

drinkers (ethanol intake <34 g/day), and current heavy drinkers (≥ 34 g/day). Leisure-time physical activity was quantified by the sum of activity time (hours per week) multiplied by the metabolic equivalents (MET) intensity for each activity.¹⁹

Resting blood pressure was measured three times with the subject in a sitting position, with a mercury sphygmomanometer at the right upper arm after at least five minutes of rest; the mean of the three measurements was used in the analysis. Diabetes was determined by the administration of antidiabetic treatment, plasma glucose levels (fasting glucose level ≥ 7.0 mmol/L or postprandial glucose level ≥ 11.1 mmol/L), or a 75 g oral glucose tolerance test using the 1998 WHO criteria,²⁰ with plasma glucose measured by the glucose-oxidase method. Total cholesterol was determined by an enzymatic autoanalyser. Body height and weight were measured while the subject was wearing lightweight clothing without shoes, and body mass index (BMI) was calculated. Electrocardiogram abnormalities were defined as left ventricular hypertrophy (Minnesota code 3-1), ST segment depression (4-1, 2, or 3), or atrial fibrillation (8-3).

Follow-up survey

The participants were followed prospectively for 19 years from December 1988 to November 2007 by repeated health examinations and by a daily monitoring system established by the study team, local physicians and members of the town's Health and Welfare Office. Vital status was checked annually by mail or telephone for any subjects who did not undergo regular examination or who moved out of town. Information about death was received via this follow-up system. When a resident died, all medical information related to a participant's illness and death, including hospital charts, physician's records and death certificate, were collected. Moreover, autopsy was performed at the Kyushu University Departments of Pathology, provided if consent for autopsy had been obtained. All medical information and autopsy findings were scrutinised, and the underlying causes of death were determined according to the International Classification of Diseases, 10th Revision (ICD-10). Cause of death was classified into the following categories: cardiovascular death (ICD-10 code of I00-I99), cancer death (C00-C97), respiratory death (J00-J99.8), and death from other causes. During the follow-up period, 783 participants (397 men and 386 women) died, of whom 564 (72.0%) underwent autopsy. Of the deceased persons, 235 (106 men and 129 women) died of cardiovascular disease, 249 (149 men and 100 women) of cancer, 154 (81 men and 73 women) of respiratory disease, and 145 (61 men and 84 women) of other causes. All individuals were completely followed-up for 19 years or until death.

Statistical analysis

All statistical analyses were performed with SAS V.9.3 software (SAS Institute, Cary, North Carolina, USA). The participants were divided into three groups on the basis of age-specific and sex-specific tertiles of handgrip strength (T1: 12.0 to 39.5, T2: 40.0 to 46.5, and T3: 47.0 to 64.0 kg for middle-aged (40–64 years) men; T1: 0.5 to 18.5, T2: 19.0 to 23.5, and T3: 24.0 to 27.5 kg for middle-aged women; T1: 3.0 to 29.5, T2: 30.0 to 36.5, and T3: 37.0 to 52.0 kg for elderly (≥ 65 years) men; T1: 0.5 to 16.0, T2: 16.5 to 20.5, T3: 21.0 to 39.0 kg for elderly women). Age- and sex-adjusted mean values of possible risk factors taken as continuous variables were estimated across handgrip strength levels using analysis of covariance, and the prevalence of risk factors taken as categorical variables were adjusted for age and sex by means of the direct method, where

overall study population was used as the standard population. Linear trends in the mean values or prevalence of risk factors across handgrip strength levels were tested using linear or logistic regression analysis. The mortality rate was calculated by the person-year method and adjusted for either age or sex using the direct method. The HR and its 95% CI across the tertiles or per 1 SD increment of handgrip strength were estimated using the Cox proportional hazards model with adjustment for potential confounding factors at baseline, namely, systolic blood pressure, use of antihypertensive agents, diabetes, total cholesterol, BMI, smoking status, alcohol intake and leisure-time physical activity, as well as either age or sex. Here, SD of handgrip strength was 7.5 kg for middle-aged men, 5.5 kg for middle-aged women, 8.4 kg for elderly men and 5.7 kg for elderly women. Heterogeneity in the relationship between men and women or between age groups was tested by adding a multiplicative interaction term to the relevant Cox model. Proportions of missing values were less than 1% for all variables in the multivariable model. A two-sided $p < 0.05$ was considered to be statistically significant in all analyses.

Ethical considerations

This study was conducted with the approval of Kyushu University Institutional Review Board for Clinical Research, and written informed consent was obtained from the participants.

RESULTS

Baseline characteristics of the study population are shown in table 1. Higher handgrip strength levels were associated with younger age, higher diastolic blood pressure, higher total cholesterol, higher BMI, lower prevalence of electrocardiogram abnormalities and increased leisure-time physical activity level.

Table 2 shows the association of all-cause and cause-specific death according to handgrip strength level by sex. In both sexes, the age-adjusted all-cause mortality in the second tertile (T2) and the highest tertile (T3) of handgrip strength was significantly lower compared to the lowest tertile (T1) (all $p < 0.05$). Handgrip strength was inversely associated with the risk of all-cause death, even after adjustment for potential confounding factors. Compared with the T1 of handgrip strength, the multivariable-adjusted HR (95% CI) for all-cause death was 0.81 (0.64 to 1.03) for T2 and 0.70 (0.53 to 0.92) for T3 in the men, and 0.66 (0.52 to 0.85) for T2 and 0.65 (0.50 to 0.84) for T3 in the women. The HR (95% CI) for all-cause death per 1 SD increment of handgrip strength was 0.72 (0.64 to 0.81) in the men and 0.74 (0.66 to 0.82) in the women. Similar associations were observed for cardiovascular death, respiratory death and death from other causes, but not for cancer death. There was no evidence of heterogeneity in the association between men and women (all P for heterogeneity > 0.2).

Next, we examined the association between handgrip strength and the risks of all-cause and cause-specific death in the middle-aged (40–64 years) and the elderly (≥ 65 years) groups (table 3). Here, the men and women were analysed together due to limited statistical power. The all-cause mortality in T2 and T3 was significantly decreased compared to T1 in both age groups (all $p < 0.05$). These associations remained significant even after adjustment for multiple confounding factors. The multivariable-adjusted HR (95% CI) for all-cause death was 0.75 (0.56 to 0.99) for T2 and 0.49 (0.35 to 0.68) for T3 in the middle-aged group and 0.50 (0.40 to 0.62) for T2 and 0.41 (0.32 to 0.51) for T3 in the elderly group. The HR (95% CI) per 1 SD increment for handgrip strength was 0.72 (0.63 to

Table 1 Baseline characteristics according to levels of handgrip strength in 1988, the Hisayama Study

| | Handgrip strength levels | | | p for trend |
|--|--------------------------|-------------|-------------|-------------|
| | T1 (n=802) | T2 (n=815) | T3 (n=910) | |
| Number of subjects | | | | |
| Middle-aged men/women (40–64 years), n | 244/314 | 248/302 | 269/366 | |
| Elderly men/women (≥65 years), n | 88/156 | 111/154 | 104/171 | |
| Age, years | 62 (0.4) | 59 (0.4) | 56 (0.4) | <0.001 |
| Systolic blood pressure, mmHg | 133 (0.7) | 134 (0.7) | 134 (0.7) | 0.71 |
| Diastolic blood pressure, mmHg | 77 (0.4) | 78 (0.4) | 79 (0.4) | 0.002 |
| Antihypertensive agents, % | 14.6 | 14.7 | 16.8 | 0.34 |
| Diabetes, % | 13.1 | 11.3 | 11.4 | 0.32 |
| Total cholesterol, mmol/L | 5.25 (0.04) | 5.38 (0.04) | 5.41 (0.04) | 0.003 |
| BMI, kg/m ² | 22.2 (0.1) | 22.7 (0.1) | 23.6 (0.1) | <0.001 |
| Electrocardiogram abnormalities, % | 20.2 | 15.2 | 15.4 | 0.02 |
| Smoking status | | | | |
| Never smoker, % | 60.6 | 59.8 | 61.7 | |
| Former smoker, % | 11.2 | 15.2 | 15.5 | |
| Current smoker (<20 cigarettes/day), % | 15.2 | 14.7 | 13.2 | |
| Current smoker (≥20 cigarettes/day), % | 13.1 | 10.4 | 9.5 | |
| Alcohol intake | | | | |
| Never, % | 65.0 | 67.2 | 65.5 | |
| Former, % | 3.7 | 2.9 | 2.7 | |
| Current (ethanol <34 g/day), % | 19.3 | 19.6 | 20.8 | |
| Current (ethanol ≥34 g/day), % | 12.1 | 10.3 | 10.9 | |
| Leisure-time physical activity, METs hour/week | 3.1 (0.4) | 4.1 (0.4) | 5.8 (0.4) | <0.001 |

Age- and sex-adjusted mean (SE) or frequencies are shown.
 BMI, body mass index; METs, metabolic equivalents.

