1.63 ± 2.01			-0.249	<0.001	***
歩幅差（%）	1.45 ± 1.29			0.130	0.015	*
歩隔差（%）	0.90 ± 0.77			0.202	<0.001	***
歩行角度差（°）	1.50 ± 1.34			0.247	<0.001	***
つま先角度差（°）	4.59 ± 5.08			0.124	0.019	*

値は女性353名の平均値±標準偏差
左右差検定：対応のないｔ検定　＊ p<0.05、＊＊＊ p<0.001、n.s. not signinificant
年齢相関：相関係数ｒと有意検定　＊ p<0.05、＊＊ p<0.01、＊＊＊ p<0.001、n.s. not signinificant

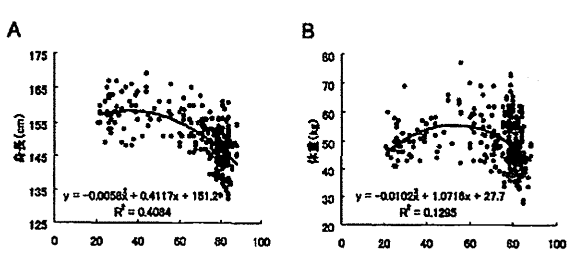

図4　身長、体重と年齢の分布
Ａ：身長と年齢分布　Ｂ：体重と年齢分布
Ｙ：２次曲線近似式、R²：重相関係数

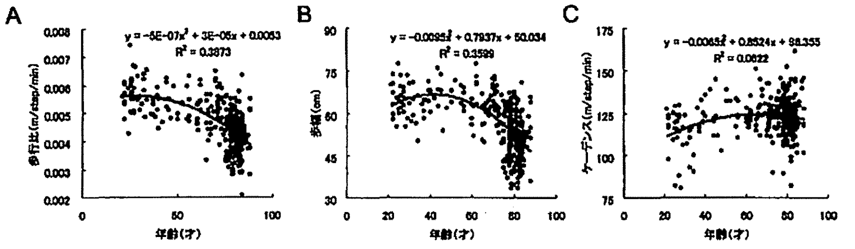

図５　歩行比、平均歩幅、ケーデンスと年齢の分布
Ａ：歩行比と年齢分布　Ｂ：平均歩幅と年齢分布　Ｃ：ケーデンスと年齢分布
Ｙ：２次曲線近似式、R²：重相関係数

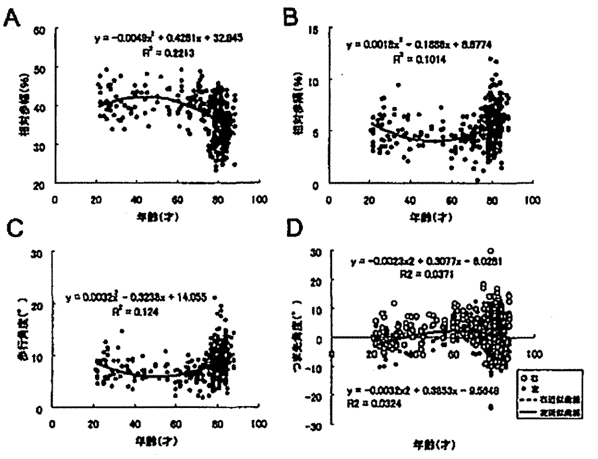

図６　平均相対歩幅、平均相対歩隔、平均歩行角度、左右つま先角度と年齢の分布
Ａ：平均相対歩幅と年齢分布　Ｂ：平均相対歩隔と年齢分布　Ｃ：平均歩行角度と年齢分布
Ｄ：左右つま先角度と年齢分布左（●）、右（○）、実線：左近似式（下）、点線：右近似式（上）
Ｙ：２次曲線近似式、R²：重相関係数