0.81) in the middle-aged group and 0.63 (0.58 to 0.69) in the elderly group. We observed similar associations for cause-specific mortality, with the exception of cancer death. There was no evidence of heterogeneity in the association between age groups (all *p* for heterogeneity >0.4).

The sensitivity analysis, which excluded participants who died within 5 years of follow-up, did not generate any substantial discrepancies with the study conclusions (data not shown).

DISCUSSION

Using data from a 19-year follow-up study of a general Japanese population, we demonstrated that greater handgrip strength levels were associated with a reduced risk of all-cause death in men and women, even after adjustments were made for other conventional risk factors. With regard to the causes of death, handgrip strength levels were inversely associated with risk of cardiovascular death, respiratory death, and death from other causes, but not with the risk of cancer death. These associations were observed in the middle-aged group as well as in the elderly group.

Many prospective studies in Western^{2–8 10–13 18} and Asian countries^{1 9 17} have examined the association between handgrip strength and the risk of all-cause mortality. Most previous studies have reported that handgrip strength is associated with all-cause death in men^{1 2 4 6 9–12} and in women.^{1 4–6 8} However, only a few population-based prospective studies have reported the association of handgrip strength levels with risk of cause-specific deaths.^{1 2 9} The Adult Health Study in Hiroshima, Japan¹ and a cohort study in the UK² found that elevated levels of handgrip strength were associated with a decreased risk of cardiovascular death, while a similar but non-significant association was found in another Japanese study.⁹ The Adult Health Study¹ also observed a significantly inverse

association between handgrip strength and the risk of death from pneumonia. Our findings are in agreement with those of these previous studies. On the other hand, there is no consensus on the association between handgrip strength and cancer death.^{1 2 9} While the study in the UK² observed a significantly inverse association between handgrip strength and cancer death, our study and two other Japanese cohort studies^{1 9} did not observe any such association.

The inverse associations were recognised concerning lower handgrip strength levels and all-cause death in observational studies of elderly populations.^{2–8} By contrast, there have been a small number of studies on this issue in middle-aged populations, and the findings were inconsistent.^{1 10–13 18} The Honolulu Heart Program,^{10 12} which observed Japanese-American men, and the Adult Health Study in Hiroshima, Japan,¹ showed a significant inverse association of handgrip strength levels with all-cause death in middle-aged populations. The Mini-Finland Health Examination Survey¹³ and our present study showed a similar inverse association in the middle-aged and elderly group. On the other hand, the Baltimore Longitudinal Study of Aging¹¹ and the Canadian Fitness Survey¹⁸ failed to show a significant association in middle-aged populations. The discrepancy between results for middle-aged populations may be due to differences in background characteristics, such as ethnicity and other confounding factors, and differences between statistical methods used.

To the best of our knowledge, there has been no previous study which examined the association of midlife handgrip strength with the risk of cause-specific mortality. In our study, the level of handgrip strength measured in midlife was associated with the risks of cardiovascular, respiratory and other non-cancer death, as was handgrip strength measured in late life. Therefore, even though the absolute risk of death (shown

Table 2 Association of handgrip strength with the risks of all-cause death and cause-specific death by sex, the Hisayama Study, 1988–2007

| | Men (n=1064) | | | Women (n=1463) | | |
|--------------------------------|----------------------------|--|------------------------------------|----------------------------|--|------------------------------------|
| | Number of events/ subjects | Age-adjusted mortality per 1000 person-years | Multivariable-adjusted HR (95% CI) | Number of events/ subjects | Age-adjusted mortality per 1000 person-years | Multivariable-adjusted HR (95% CI) |
| All-cause death | | | | | | |
| T1 (lowest) | 164/332 | 34.8 | 1.00 (reference) | 162/470 | 22.3 | 1.00 (reference) |
| T2 | 134/359 | 26.9* | 0.81 (0.64 to 1.03) | 117/456 | 15.8* | 0.66 (0.52 to 0.85)* |
| T3 (highest) | 99/373 | 21.7* | 0.70 (0.53 to 0.92)* | 107/537 | 14.9* | 0.65 (0.50 to 0.84)* |
| Per 1 SD increment | | | 0.72 (0.64 to 0.81)† | | | 0.74 (0.66 to 0.82)† |
| Cardiovascular death | | | | | | |
| T1 (lowest) | 54/332 | 11.4 | 1.00 (reference) | 50/470 | 6.9 | 1.00 (reference) |
| T2 | 31/359 | 6.1* | 0.51 (0.32 to 0.82)* | 43/456 | 5.9 | 0.74 (0.48 to 1.12) |
| T3 (highest) | 21/373 | 4.4* | 0.38 (0.22 to 0.66)* | 36/537 | 5.2 | 0.67 (0.43 to 1.05) |
| Per 1 SD increment | | | 0.52 (0.41 to 0.66)† | | | 0.77 (0.64 to 0.93)† |
| Cancer death | | | | | | |
| T1 (lowest) | 46/332 | 9.6 | 1.00 (reference) | 35/470 | 4.5 | 1.00 (reference) |
| T2 | 51/359 | 10.1 | 1.16 (0.77 to 1.75) | 29/456 | 3.9 | 0.79 (0.47 to 1.31) |
| T3 (highest) | 52/373 | 10.9 | 1.43 (0.93 to 2.18) | 36/537 | 4.7 | 1.07 (0.66 to 1.74) |
| Per 1 SD increment | | | 1.11 (0.92 to 1.35) | | | 0.98 (0.79 to 1.22) |
| Respiratory death | | | | | | |
| T1 (lowest) | 34/332 | 7.5 | 1.00 (reference) | 36/470 | 5.1 | 1.00 (reference) |
| T2 | 28/359 | 5.9 | 0.91 (0.53 to 1.55) | 22/456 | 3.0* | 0.60 (0.35 to 1.05) |
| T3 (highest) | 19/373 | 4.8* | 0.81 (0.43 to 1.51) | 15/537 | 2.2* | 0.45 (0.24 to 0.84)* |
| Per 1 SD increment | | | 0.60 (0.46 to 0.79)† | | | 0.61 (0.49 to 0.78)† |
| Death from other causes | | | | | | |
| T1 (lowest) | 30/332 | 6.2 | 1.00 (reference) | 41/470 | 5.8 | 1.00 (reference) |
| T2 | 24/359 | 4.7 | 0.75 (0.43 to 1.32) | 23/456 | 3.1* | 0.55 (0.32 to 0.92)* |
| T3 (highest) | 7/373 | 1.6* | 0.21 (0.09 to 0.50)* | 20/537 | 1.5* | 0.48 (0.27 to 0.84)* |
| Per 1 SD increment | | | 0.54 (0.40 to 0.73)† | | | 0.62 (0.50 to 0.77)† |

*p<0.05 vs T1. †p<0.05 for 1 SD increment of handgrip strength.

HRs were adjusted for age, systolic blood pressure, use of antihypertensive agents, diabetes, total cholesterol, body mass index, electrocardiogram abnormalities, smoking status, alcohol intake and leisure-time physical activity.

as mortality rates in table 3) among the middle-aged was much lower than that of the elderly, handgrip strength measured in midlife may be a good predictive marker that could be used to identify people at higher risk of non-cancer diseases, and subsequent risk of mortality.

The mechanisms underlying the association between handgrip strength and risk of all-cause and cause-specific death have not been clearly defined, but a lower level of handgrip strength, which reflects a weaker whole-body muscle strength, is known to be associated with traditional risk factors for death or cardiovascular disease, that is, lower body weight,²¹ physical inactivity²² and chronic diseases, such as diabetes and hypertension.²³ However, our findings showed that the association of handgrip strength levels with all-cause and cardiovascular death remained significant, even after adjustment for these factors. A population-based study reported a positive correlation of handgrip strength with the serum concentration of insulin-like growth factor 1 (IGF-1),²⁴ which is a key regulator of muscle cell proliferation and differentiation, and an inhibitor of cell apoptosis and necrosis.²⁵ Other epidemiological studies have shown an association between decreased IGF-1 concentration and elevated risk of insulin resistance,²⁶ impaired glucose tolerance including type 2 diabetes,²⁷ ischaemic heart disease,²⁸ and mortality.²⁹ Therefore, IGF-1 may potentially mediate the association between muscle strength and risk of cardiovascular death. The mechanisms which account for the link between

handgrip strength and respiratory death remain unclear, but a case-control study³⁰ demonstrated that patients with chronic obstructive pulmonary disease, a common cause of respiratory death, had decreased expiratory muscle endurance and lower handgrip strength, compared to control subjects with normal lung function, indicating that weaker handgrip strength may be a marker of reduced respiratory muscle function. In our cohort, pneumonia was also an important cause of respiratory death, and death from other causes primarily included infectious diseases such as sepsis. Lower handgrip strength may reflect lower body weight,²¹ and may be associated with higher risk of pneumonia and sepsis due to undernourished and immunocompromised conditions.

The strengths of the present study include a longitudinal population-based design, long duration of follow-up, perfect follow-up of the participants, and accurate diagnosis for cause of death on the basis of medical information and autopsy. However, some limitations should be noted. First, handgrip strength levels were determined on the basis of measurements at baseline examination only. Possible changes in handgrip strength levels during the follow-up period were not taken into consideration. Therefore, the risk estimates reported in this study might be underestimated. Second, socioeconomic information, such as educational level and occupation, which might affect the association between handgrip strength and the risk of death, was not available in our cohort. Third, we could not

Table 3 Association of handgrip strength with the risks of all-cause death and cause-specific death by age groups, the Hisayama Study, 1988–2007

| | Middle-aged (40–64 years) (n=1743) | | | Elderly (≥65 years) (n=784) | | |
|-------------------------|------------------------------------|--|------------------------------------|-----------------------------|--|------------------------------------|
| | Number of events/ subjects | Sex-adjusted mortality per 1000 person-years | Multivariable-adjusted HR (95% CI) | Number of events/ subjects | Sex-adjusted mortality per 1000 person-years | Multivariable-adjusted HR (95% CI) |
| All-cause death | | | | | | |
| T1 (lowest) | 118/558 | 12.7 | 1.00 (reference) | 208/224 | 88.2 | 1.00 (reference) |
| T2 | 84/550 | 8.6* | 0.75 (0.56 to 0.99)* | 167/265 | 46.6* | 0.50 (0.40 to 0.62)* |
| T3 (highest) | 58/635 | 5.0* | 0.49 (0.35 to 0.68)* | 148/275 | 36.3* | 0.41 (0.32 to 0.51)* |
| Per 1 SD increment | | | 0.72 (0.63 to 0.81)† | | | 0.63 (0.58 to 0.69)† |
| Cardiovascular death | | | | | | |
| T1 (lowest) | 32/558 | 3.5 | 1.00 (reference) | 72/224 | 30.5 | 1.00 (reference) |
| T2 | 20/550 | 2.0 | 0.62 (0.35 to 1.11) | 54/265 | 14.8* | 0.44 (0.31 to 0.64)* |
| T3 (highest) | 14/635 | 1.2* | 0.41 (0.21 to 0.80)* | 43/275 | 10.3* | 0.32 (0.22 to 0.48)* |
| Per 1 SD increment | | | 0.65 (0.50 to 0.84)† | | | 0.60 (0.51 to 0.70)† |
| Cancer death | | | | | | |
| T1 (lowest) | 40/558 | 4.3 | 1.00 (reference) | 41/224 | 17.7 | 1.00 (reference) |
| T2 | 37/550 | 3.8 | 0.97 (0.61 to 1.53) | 43/265 | 12.1* | 0.69 (0.44 to 1.08) |
| T3 (highest) | 36/635 | 3.1 | 0.94 (0.59 to 1.51) | 52/275 | 13.0* | 0.76 (0.49 to 1.18) |
| Per 1 SD increment | | | 0.99 (0.81 to 1.22) | | | 0.92 (0.76 to 1.11) |
| Respiratory death | | | | | | |
| T1 (lowest) | 13/558 | 1.4 | 1.00 (reference) | 57/224 | 24.8 | 1.00 (reference) |
| T2 | 10/550 | 1.0* | 0.85 (0.37 to 1.98) | 40/265 | 11.3* | 0.43 (0.28 to 0.65)* |
| T3 (highest) | 1/635 | 0.1* | 0.08 (0.01 to 0.59)* | 33/275 | 8.2* | 0.35 (0.22 to 0.56)* |
| Per 1 SD increment | | | 0.46 (0.31 to 0.70)† | | | 0.55 (0.45 to 0.66)† |
| Death from other causes | | | | | | |
| T1 (lowest) | 33/558 | 3.5 | 1.00 (reference) | 38/224 | 15.3 | 1.00 (reference) |
| T2 | 17/550 | 1.7* | 0.58 (0.32 to 1.05) | 30/265 | 8.3* | 0.57 (0.35 to 0.94)* |
| T3 (highest) | 7/635 | 0.6* | 0.21 (0.09 to 0.49)* | 20/275 | 4.8* | 0.33 (0.19 to 0.59)* |
| Per 1 SD increment | | | 0.52 (0.40 to 0.68)† | | | 0.56 (0.45 to 0.70)† |

* $p < 0.05$ vs T1. † $p < 0.05$ for 1 SD increment of handgrip strength.

HRs were adjusted for sex, systolic blood pressure, use of antihypertensive agents, diabetes, total cholesterol, body mass index, electrocardiogram abnormalities, smoking status, alcohol intake and leisure-time physical activity.

determine the cut-off level of handgrip strength to predict the mortality risk (which might be clinically useful information), because we did not have an adequate number of mortality events to analyse.

In conclusion, handgrip strength levels were associated with the risk of all-cause and cause-specific mortality, except for cancer mortality, in middle-aged and elderly subjects in a Japanese population. Our results suggest that handgrip strength measured in midlife may be a good predictive marker that could be used to identify individuals at high risk for death from non-cancer diseases.

What is already known on this subject

- ▶ Most previous studies have reported an inverse association between handgrip strength and all-cause mortality in elderly populations (approx 65 years or older).
- ▶ A small number of studies have evaluated the association of handgrip strength with all-cause mortality in a middle-aged population, and their findings have been inconsistent.
- ▶ The association of handgrip strength with cause-specific mortality in the middle-aged population has been unknown.

What this study adds

- ▶ Handgrip strength measured in midlife, as well as in late life, was significantly and inversely associated with the risk of cardiovascular, respiratory and other non-cancer death, and these associations were independent of other potential risk factors.
- ▶ Handgrip strength levels in midlife may be a good predictive marker for the future risk of non-cancer death.

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Competing interests None.

Patient consent Obtained.

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【原 著】

地域在住高齢者における3軸加速度計で測定した
座位時間と肥満との関連

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【要約】目的：地域在住高齢者において、加速度計によって測定された座位行動時間と肥満との関係を明らかにする。

方法：追跡中の前向きコホート研究である篠栗元気もん研究のベースラインデータを用いて横断解析を行った。対象者は福岡県糟屋郡篠栗町に居住する要介護認定を受けていない65歳以上の高齢者1,401名(女性849名)であった。座位行動時間の測定には、3軸加速度計Active Style Pro(HJA-350IT, オムロンヘルスケア)を用い、1.5メッツ以下の活動の合計時間(分/日)を算出した。体重、体脂肪量の測定には、生体インピーダンス法(DC-320, タニタ)を用いた。Body mass index(BMI) ≥ 25 を肥満と判定した。

結果：年齢、教育年数、仕事の有無、現在の飲酒・喫煙状況、手段的日常生活動作、および中高強度身体活動量を調整した回帰分析を行った結果、男性では座位行動時間は体重、体脂肪量、および体脂肪率と関連した(すべて $p < 0.01$)。更に女性では、これらに加えてBMIも正の関連を示した(すべて $p < 0.01$)。男女ともに、座位行動の長い群では、肥満のオッズ比が有意に高い値を示した。

結論：地域在住高齢者において、座位行動時間と肥満指標との間に正の関連が示された。肥満、体脂肪の蓄積予防を目的としたポピュレーション・アプローチにおいて、座位行動に注目することの有用性が示唆された。

Key words：座位行動、加速度計法、身体活動エネルギー消費

1. 緒 言

高齢期の肥満は、糖・脂質代謝異常や動脈硬化性疾患、ならびに膝痛のリスクを高める要因であり、健康寿命の延伸にとって適切な体重管理が果たす役割は大きい¹⁾。Body mass index (BMI)が 25 kg/m^2 以上の肥満の割合は、70歳以上の男性で26.2%、女性で26.4%であり、高齢期肥満は我が国において広範に認められるといえよう^{1,2)}。

近年、座位行動が肥満をはじめとしたさまざまな代謝性疾患の危険因子であることを示すエビデンスが蓄積されつつあり³⁾、高齢者のメタボリックシンドローム^{4,5)}や糖・脂質系代謝因子^{6,7)}との関連が既に報告されている。我が国でも高齢者を対象とした郵送調査により、座位行動の指標とし