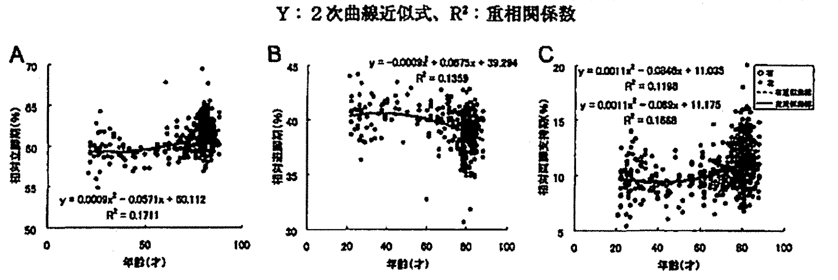

図７　平均相対立脚期、平均相対遊脚期、左右相対両脚支持期と年齢の分布
Ａ：平均相対立脚期と年齢分布　Ｂ：平均相対遊脚期と年齢分布
Ｃ：左右相対両脚支持期と年齢分布左（●）、右（○）、実線：左近似式（上）、点線：右近似式（上）
Ｙ：２次曲線近似式、R²：重相関係数

かった（図６D)。

時間指標の結果を示した。平均相対立脚期、平均相対遊脚期、左右相対両脚支持期と年齢の相関分布図を示した（図７）。加齢にともない平均相対立脚期は延長し、平均相対遊脚期は短縮した（図７A、B)。また、左右両脚支持期は加齢にともない延長した。(図７C)。

左右差指標を示した。歩幅差、歩隔差、歩行角度差を図８に示した。歩幅左右差、歩隔左右差および歩行角度左右差は、加齢にともない増加した（図８A、B、C)。

総合的な古典的歩行指標であるスピードの相関を図９に示した。スピードは年齢とともに低下を示した（図９）。

歩容指標で年齢を説明する式を作成するため選出された指標は、総合指標から歩行比、空間指標から平均相対歩幅、左右差指標から歩行角度差そして時間指標からは平均相対立脚期であった。これらの歩容指標を目的変数、年齢を説明変数とした重回帰分析を実施した（表３）。歩行比と歩行角度差は有意な説明変数とされ、得られた回帰式の説明率は38％（r=0.618、r²=0.382、補正 r²=0.375、s.e.=14.2）であった。

表３　多変量解析結果

変　数	調整済み係数	標準誤差	t 値	P-値	下限 95%	上限 95%
歩行比（m/cpm）	-11674	1731	-6.74	<0.001	-15078	-8270
平均立脚期（%）	0.990	0.552	1.79	0.0737	-0.0954	2.08
平均歩幅（%）	0.0448	0.182	0.246	0.806	-0.313	0.403
歩行角度差（°）	1.41	0.586	2.40	0.0168	0.255	2.56
切　片	59.3	38.1	1.56	0.121	-15.7	134

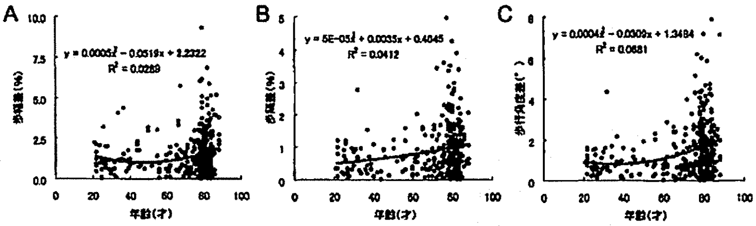

図８　歩幅差、歩隔差、歩行角度差と年齢の分布
A：歩幅差と年齢分布　B：歩隔差と年齢分布　C:歩行角度差と年齢分布
Y：２次曲線近似式、R^2：重相関係数

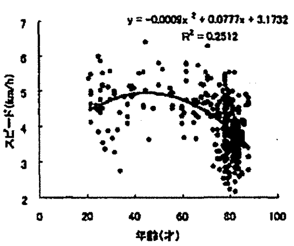

図９　スピードと年齢の相関分布
Y：２次曲線近似式、R^2：重相関係数

考　察

被験者の身体特徴の加齢変化は先行研究と一致し、標準的な加齢傾向の見られた集団であることが示された。まず初めに、身長は50代から90代にかけて経年的に低下傾向を示した。50代から90代の先行研究においても、男性は年間0.19cm、女性は年間0.41cm の身長低下が躯間長低下により認められたと報告されている[23]。次に、体重は50代にピークを持ちながらそれ以降は低下した。50代以降の体重低下は、高齢者に顕著な低体重、低筋力を特徴とするサルコペニア[24] や、虚弱[25] で引き起こされるといわれ、先行研究と一致している。