てのテレビ視聴時間とBMI ≥ 25 の肥満保有リスクとの関係が検討されており、テレビ視聴時間の長さとの間に有意な正の関連が報告されている⁸⁾。更にこの関係は、推奨身体活動量を充足しているか否かにかかわらず認められており、高齢者の肥満予防に向けた取り組みとして、身体活動量とともに座位行動を評価することの重要性が指摘されている。

座位行動は、若年者に比べて高齢者において長くなる傾向にあり⁹⁾、疾病に与えるインパクトはより大きいと予想される。しかし、高齢者においては、質問票を用いた評価はバイアスを生じやすいことも指摘されており¹⁰⁾、この欠点を克服するため、加速度計を用いた評価が勧められている。加速度計は複雑な操作を必要としないことから、調査対象者にかかる負担が比較的少なく、また記憶バイアス等の問題を生じないことから、特に比較的大規模な疫学的研究で多く利用されてきている¹¹⁾。

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しかしながら、我々の知る限り、我が国における高齢期の肥満と座位行動の関係について、客観的な測定に基づいた知見は見当たらない。そこで本研究では、我が国の地域在住高齢者を対象として3軸加速度計を用いて測定した座位行動時間と肥満との関係を明らかにすることを目的とする。

2. 方 法

2-1. 研究デザインとセッティング

本研究は現在進行中の前向きコホート研究である篠栗町研究¹²⁾より、ベースライン調査データを用いた横断研究とした。篠栗町研究は、介護予防施策にかかわる身体的、社会的、心理行動的諸要因を探ることを目的として開始された。本調査は2011年5月から8月にかけて行われ、町内各地区の公民館において調査測定会を実施し、データを収集した。

2-2. 対象者

福岡県糟屋郡篠栗町に居住し、2011年1月末時点で65歳以上かつ要介護認定を受けていない全高齢者4,979名のうち、同年5月の調査開始時点までに死亡、入院または町外に転居した66名を除いた4,913名(うち女性2,771名)を初期調査対象とした。調査への同意が得られた者は2,629名であった。アンケート回答のみ、または自宅での訪問測定を行った662名を除き、地区調査会場を訪れた者は1,967名であった。日常生活に介護・介助を必要とすると自己回答したもの、および外傷、うつ病、認知症、パーキンソン病のうち1つ以上を有する者128名は、加速度計を用いた身体活動の測定がうまく行えない可能性があるかと判断し解析から除外した。体組成計、または加速度計の有効データを得られなかった者394名、およびその他の解析項目で有効回答の得られなかった者44名を除き、最終的に1,401名(女性849名、有効回答率53%)を解析対象とした。

2-3. 測定項目

2-3-1. 身体計測

身長は調査測定会の会場において立位姿勢で実測した。体重、身体組成の測定にはデュアル周波数体組成計DC-320(タニタ)を用いた。本機器は、静止立位姿勢で周波数6.25kHzおよび50kHzの信号成分を含んだ電流を両足底より通電することで、

身体組成の測定を行うものである。本機器は6~99歳までを測定対象年齢としており、更に両足間生体インピーダンス法体組成計は、DXA法との相関から高い精度で体脂肪量を評価しうることが示されている¹³⁾。

BMIは体重(kg)を身長(m)の二乗で除して算出し、BMI 25以上を肥満(OB)と判定した。本研究では、体組成計の測定値から体重、BMI、体脂肪量、体脂肪率、およびOBの判定結果を解析に用いた。

2-3-2. 座位行動時間と身体活動量

座位行動時間と身体活動量の測定には、3軸加速度計を内蔵した活動量計(Active Style Pro HJA-350IT, オムロンヘルスケア, 京都。以下、加速度計)を用いた。本機器は3軸方向の合成加速度を用いた独自のアルゴリズムにより、身体活動を(1)低強度活動、(2)歩・走行活動、(3)歩・走行以外の活動に分類し、それぞれに異なる推定式を当てはめることで精度の高い強度推定を可能としている^{14,15)}。加速度計は調査測定会で配布し、入水時を除いて起床時点から就寝時点までの装着を求め、7日間以上の装着期間を経て回収した。なお、身体活動量をモニタリングすることで身体活動が促進されないよう、調査時には加速度計のディスプレイは時計のみを表示するよう設定し、身体活動量や歩数が表示されないように配慮した。加速度計のepoch lengthは60秒とした。単位時間ごとに推定される活動強度が1.0メッツ未満の場合にはゼロカウントとし、『ゼロカウントの継続時間が60分以上連続した場合』に、その時間帯を非装着時間と判定とした⁹⁾。なお、このときにゼロカウントの間で、2分以内の短い身体活動が挟まれる場合には、その身体活動時間も含めて、60分以上継続するかどうか判定を行った⁹⁾。装着時間は1,440(分)から非装着時間を引くことで求めた。成人および高齢者を対象とした先行研究に準じ、1日当たりの装着時間が10時間以上であればそのデータを採用し、基準を満たす日が4日以上ある者のみを解析対象とした^{9,16,17)}。本研究においては、平日と休日でわずかに座位行動時間および中高強度の身体活動量に差が認められたものの(10分、0.3メッツ・時)、この基準により52名を除外した場合にも解析結果は変わらなかったため、休日のデータが得られなかった者も含めた結果を示した。

座位行動は1.5メッツ以下の活動^{3,9)}と定義し、

1日当たりの座位行動時間(分/日, sedentary time; ST)を算出した。中高強度身体活動は3メッツ以上の活動と定義し、活動強度と持続時間の積和から、中高強度身体活動量(moderate-to-vigorous physical activity; MVPA, メッツ・時/日)を算出した。同様に1.6~2.9メッツの活動を軽強度身体活動と定義し、軽強度身体活動量(Light intensity physical activity; LPA, メッツ・時/日)を算出した。身体活動によるエネルギー消費量(physical activity energy expenditure; PAEE)は、体重当たりの消費量(kcal/kg/日)を算出した。

2-3-3. その他の調整項目

性別および年齢(2011年1月時点)の情報は、調査開始時に町より提供を受けた。その他の調整因子として、以下の項目を質問紙法により調査を行った。教育年数は、教育を受けていた合計年数について回答を得た。収入のある仕事の有無は、2件法で回答を得た。飲酒習慣は4件法で回答を求め「もともと飲まない」、「ほとんど飲まない」を0(現在の飲酒なし)、「ときどき飲む」、「ほぼ毎日飲む」を1(現在の飲酒あり)とコード化した。喫煙習慣は「もともと吸っていない」、「吸っていたがやめた」を0(現在の喫煙なし)、「ときどき吸っている」、「ほぼ毎日吸っている」を1(現在の喫煙あり)とコード化した。手段的日常生活活動(instrumental activities of daily living; IADL)は、老研式活動能力指標¹⁸⁾を用いて測定を行った。本尺度は、高次生活機能を測定するために開発された質問票であり、「手段的自立」「知的能動性」「社会的役割」の下位指標からなる合計13項目で構成されている。各項目について、「はい」に1点、「いいえ」に0点を与える。本研究ではこのうち「手段的自立」に関する5項目の合計得点(得点範囲0~5点)をIADLの指標として用いた。経済状況は、現在の家庭の経済的状態について「苦しい」、「やや苦しい」、「ややゆとりがある」、「ゆとりがある」の4件法で回答を得た。本研究では「苦しい」、「やや苦しい」を0、「ややゆとりがある」、「ゆとりがある」を1とコード化した。

2-4. 解析方法

対象者を、男女ごとにSTの四分位に基づく4群(Q1~Q4)に分け、測定結果を群別に示した。それぞれの項目について、平均値±標準偏差または頻度(%)で表した。

身体活動指標間の関連を検討するため、STと

LPA, MVPA, PAEEについて性、年齢、および加速度計装着時間を統制した偏相関分析を行った。MVPAの分布に偏りがみられたため、スピアマンの順位相関係数を用い、偏順位相関係数 ρ を求めた。

次に、座位行動時間と肥満関連指標の関係を明らかにするため、男女ごとにSTを説明変数、体重、BMIおよび体脂肪量、体脂肪率を目的変数とした重回帰分析を行い、非標準化回帰係数とその95%信頼区間を示した。モデル1では年齢、装着時間を調整因子として投入した。モデル2ではモデル1に加え、教育年数、収入のある仕事の有無、現在の飲酒・喫煙状況、IADL、経済状況を調整因子として投入した。モデル3では、モデル2に加えてMVPAを調整因子として投入した。各モデルで分散拡大係数の最大値は2.3であったため、多重共線性はないと判断して調整因子を同時に投入した。なお、年齢とSTの交互作用は有意でなかったことから($p>0.05$)、解析にはこれらの交互作用項を含めなかった。更に、座位行動時間と肥満との関係を明らかにするため、男女別にSTの4群を説明変数、OBを目的変数としたロジスティック回帰分析を行い、オッズ比および95%信頼区間を算出した。調整因子の投入手順は重回帰分析と同様とした。

最後に、本研究の解析対象者と、解析に含まなかった研究対象者の個人属性要因(性、年齢、教育歴、仕事の有無)について比較を行った。カテゴリ変数の比較には χ^2 乗検定、連続変数の比較にはt検定を用いた。

すべての統計解析はSAS ver 9.3 (SAS Institute, Cary, US)を用いた。統計的有意水準は $\alpha=0.05$ とした。

2-5. 倫理的配慮

本研究は九州大学健康科学センター倫理委員会の承認を得て実施された。ヘルシンキ宣言の精神に基づいて、調査参加者に調査の目的と内容の説明を実施し、同意の署名を得た。

3. 結 果

全対象者における加速度計の平均装着日数は7.1±1.4日であった。また、平均装着時間は14.1±1.6時間/日であった。OBの割合は25.6%(男性24.3%, 女性26.5%)であった。STの平均値は486.9

表1 Characteristics of the study participants by sedentary time quartile.

| Variables | Total | Men | | | | | Women | | | | |
|---|---------------|--------------|--------------|--------------|---------------|-------------|--------------|--------------|--------------|---------------|-------------|
| | | Q1 (<415) | Q2 (415-489) | Q3 (490-559) | Q4 (>559) | p for trend | Q1 (<356) | Q2 (356-421) | Q3 (422-499) | Q4 (>499) | p for trend |
| n | 1401 | 138 | 138 | 138 | 138 | | 212 | 212 | 213 | 212 | |
| Age, years | 73.1 ± 6.0 | 71.6 ± 5.2 | 73.2 ± 5.5 | 73.8 ± 6.3 | 73.9 ± 6.4 | <0.001 | 72.0 ± 5.5 | 72.3 ± 5.5 | 73.1 ± 5.8 | 75.0 ± 6.7 | <0.001 |
| Height, cm | 154.3 ± 8.8 | 161.4 ± 6.1 | 162.2 ± 6 | 163.6 ± 5.4 | 162.5 ± 5.9 | 0.052 | 148.6 ± 6.2 | 149.6 ± 5.2 | 149.7 ± 6 | 148.4 ± 6.5 | 0.606 |
| Weight, kg | 55.4 ± 9.7 | 60.8 ± 7.2 | 61.0 ± 8.5 | 62.2 ± 7.9 | 61.5 ± 8.9 | 0.309 | 50.2 ± 7.9 | 51.6 ± 8.1 | 52.3 ± 8.5 | 52.2 ± 9.3 | 0.015 |
| BMI, kg/m ² | 23.2 ± 3.2 | 23.3 ± 2.4 | 23.2 ± 2.9 | 23.2 ± 2.6 | 23.3 ± 3.2 | 0.998 | 22.7 ± 3.1 | 23.0 ± 3.3 | 23.3 ± 3.3 | 23.7 ± 3.9 | 0.002 |
| Fat-free mass, kg | 39.7 ± 7.7 | 47.0 ± 4.8 | 47.2 ± 5.3 | 48.1 ± 5.1 | 47.4 ± 5.2 | 0.300 | 34.0 ± 3.6 | 34.7 ± 3.8 | 34.7 ± 4.0 | 35.1 ± 4.9 | 0.006 |
| Fat mass, kg | 15.8 ± 5.3 | 13.8 ± 3.6 | 13.8 ± 4.2 | 14.1 ± 3.9 | 14.1 ± 4.6 | 0.467 | 16.3 ± 5.1 | 16.9 ± 5.4 | 17.5 ± 5.5 | 17.1 ± 6.4 | 0.098 |
| Body fat percentage, % | 28.3 ± 7.4 | 22.5 ± 4.1 | 22.2 ± 4.7 | 22.4 ± 4.3 | 22.5 ± 5.0 | 0.964 | 31.7 ± 5.5 | 32.1 ± 6.0 | 32.9 ± 5.8 | 31.9 ± 7.6 | 0.619 |
| OB, n (%) ^a | 359 (25.6) | 27 (19.6) | 37 (26.8) | 32 (23.2) | 38 (27.5) | 0.173 | 42 (19.8) | 54 (25.5) | 57 (26.8) | 72 (34.0) | 0.001 |
| Accelerometer wear time, min/d | 829.1 ± 99.4 | 743.1 ± 67.9 | 788.9 ± 69.8 | 809.8 ± 83.8 | 880.3 ± 104.0 | <0.001 | 800.2 ± 76.3 | 825.2 ± 76.4 | 846.3 ± 76.9 | 906.2 ± 123.3 | <0.001 |
| Absolute sedentary time, min/d | 451.9 ± 120.6 | 331.1 ± 61.8 | 454.7 ± 22.6 | 523.0 ± 20.1 | 638.9 ± 86.1 | <0.001 | 294.6 ± 49.4 | 390.4 ± 19.6 | 456.2 ± 22.5 | 575.2 ± 75.1 | <0.001 |
| Relative sedentary time, % of wear time | 54.5 ± 12.9 | 44.7 ± 8.3 | 58.1 ± 5.7 | 65.2 ± 6.6 | 72.8 ± 7.2 | <0.001 | 37.0 ± 6.6 | 47.7 ± 5.1 | 54.4 ± 5.9 | 64.0 ± 7.4 | <0.001 |
| MVPA time, min/d | 45.5 ± 34.4 | 57.1 ± 37.1 | 40.2 ± 25.9 | 35.5 ± 24.4 | 30.0 ± 27.6 | <0.001 | 70.4 ± 42.6 | 53 ± 32.9 | 42.5 ± 28.3 | 28.9 ± 24.9 | <0.001 |
| MVPA, METs·h/d | 2.7 ± 2.1 | 3.4 ± 2.4 | 2.4 ± 1.7 | 2.1 ± 1.6 | 1.8 ± 1.9 | <0.001 | 4.0 ± 2.5 | 3.1 ± 2.1 | 2.5 ± 1.8 | 1.7 ± 1.5 | <0.001 |
| LPA, METs·h/d | 11.8 ± 3.6 | 12.6 ± 2.5 | 10.3 ± 2.3 | 8.8 ± 2.6 | 7.3 ± 2.4 | <0.001 | 15.8 ± 2.6 | 13.6 ± 2.5 | 12.3 ± 2.6 | 10.5 ± 3.1 | <0.001 |
| PAEE, kcal/kg/d | 9.2 ± 2.8 | 10.6 ± 2.4 | 8.8 ± 2.2 | 7.9 ± 2.3 | 7.0 ± 2.3 | <0.001 | 11.6 ± 2.5 | 10.1 ± 2.2 | 9.1 ± 2.3 | 7.7 ± 2.4 | <0.001 |
| IADL, point | 4.9 ± 0.4 | 4.9 ± 0.4 | 4.8 ± 0.5 | 4.8 ± 0.6 | 4.7 ± 0.6 | 0.002 | 5.0 ± 0.1 | 4.9 ± 0.4 | 5.0 ± 0.2 | 4.9 ± 0.4 | 0.165 |
| Formal education, year | 11.2 ± 2.4 | 11.5 ± 2.9 | 11.5 ± 2.7 | 11.8 ± 2.7 | 12.3 ± 2.8 | 0.016 | 10.9 ± 2.1 | 10.9 ± 2.2 | 10.7 ± 1.9 | 10.5 ± 2.4 | 0.036 |
| Job status, n with having job (%) | 239 (17.1) | 53 (38.4) | 39 (28.3) | 31 (22.5) | 15 (10.9) | <0.001 | 38 (17.9) | 26 (12.3) | 23 (10.8) | 14 (6.6) | <0.001 |
| Current drinker, n (%) | 548 (39.1) | 96 (69.6) | 97 (70.3) | 82 (59.4) | 71 (51.5) | <0.001 | 56 (26.4) | 59 (27.8) | 43 (20.2) | 44 (20.8) | 0.074 |
| Current smoker, n (%) | 112 (8.0) | 24 (17.4) | 16 (11.6) | 25 (18.1) | 22 (15.9) | 0.987 | 8 (3.8) | 3 (1.4) | 7 (3.3) | 7 (3.3) | 0.953 |
| Economic status, n with straitened or relatively straitened (%) | 843 (60.2) | 95 (68.8) | 88 (63.8) | 77 (55.8) | 83 (60.1) | 0.068 | 131 (61.8) | 131 (61.8) | 122 (57.3) | 116 (54.7) | 0.092 |

BMI; body mass index, MVPA; moderate-to-vigorous physical activity, LPA; light intensity physical activity, METs; metabolic equivalents, PAEE; physical activity energy expenditure, IADL; instrumental activity of daily living. Data were represented as mean ± SD or n (%). ^a Obesity defined as body mass index ≥ 25 kg/m².