本試験の歩容変数と年齢の相関解析から、高齢者のスクリーニングにはスピード（r=-0.418）よりも歩行比（r=-0.603）が有用である可能性が示唆された。サルコペニアや虚弱を代表とする老年症候群の予備群をスクリーニングするため、これまでは多くの試験でスピードに着目してきた[26][27][28]。これは、スピードが老化に伴う下肢筋力の低下を原因とする歩幅の減少や体力低下と相関が高かったためである。スピードが歩幅とケーデンスの積で算出するのに対して、歩行比は歩幅とケーデンスの除で算出される。本試験結果では加齢による有意な歩幅の短縮（r=-0.546）とゆるやかなケーデンスの増加（r=0.194）を示したため、スピードに比べ、歩行比のほうが高い加齢相関を示した。歩行比は健常成人では0.006m/step/min となり、歩行効率を示す指標である[29] ことから、高齢者の歩行エネルギー効率の低下現象を的確にとらえたと考えられた。

また、相対両脚支持期は左脚に比べて右脚が長く、つま先角度は左脚に比べて右脚が外側を向くことが本試験で初めて明らかとなった。従来、歩容解析に用いられていたモーションキャプチャーシステムは被験者と解析者の負担を減らすため、片側計測が多く行われている[30]。これは、健常成人においては対称性が高いという報告を根拠としている[20]。しかし、本試験結果から、健常者においても全ての歩容変数の対称性が高いのではなく、少なくとも両脚支持期とつま先角度には左右機能差が存在することが明らかとなった。相対両脚支持期の延長は、先行研究においてバランス能力の低下を示す[14] ことから、本被験者の集団においては、左脚よりも右脚のバランス能力が低い可能性が示唆された。先行研究によると女性は男性よりも手足ともに右利きが多いとされているが、利き脚と脚力が相関する一方で、利き脚に関わらず右脚に比べて左脚の平行機能が高いと報告され[31]、本試験結果と一致した。また、つま先角度の左右機能差については先行報告がない。右脚のバランス能力の低下を前提とすると、つま先角度を外側に広げることにより、進行方向に対して横方向の安定性を増加させたと考えられるが、確認が必要である。

次いで、歩容の左右差と年齢について着目すると、

歩行周期差、ストライド差、歩幅差、歩隔差、歩行角度差とつま先角度差の６項目の左右差は加齢による有意な増加が認められた。先行研究において健常成人で対称性が高いとされていた歩幅[20]などで、本試験においては加齢による有意な左右差増加が確認された。このことは、老化現象である筋力低下に伴う歩幅低下とは別視点で老化指標となりうる可能性を示唆した。

さらに、左右差を含めた複数の項目で年齢を推定することにより、従来のスピードに依存した歩容評価よりも多角的な歩容評価が可能になった。多変量解析の結果から左右差を含む歩容変数を用いた有意な年齢推定式が作成されたためである。この推定式は、歩行効率を示す歩行比、空間変数である歩幅、時間変数である相対立脚期および左右差変数である歩行角度左右差といった質の異なる歩容変数を組み合わせ、多角的に歩容を評価している。その上、これら４つの歩容変数による推定年齢と実際の年齢の相関係数は r=0.618を示し、スピードと年齢の相関係数 r=-0.418を上回ることから、精度の向上も確認された。多角的な歩容の評価と精度の向上は、多様化した高齢者のスクリーニングに適している可能性が考えられ、予防医学的な貢献が期待できる。