表 2 Multiple regression analysis of sedentary time with obesity-related indicators.

| Dependent variables | Model 1 ^a | | Model 2 ^b | | Model 3 ^c | |
|---------------------|-------------------------|---------|-------------------------|---------|-------------------------|---------|
| | B (95% CI) ^d | p value | B (95% CI) ^d | p value | B (95% CI) ^d | p value |
| Men | | | | | | |
| Weight | 0.75 (0.34-1.16) | <0.001 | 0.83 (0.41-1.27) | <0.001 | 0.79 (0.31-1.27) | 0.002 |
| BMI | 0.16 (0.02-0.30) | 0.028 | 0.21 (0.07-0.36) | 0.006 | 0.17 (0.00-0.33) | 0.125 |
| Fat mass | 0.49 (0.29-0.70) | <0.001 | 0.54 (0.33-0.76) | <0.001 | 0.43 (0.19-0.67) | <0.001 |
| Body fat percentage | 0.47 (0.25-0.70) | <0.001 | 0.52 (0.28-0.76) | <0.001 | 0.35 (0.09-0.62) | 0.009 |
| Women | | | | | | |
| Weight | 0.95 (0.60-1.30) | <0.001 | 1.04 (0.67-1.39) | <0.001 | 1.06 (0.63-1.48) | <0.001 |
| BMI | 0.34 (1.95-4.88) | <0.001 | 0.37 (0.22-0.51) | <0.001 | 0.38 (0.21-0.55) | <0.001 |
| Fat mass | 0.59 (0.36-0.82) | <0.001 | 0.65 (0.41-0.88) | <0.001 | 0.70 (0.42-0.98) | <0.001 |
| Body fat percentage | 0.50 (0.24-0.76) | <0.001 | 0.55 (0.28-0.82) | <0.001 | 0.65 (0.34-0.97) | <0.001 |

BMI; body mass index.

^a Adjusted for age and accelerometer wearing time.^b Also adjusted for years of formal education, job status, drinking and smoking habit, instrumental activity of daily living and economic status.^c Also adjusted for amount of moderate-to-vigorous physical activity (METs·h/d).^d Unstandardized regression coefficient and 95% confidence interval (CI). It represents the mean difference in each dependent variable per 60 minutes greater sedentary time.

±124.4 分/日であり，装着時間に占める割合は 60.2±12.5%であった。

1 日当たりの ST の四分位点は男性で低いほうから順に 415 分，490 分，560 分，女性で順に 356 分，422 分，500 分であった。群別の対象者の諸特性は表 1 に示したとおりである。

性，年齢，装着時間を統制後，ST と MVPA，LPA および PAEE の偏相関係数はそれぞれ $\rho = -0.51$ ($p < 0.001$)， $\rho = -0.90$ ($p < 0.001$)， $\rho = -0.84$ ($p < 0.001$)であった。また，LPA と MVPA および PAEE の偏相関係数はそれぞれ $\rho = -0.35$ ($p < 0.001$)， $\rho = -0.80$ ($p < 0.001$)，MVPA と PAEE の偏相関係数は， $\rho = 0.72$ ($p < 0.001$)であった。

ST と肥満関連指標の重回帰分析の結果を表 2 に示す。男性においては，年齢，教育年数，仕事の有無，現在の飲酒・喫煙状況，および IADL を調整後に，ST とすべての指標の間に有意な正の関係が認められた ($p < 0.001$)。このうち，体重，体脂肪量，および体脂肪率については，MVPA を調整してもなお関係は有意なままであった ($p < 0.001$)。ST と BMI は，MVPA を調整すると，その関係の有意性は消失した ($p = 0.125$)。

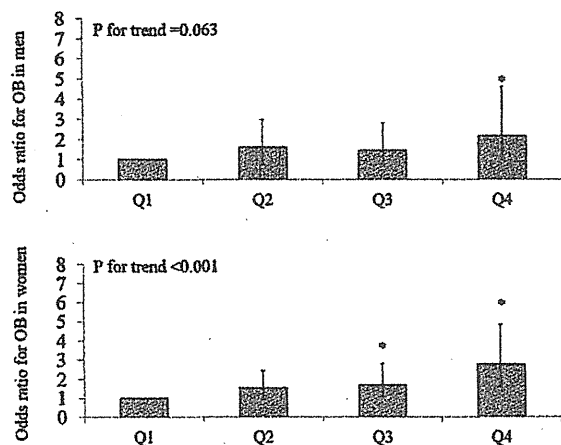


図 1 Odds ratios for obesity (OB) by sedentary time quartile.

Odds ratios were calculated after adjustment for age, years of education, employment status, drinking and smoking habit, instrumental activities of daily living and moderate-to-vigorous physical activity.

OB: Obesity defined as body mass index $\geq 25 \text{ kg/m}^2$.

女性においては，多変量調整後に ST とすべての指標の間に有意な正の関係が認められ

($p<0.001$), その関係は MVPA を調整後も変わらなかった($p<0.001$)。

男女ごとの ST の四群別にみた, OB の多変量調整オッズ比を図 1 に示した。男性で Q1 を基準にしたときの Q2~Q4 における OB の調整済みオッズ比と 95%信頼区間は, 順に 1.61 (0.78-2.96), 1.46 (0.76-2.80), 2.16 (1.02-4.58) であり, Q4 で有意に高いオッズ比が観察された。女性における OB の調整済みオッズ比と 95%信頼区間は, 順に 1.52 (0.95-2.36), 1.70 (1.04-2.79), 2.75 (1.57-4.83) であり, 有意な正の傾向性が認められた($p<0.001$, 図 1)。なお, すべてのモデルは適合していると考えられた(Hosmer-Lemeshow 検定, すべて $p>0.05$)。

解析対象者 1,401 名は, 解析に含まれなかった 3,512 名と比較して女性の割合が多く($p=0.002$), 年齢が若かった($p<0.001$)。また, 調査会参加者 1,967 名のなかで, 解析に含まれなかった 566 名と比較して, 女性の割合が多く($p=0.006$), 年齢が若く($p<0.001$), 教育歴が長かった($p<0.001$)。仕事の有無に差は認められなかった($p=0.56$)。

4. 考 察

本研究の目的は, 地域在住高齢者を対象として加速度計で測定した座位行動と肥満との関係を明らかにすることであった。体重, BMI, 体脂肪量, 体脂肪率について, 座位行動時間との関連を検討したところ, 女性では座位行動時間と全指標との間に正の関連が認められた。男性においては, 座位行動時間と体重, 体脂肪量, および体脂肪率との間に正の関連が認められた。また男女ともに, 座位時間の長い群で, 肥満(OB, BMI $\geq 25\text{kg/m}^2$)のオッズ比が有意に高い値を示した。

まず女性においては, 最も座位行動時間が短い群(Q1)に比べて上位2群(Q3,4)でOBの有意に高いオッズ比が観察された。Q1に対するQ4のOBのオッズ比は2.8 (1.6-4.8)であり, 比較的強固な関連があるといえよう。また, 有意な傾向性が認められており, 女性においては座位行動時間の長さや脂肪の蓄積の間には一貫した正の関係があると考えられる。男性では, 座位行動時間の最も短い群に比べて, 最も長い群でOBの有意に高いオッズ比が観察された。体脂肪についてみると, 女性と同様に座位行動時間と体脂肪率・体脂肪量の間に有意な正の関係が示された。以上から, 男女ともに肥満, および体脂肪指標との間に正の関連

が認められる点で一貫していたといえる。

座位行動と肥満およびBMIに関しては, Inoue et al.⁸⁾が, 我が国の高齢者を対象として長時間の座位行動(テレビ視聴時間)と肥満(BMI ≥ 25)との有意な関連を報告した。また, 加速度計を用いた先行研究としては, Gennuso ら⁷⁾が米国の65歳以上の一般高齢者1,914名を対象とした横断研究を行っており, 1軸加速度計で測定された座位行動時間が体重, BMI, および腹囲と関連することを示している。本研究では, 男女ともに肥満, 体重, 体脂肪量・率と座位行動時間の間に有意な関係が認められており, 先行研究を支持する結果であった。一方で, 英国の60歳以上の高齢者649名において行われた調査⁶⁾では, 1軸加速度計を用いて座位行動と心血管代謝因子の関係が検討されたが, 座位行動時間とBMIの関係は, 中高強度活動を調整することで消失した。本研究の男性においても中高強度活動を調整すると, 座位行動時間とBMIの関係は有意でなくなった。高齢者は身体組成にばらつきが大きく, 低BMIは除脂肪量の少なさを反映するといわれている¹⁾。特に男性では, 体格に占める脂肪量の割合が低いことから, BMIが体脂肪のばらつきを十分に反映していなかった可能性がある。高齢期の肥満およびBMIと座位行動の関連については, まだ一貫した知見が得られていないとはいえず, 体組成成分の違いや, 中高強度活動の影響を精査する必要があると考えられた。