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Effectiveness of exercise with or without thermal therapy for community-dwelling elderly Japanese women with non-specific knee pain: A randomized controlled trial

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HSGS

ABSTRACT

Knee pain is a common health problem in the elderly population, for which non-invasive treatments are recommended as a first line treatment in the management of knee pain. A randomized controlled trial was conducted to determine the effects of exercise with or without thermal therapy in community-dwelling elderly women with chronic knee pain. Women over 75 years of age with knee pain ($n = 150$) were randomly assigned into four groups: exercise (Ex) and heat/steam generating sheet (HSGS) ($n = 38$), Ex ($n = 37$), HSGS ($n = 38$), or health education (HE) ($n = 37$). The Ex group attended a 60-min comprehensive training program twice a week for 3-months. The HSGS group placed two sheets on the knee for five hours per day. Functional fitness, visual analog scale (VAS), and Japanese knee osteoarthritis measure (JKOM) were assessed at baseline and post-intervention. The results showed VAS improvements in the Ex + HSGS and HSGS groups. Total JKOM score, muscle strength, and functional mobility significantly improved in the Ex + HSGS group compared with the HE group. The odds ratio (OR) for VAS and functional mobility improvement was more than eight times as great in the Ex + HSGS group (OR = 8.60, 95% confidence interval (CI) = 2.82–32.73) compared with the education group. Ex or HSGS alone were insufficient in enhancing functional fitness or improving pain and quality of life. The combined effects of both Ex and heat therapy seems to have an added benefit of decreasing pain, improving physical function and increasing quality of life. Trial Registration Number: JMA-IIA00110.

1. Introduction

Knee pain is one of the most common knee problems experienced by elderly people (Hadler, 1992), and chronic knee pain has been associated with mobility limitations, and future dependence in activities of daily living (Davis, Ettinger, Neuhaus, & Mallon, 1991; Nishiwaki, Michikawa, Yamada, Eto, & Takebayashi, 2011). Risk factors including obesity, weakness of the knee extensor muscles, extreme physical activity levels (i.e. over-exercising, total sedentariness), and chronic diseases for knee pain are well documented (Jinks, Jordan, Blagojevic, & Croft, 2008; Lamb et al., 2000). The risk of developing knee pain is influenced by the presence of multiple risk factors (Dekker, Tola, Aufdemkampe, & Winckers, 1993; Jinks et al., 2008; Lamb et al., 2000; O'Reilly, Jones, Muir, & Doherty, 1998), and eliminating these risk factors may reduce symptoms and disability associated with knee pain. Some factors, such as age and sex are fixed and unchangeable, but others including obesity, muscle weakness, over-exercising, as well as sedentariness, can be modified with non-pharmacologic therapies (Doi et al., 2008; Fransen & McConnell, 2008).

Several previous investigations have focused on treatments for radiographic osteoarthritis (OA). However, Hadler suggested that knee pain, not OA, is the malady, as a greater percentage of elderly people suffer from knee pain than knee OA. It has been suggested that symptoms of knee OA, i.e. pain, can exacerbate or regress regardless of radiographic progression (Hadler, 1992). Many studies have suggested that exercise should be one of the mainstays of treatment (Ettinger et al., 1997; Fransen & McConnell, 2008; Minns Lowe, Barker, Dewey, & Sackley, 2007) for knee OA. The recommendations for exercise are based on several randomized controlled trials showing that both aerobic and resistance exercises improve physical fitness and can reduce pain symptoms in elderly people with chronic knee pain caused by OA (Deyle et al., 2000; Ettinger et al., 1997; Kovar et al., 1992; Roddy et al., 2005).

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These previous studies were conducted on populations with wide age ranges, including middle-aged adults, from 40 to 50 years old (Hay et al., 2006; Hurley et al., 2007; O'Reilly, Muir, & Doherty, 1999; Thomas et al., 2002), and very few trials, if any, have studied the effects of exercise on non-specific knee pain focusing on community-dwelling elderly people over the age of 75. Other methods of treatments besides exercise can be used to treat pain. One such treatment method, topical heat therapy, has been reported to be effective and safe in the treatment of low back (Nadler et al., 2002), knee (Giombini, Di Cesare, Di Cesare, Ripani, & Maffulli, 2011; Mazzuca, Page, Meldrum, Brandt, & Petty-Saphon, 2004; Seto, Ikeda, Hisaoka, & Kurosawa, 2008; Yildirim, Filiz Ulusoy, & Bodur, 2010) and wrist pain (Michlovitz, Hun, Erasala, Hengehold, & Weingand, 2004). A recently developed HSGS has been suggested as an effective method for alleviating pain and improving stiffness and gait impairment in patients with knee OA (Oda et al., 2006; Seto et al., 2008). While several studies have confirmed the separate effects of thermal therapy and exercise treatment on symptoms of knee OA and physical function, the combined effects of both heat and exercise on non-specific knee pain and lower-extremity function is unknown in the elderly population.

We hypothesize that the combination of both heat therapy and exercise will be more beneficial for reducing knee pain and improving function. The purpose of this study was to determine the combined and separate effects of heat therapy and exercise on knee pain relief, physical function, and quality of life (QOL) in community-dwelling elderly women with chronic knee pain.

2. Methods

2.1. Subjects

The baseline survey was conducted in October 2010, on a sample of 859 women who were randomly selected from the Basic Resident Register of women aged 75 and older residing in the Itabashi ward of Tokyo as of April 1, 2010. Three hundred and two (35.2%) who reported knee pain in the baseline survey were classified as potential participants.

The inclusion criteria were: (1) age $\geq$ 75 years; (2) have knee pain at baseline; and (3) no missing baseline knee pain and functional fitness data. The exclusion criteria included: (1) severely impaired mobility (e.g. unable to walk without assistance from another person); (2) physician enforced restriction of exercise (e.g. post-knee surgery or chronic disease); (3) known dermal allergy to heat; and (4) unstable cardiac conditions such as ventricular dysrhythmias, pulmonary edema, or other musculoskeletal conditions. One hundred fifty women (150/302, 49.7%) were included in this trial, and 152 women were excluded based on the exclusion criteria.

The study protocol was approved by the Clinical Research Ethics Committee of the Tokyo Metropolitan Institute of Gerontology (TMIG). The procedures were fully explained to all participants, and written informed consent was obtained.

2.2. Randomization

Randomization was performed after the baseline assessment, and any variable such as name, age, address, and telephone number that identified personal information was not included in the randomization process. The assigned identification numbers of 150 participants were divided into four groups based on computer-generated random numbers. The groups were randomly assigned to one of the four interventions: Ex ($n = 37$), HSGS ($n = 38$), Ex + HSGS ($n = 38$), or HE ($n = 37$). There was no attempt to equalize the size of the groups based on their characteristics or to recruit subjects with specific characteristics. The co-investigators were blind to the randomization procedure and group allocations, and data collection was conducted by separate physical therapy staff members who were also blind to the allocation of interventions.

2.3. Data collection

2.3.1. Interview survey

A face to face interview survey was conducted to assess the following variables: presence of knee pain, degree of knee pain, JKOM, history of falls, fear of falling, urinary incontinence, and chronic medical conditions. Knee pain was assessed by the question "Do you have knee pain?" A person who responded "yes" was defined as having knee pain, and the degree of pain was evaluated as light, medium, or severe. As the focus was on knee pain based on the subjective response to the questionnaire, there were no definite clinical diagnostic measures or X-ray assessments to define knee pain. Since the origin of the pain could not be determined, the term 'non-specific' knee pain was used.