座位行動時間と体脂肪については, 小規模ながらいくつかの研究で検討がなされている。例えば我が国では109名の女性虚弱高齢者を対象とした研究から, 座位行動時間と体脂肪率の間に有意な正の相関が認められている¹⁹⁾。また, Swartz ら²⁰⁾は, 232名の中高齢者ボランティア(50~87歳, 男性24%)を対象として加速度計を用いて測定した座位行動とDXA法による体脂肪成分の間に有意な正の関連を示している。同様にChastin ら²¹⁾も, 30名の健康な高齢者を対象とした横断調査から, 男性において座位時間と体脂肪率との間に有意な関連を認めている。先行研究では対象集団に限られているものの, 体脂肪と座位行動はおおよそ一貫して正の関連があり, 本研究は比較的大規模な集団においてこの関係を支持する結果を提示したといえる。

これらの関係の背景には, 座位行動の長さに起因するエネルギー消費の減少が考えられる。日中の多くの時間は座位行動と軽度の身体活動が占め

ており、座位行動が長ければ、軽度身体活動が短くなるという関係性を示す²²⁾。実際に座位行動時間と軽度身体活動量の間には、 $\rho = -0.90$ と強い負の相関関係が認められた。本研究の解析対象者において、中高強度活動は平均して1時間に満たず、睡眠時間を8時間と見積っても、軽強度以下の活動は1日当たり15時間以上を占めるものと想定される。この時間の長さから、活動強度は必ずしも高くないものの、ヒトのエネルギー消費において座位行動および軽強度活動が寄与するところは大きい。本研究でも座位行動と身体活動によるエネルギー消費量との相関係数は $\rho = -0.84$ であり、軽強度および中高強度身体活動のそれ(0.80, 0.72)と比べても座位行動がエネルギー消費に強く関与するといえよう。身体活動によるエネルギー消費量は、Q1とQ4の間で、体重1kg当たり男性で3.6kcal/日、女性で3.9kcal/日と大きな差が認められており、座位行動が影響したものと考えられた。また、異なるメカニズムとして、長時間にわたって下肢の筋収縮が生じない不活動状態に曝されることで、筋中のリポ蛋白リパーゼ活性の低下をきたすことが指摘されている²³⁾。高齢者においても座位時間が脂質代謝異常と関連するという結果も報告されており^{4,7)}、間接的ではあるものの、この仮説を支持するものと考えられる。

本研究の強みは、座位行動を定量的に測定した点にある。我々の知る限り、我が国の地域高齢者において加速度計によって測定された座位行動と肥満との関係を示した研究は見当たらない。本研究で用いた3軸加速度計は、感度3mGとごくわずかな身体の動きもとらえられるものであり、更に低強度活動のための推定式を含む強度推定アルゴリズムを備えていることから¹⁵⁾、座位行動時間を高い精度で推定可能といえる。加速度計のデータ選択の手続きに関する明確な基準がないことから、先行研究^{9,16,17)}に従って1日10時間以上かつ4日以上の装着があった者を解析対象としたが、結果として1日当たり平均装着時間14時間以上かつ平均装着日数7日以上となっていたことから、装着へのコンプライアンスは十分に高かったと考えられる。また、BMIだけでなく体脂肪率の測定を行っている点も本研究の強みとしてあげられる。高齢者では、若年者と比べて身体組成のばらつきが大きいため、BMIだけでは体格の評価に不十分な可能性がある。生体インピーダンス法は測定精度に課題はあるものの、千人を超える規模の調査

においては妥当な方法であったと考えられる。

一方で、本研究はいくつかの課題を有している。第1に、本研究は横断研究であることから因果関係は明らかでない。本稿で述べたメカニズムとは反対に、肥満・体重増加が座位行動の先行要因だとする報告もあり²⁴⁾、いまだに十分な知見は蓄積されていないことから、今後の前向き研究を通して検証を続けることが求められる。第2に、調査は特定の町で実施されたものであり、本研究の知見をそのまま一般高齢者に適用できるとは限らない。また、解析対象者は、地区で行われた測定会に参加できた者であったことから、比較的健康かつ活動的な集団に偏っている可能性が否定できない。解析対象者の年齢が若く、教育歴も長かったことを踏まえると、地域における代表性も課題があるといえる。第3に、本研究では服薬歴や食事の影響を考慮していないことも課題としてあげられる。

このような課題がありつつも、高齢期の肥満対策においては運動や身体活動促進の代替策として、座位行動に注目することは公衆衛生的な意義があると考えられる。肥満・体脂肪蓄積の予防において、運動や活発な身体活動の有益さについては既に多くの知見が得られているが、高齢期において活発な身体活動や運動を実践に結びつけるのは必ずしも容易ではない場合がある。これに対して、本研究のように活動的と考えられる自立高齢者においても、座位行動時間は最も短い群で40%、最も長い群で70%近くを占めていた。このように、座位行動はあらゆる人が行っている活動であり、かつ個人間の変動幅も大きいため、行動を変容できる潜在的な人口は十分に大きいと予想される。このことから、座位行動は肥満・体脂肪蓄積に向けたポピュレーション・アプローチにおいて有用な指標となりうるだろう。

5. 結 論

地域在住高齢者において、座位行動時間は肥満リスクと有意に関連していた。座位行動と体脂肪との関連は先行研究とも一致しており、座位行動が身体活動エネルギー消費を反映していると考えられた。以上の成績から、高齢期において過度の脂肪蓄積を抑制するためのポピュレーション・アプローチとして、座位行動に注目することの有効性が示唆された。

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【Original Article】

Association between Tri-axial Accelerometer-derived Sedentary Time and Obesity in a Japanese Community-dwelling Older Population

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Abstract

Objective: Previous studies have shown that time spent in sedentary behaviors is a risk factor of obesity, independent of lack of moderate-to-vigorous physical activity (MVPA). However, few studies have been conducted to examine relationship between objectively measured time spent in sedentary behaviors and obesity. The aim of this study was to investigate the relationship of objectively measured sedentary time and obesity in community-dwelling older adults.

Methods: Cross-sectional analyses were completed on 1,401 (female n=849) participants of the baseline survey of the Sasaguri Genkimon Study (SGS), a longitudinal cohort study of community-dwelling older adults aged 65+ who were not certified as requiring nursing care. Sedentary behaviors were defined as activities with intensity ≤ 1.5 METs (metabolic equivalents). Sedentary time was assessed by a tri-axial accelerometer. Obesity was defined as body mass index (BMI) of 25 or higher. Body weight and fat mass was measured by bioelectrical impedance analysis.

Results: Sedentary time was positively associated with body weight, fat mass, body fat percentage and obesity in both men and women ($p < 0.01$), and positively associated with BMI in women as well ($p < 0.01$), after adjusting for socio-demographic and lifestyle factors, instrumental activities of daily living, and MVPA.

Conclusion: Prolonged sedentary behaviors were associated with increased risk of obesity and its related indicators in Japanese community-dwelling elderly. Decreasing sedentary behaviors can be an effective strategy for preventing obesity in population approach.

Key words: sedentary behavior, accelerometry, physical activity energy expenditure

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Research article

Physical Fitness Measures As Potential Markers of Low Cognitive Function in Japanese Community-Dwelling Older Adults without Apparent Cognitive Problems

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Abstract

Detecting signs of cognitive impairment as early as possible is one of the most urgent challenges in preventive care of dementia. It has still been unclear whether physical fitness measures can serve as markers of low cognitive function, a sign of cognitive impairment, in older people free from dementia. The aim of the present study was to examine an association between each of five physical fitness measures and global cognition in Japanese community-dwelling older adults without apparent cognitive problems. The baseline research of the Sasaguri Genkimon Study was conducted from May to August 2011 in Sasaguri town, Fukuoka, Japan. Of the 2,629 baseline subjects who were aged 65 years or older and not certified as individuals requiring nursing care by the town, 1,552 participants without apparent cognitive problems (Mini-Mental State Examination score ≥ 24) were involved in the present study (59.0% of the baseline subjects, median age: 72 years, men: 40.1%). Global cognitive function was measured by the Japanese version of the Montreal Cognitive Assessment. Handgrip strength, leg strength, sit-to-stand rate, gait speed, and one-leg stand time were examined as physical fitness measures. In multiple linear regression analyses, each of the five physical fitness measures was positively associated with the Montreal Cognitive Assessment score after adjusting for age and sex ($p < 0.001$). These associations were preserved after additional adjustment for years of formal education, body mass index, and other confounding factors ($p < 0.001$). The present study first demonstrated the associations between multiple aspects of physical fitness and global cognitive function in Japanese community-dwelling older people without apparent cognitive problems. These results suggest that each of the physical fitness measures has a potential as a single marker of low cognitive function in older populations free from dementia and thereby can be useful in community-based preventive care of dementia.