2.3.2. Anthropometric and physical function measurements

Height and body weight measurements were converted to BMI (kg/m^2). Bone mineral density (BMD) of the distal radius and ulna of the non-dominant forearm was measured by the dual-energy X-ray absorptiometry (DEXA) method using a DTX-200 osteometer (Osteometer MediTech, Inc., USA) (Kelly, Crane, & Baran, 1994). Grip strength was measured using a hand-held Smedley type dynamometer. Usual walking speed was measured on a flat walking path of 11 m, with markers at the 3 m and 8 m points. A stopwatch was used to measure the time taken to walk 5 m between the markers, and the faster time of two trials was recorded. Stride length was measured using a WalkWay device (WalkWay MW-1000, Anima Co., Tokyo, Japan). The participants walked on the WalkWay at their normal pace for 3 m, with a 1.5 m approach before reaching the starting edge of the Walkway to ensure the participants were walking at their normal pace (Shimada et al., 2010). To measure one leg standing time with eyes open, participants were asked to stand on their preferred foot, with one foot lifted off the ground, while gazing at a point set at eye level 1 m away until they placed the other foot down. The longer of two trials was recorded. The timed up & go (TUG) was used to measure physical mobility, balance, gait speed, and functional ability. TUG was measured in seconds, as the time taken for the subject to stand up from a chair, walk a distance of 3 m to a cone, walk around the cone (turn), walk back to the chair, and sit down again. The trial was repeated, and the faster time was recorded. Participants were allowed to use assistive walking devices during the physical function measurements if they expressed strong concerns of walking without a device, or if there was any danger of falling.

2.3.3. Outcome measures

The primary outcome variable of this trial was the change in degree of pain as measured by the VAS. Secondary outcome measures included changes in functional mobility, muscle strength, and JKOM total score and the subscales of the JKOM. The subscales within the JKOM measure included: pain and stiffness in the knees, which included questions regarding knee function; condition in daily life, where participants were asked about difficulties performing daily routine activities; general activities; and health conditions. These assessments were conducted at baseline and after the 3-month intervention. All data were collected at the TMIG in Tokyo, Japan.

2.4. Intervention

2.4.1. Exercise

The Ex group attended a group-based 60-min exercise class focusing on strengthening of the muscles around the knee such as the quadriceps and hamstrings, as well as the tibialis anterior, gastrocnemius and soleus. The classes were held at the TMIG health promotion center, twice a week for 3-months. Each exercise session consisted of a five minute warm-up, 30 min of strengthening exercise, followed by 20 min of balance and gait training, and 5 min of cool-down. The strengthening exercises were performed in a progressive sequence from the seated to standing positions. For each type of exercise, participants were instructed to complete up to eight repetitions of the movements. When the exercises were properly executed without significant fatigue or loss of proper execution, the resistance was increased. The progressive resistance was provided through the use of the Thera-bands and ankle-weights, and each individual's ability to increase resistance was assessed by the principal investigator, along with the exercise instructor and assistant trainers who supervised the group classes. The intensity was maintained at approximately 12–14 on the Borg rate of perceived exertion (RPE) scale (Borg, 1982). Participants exercised together within their intervention groups, and those who attended at least 15 or more sessions out of the 24 exercise sessions (60%) were considered to have completed the trial.

2.4.1.1. Muscle strength training.

Chair exercise. The chair-seated exercises were used in the early stages of the program as they provided a secure and stable position without putting any pressure on the knee joint. Repetitions of toe raises, heel raises, knee lifts, knee extensions and others, were performed while seated on a chair. While standing upright behind the chair and holding the back of the chair for stability; hip flexions, lateral leg raises, and repetitions of other exercises were performed.

Ankle-weight exercise. To strengthen lower extremities, a fixed weight was placed on the ankle while the participants performed strengthening exercises. Weights of 0.50 kg, 0.75 kg, 1.00 kg, 1.50 kg were prepared and used in accordance with each participant's strength level to strengthen lower extremities. The exercises performed with these ankle-weights included seated knee flexion/extensions, standing knee flexion/extensions, ankle dorsiflexions and others.

Resistance band (Thera-Band) exercise. Resistance bands were used to strengthen the upper and lower body. Lower body exercises consisted of leg extensions, hip flexions, looped ankle presses, looped toe lifts, and more. Upper body exercises included double-arm pull backs holding the band horizontally in front of the chest, bicep curls, and others.

Balance training. The training was focused on the improvement of static and dynamic balancing ability. Exercises included standing on one leg, multidirectional weight shifts, tandem stand, tandem walk, side stepping on alternate legs, and other items.

2.4.2. HSGS group

The HSGS is a thin (89 mm × 173 mm), flexible sheet (Kao, Tokyo, Japan), that generates heat and steam via reaction of iron and atmospheric oxygen. When the sheet is placed on the skin, the temperature of the skin surface rises to around 40 °C within 30 min and it continues to generate heat and steam for over 5 h. The HSGS produces high heat flux and warms the skin more widely and deeply than the heat-generating sheet without steam (Oda et al., 2006). The participants in the HSGS group were asked to place the HSGS on the painful knee for 6 h a day immediately after waking up, and if they had pain in both knees they were asked to place the HSGS on the most painful knee. Two HSGS were applied to around the patella, and a thin supporter was worn over the two sheets. The participants recorded the time of day they placed and removed the sheet on a HSGS monitoring log, which were collected at TMIG classes every two weeks, and HSGS were provided for two weeks.

2.4.3. Ex + HSGS group

The participants were instructed to perform a combination of the same intervention as the Ex group as well as the HSGS group.

2.4.4. HE

Participants in the education group took a 60-min class once a month for 3-months, a total of three times. The classes focused on nutrition, cognitive function, and oral hygiene. Participants were asked to continue their usual life-style habits, and no specific instructions on physical activity or heat therapy were given.

2.5. Data analysis

Sample size was calculated for changes in the primary outcome variable of VAS. Setting the power at 0.80 and an alpha value of 0.05, the total sample size required was estimated to be 128 subjects (Cohen, 1992). When considering a potential attrition rate of 15% (Doi et al., 2008), 150 subjects were required.

Means and standard deviations were calculated for continuous variables, and a one-way analysis of variance (ANOVA) was performed to measure significant differences in baseline and post treatment values between the intervention groups, and the chi-square test was used for categorical variables. The normality of the distribution was examined by the Komogorov–Smirnov test for primary and secondary outcomes. A repeated-measures ANOVA (4 × 2) was performed on normally distributed variables including VAS, total JKOM score, stride, normal walking speed, grip strength and TUG, and the generalized linear model (GLM) was used to assess non-normal variables including JKOM subscale scores and one leg standing time, to find differences in pre- and post-intervention between groups. Paired *t*-tests were done on pre- and post-intervention measures to find changes within groups. Percent change was calculated for each JKOM measure using the following formula: % change = ((post-intervention value − baseline value)/ baseline value) × 100). One-way ANOVAs were performed to determine significant differences in percent changes between the groups. The Scheffe post hoc method was used when significance was found. Multiple logistic regressions were performed to compare the effects of the four intervention groups on VAS, usual walking speed, and combined outcome variables after the 3-month intervention. All analyses were performed using SPSS 19.0 and SAS 9.2 version for Windows and $P < 0.05$ was considered statistically significant.

3. Results

The mean attendance rates during the 3-month intervention were 71.1% (range 57.9–84.2%) in the Ex + HSGS group, 82.9% (78.4–89.2%) in the Ex group, 88.2% (84.2–92.1%) in the HSGS group, and 81.1% (78.4–83.8%) in the HE group. The mean ± SD for the duration of HSGS use for the Ex + HSGS group was 6.49 ± 0.79 h/day, and 6.41 ± 0.59 h/day for the HSGS group ($P = 0.660$). Thirteen participants (Ex + HSGS = 5, Ex = 3, HSGS = 3, HE = 2) were unable to complete the study after randomization because of admission to nursing home ($n = 1$), lack of motivation ($n = 4$), hip fracture ($n = 1$), spouse care ($n = 3$), severe back pain ($n = 1$), and other unknown reasons ($n = 3$) (Fig. 1). These 13 subjects were excluded from all post-intervention analyses.

Table 1 shows the baseline comparisons in anthropometric values, physical fitness measures, and interview survey results