Key words: Cognitive screening, community-based study, cross-sectional study, mild cognitive impairment, physical function, primary prevention.

Introduction

Dementia has been perceived as a burdensome public health issue in aging societies (Wimo et al., 2013; Wimo and Prince, 2011). One of the most urgent challenges in the primary care field is to detect signs of cognitive impairment as early as possible before clinical diagnosis. Earlier detection has been suggested to allow for effective medical treatments preventing or slowing the onset of dementia (Siemers, 2011; Sperling et al., 2011). Hence, there is a great need for identifying biomarkers and other

lifestyle-related markers which help the detection of subtle cognitive impairment occurring in the preclinical or earlier phase of the disease.

Physical fitness has been reported to be a lifestyle-related factor predicting future incidence of dementia and cognitive impairment (Alfaro-Acha et al., 2007; Buchman et al., 2007; Sattler et al., 2011; Wang et al., 2006). In contrast, it has not been fully understood whether physical fitness measures can serve as markers of low cognitive function, a sign of cognitive impairment, in older people free from dementia. Two recent population-based studies suggested a role of gait speed as a marker of low cognitive function in the pre-dementia stage by demonstrating its association with global cognition in cognitively intact older people (Fitzpatrick et al., 2007; Mielke et al., 2013). However, the knowledge for other physical fitness measures has still been limited. The other measures not yet investigated include those often administered in community-based health checkups to evaluate different aspects of physical fitness. Because the primary detection essentially needs to cover community-dwelling older individuals having diverse physical functional status, it is worth understanding abilities of the other physical fitness measures as single markers of low cognitive function in the pre-dementia stage. Therefore, the aim of the present study was to examine if each of the physical fitness measures determined by five common tests would be associated with global cognitive function in Japanese community-dwelling older people without apparent cognitive problems.

Methods

Participants

The present study was performed as part of the baseline research of the Sasaguri Genkimon Study (SGS) conducted from May to August 2011. The design of the SGS has been described in detail elsewhere (Narazaki et al., 2013). Briefly, it is an ongoing community-based prospective cohort study in Sasaguri Town, a regional town on Kyushu Island located in the southwest part of Japan, aiming to explore modifiable lifestyle-related factors causing older people to require nursing care. Subjects of the baseline research were 2,629 town residents who were aged 65 years or older and not certified as individuals requiring nursing care by the town at the end of January 2011. Of the baseline subjects, we excluded 17 individuals with a medical history of dementia or Parkinson's

disease, 526 individuals who refused or did not complete cognitive tests, 146 individuals with signs of apparent cognitive problems determined by a Mini-Mental State Examination (MMSE) score of <24 , 177 individuals who refused physical fitness tests, and 211 individuals with incomplete data on other measurements (Figure 1). Accordingly, 1,552 participants were involved in the present study (59.0% of the baseline participants). Written informed consent was obtained from all the baseline subjects prior to their participation. This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the Institute of Health Science, Kyushu University.

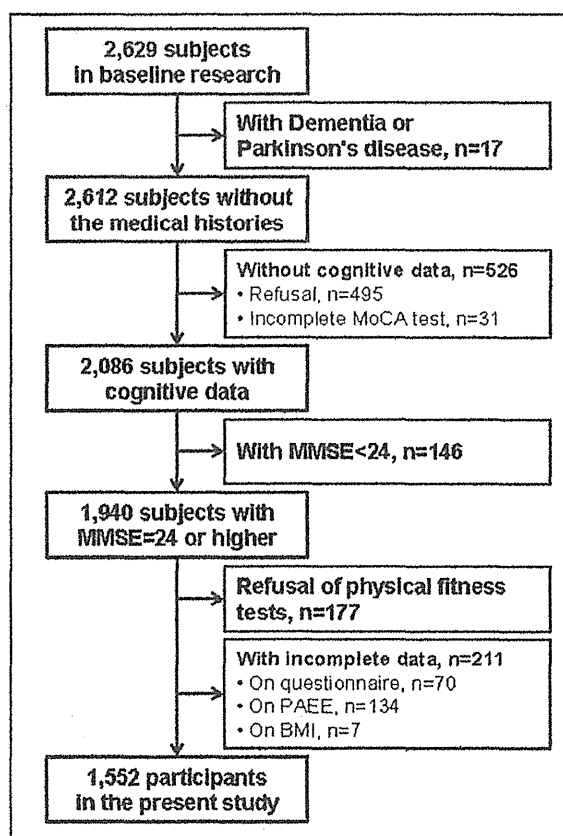


Figure 1. Flow chart of participation. This figure shows the flow of participation in the present study. MoCA, MMSE, PAEE, and BMI denote Montreal Cognitive Assessment, Mini-Mental State Examination, physical activity energy expenditure, and body mass index, respectively.

Cognitive function measures

Cognitive function was measured with the Japanese version of the Montreal Cognitive Assessment (MoCA). The details of this instrument are explained elsewhere (Fujiwara et al., 2010). Like the original one (Nasreddine et al., 2005), it is a 30-point tool for measuring global cognition in the nine domains of attention, calculations, concentration, conceptual thinking, executive functions, language, memory, orientation, and visuoconstructional ability. A higher MoCA score indicates better cognitive function. All MoCA tests were administered to the participants by trained examiners in accordance with the official instruction (Suzuki, 2010). After the measure-

ment, MoCA scores were independently evaluated by two trained authors (K.N and T.H: 93.2% of agreement). Inconsistent evaluations between the two were judged together before final scores were determined. For the present study, MoCA scores without the 1-point correction for years of education were used. In addition to the MoCA, we performed the Japanese version of MMSE to screen apparent cognitive problems with the cut-off score of <24 , as explained in the above section. This MMSE cut-off score has been widely used to detect abnormal cognitive status and to screen dementia in previous studies (Holsinger et al., 2007).

Physical fitness measures

Multiple aspects of physical fitness were objectively measured through five tests in a random manner: the handgrip test for measuring upper-extremity strength, the isometric knee extension test for lower-extremity strength, the five-times sit-to-stand test for lower-extremity agility, the 5-meter gait test for locomotive coordination, and the open-eyed one-leg stand test for postural balance. These five tests were selected because they are commonly administered in community-based regular checkups for older people in Japan. The handgrip test was performed twice for each hand using a digital grip dynamometer (TKK5401; Takei Scientific Instruments, Niigata, Japan) in a standing position. In this test, the participants were asked to grip the dynamometer as strongly as possible. The handgrip strength (HS: kg) was determined as an average of the highest scores of the left and right hands. The isometric knee extension test was also performed twice for each leg using a digital tension meter (TKK5710e; Takei Scientific Instruments, Niigata, Japan) in a seated position with the knee flexed at 90 degrees. During the test, the participants were asked to exert knee extensor force as strongly as possible against an ankle extended from the tension meter while crossing their arms on their chest. The leg strength (LS: kg) was defined in the same way as for the HS. In the five-times sit-to-stand test, the participants were requested to perform five consecutive chair stands as quickly as possible while crossing their arms on their chest, and the time (sec) spent to complete the task was recorded using a digital stopwatch. Only one trial was made for this test due to its strenuous nature. The sit-to-stand rate (SR: reps/sec) was determined by dividing 5 (reps) by the task time. The 5-meter gait test was conducted over a straight 11m lane with taped marks at the 3m and 8m points. The participants were asked to walk on the entire lane as fast as possible (but without running) in two trials, and the time (sec) for walking between the two marks was measured in each trial using a digital stopwatch. The gait speed (GS: m/sec) was calculated by dividing 5 (m) by the shortest task time in the two trials. In the open-eyed one-leg stand test, the participants tried to stand as long as possible up to 120 sec with a preferred leg while watching a taped mark on the wall 1m away from a toe line. This test was performed twice, and the time (sec) to failure of the task was measured in each trial using a digital stopwatch. The longer task time in the two trials was selected as the one-leg stand time (OT: sec). All of the five tests were admin-

istered by trained examiners with standardized procedures including standard instruction and practice. Additionally, the participants were encouraged to ask questions, if needed, throughout the procedures for better understanding and compliance. Higher values indicate better physical fitness in all of the five measures.

Other measurements

Age, sex, years of formal education, and economic status (comfortable, relatively comfortable, relatively uncomfortable, and uncomfortable) were obtained from a questionnaire. The physical activity energy expenditure (PAEE: kcal/day) was defined as average daily energy expenditure due to physical activity and objectively measured by a tri-axial accelerometer device (Active Style Pro HJA-350IT; Omron Healthcare, Kyoto, Japan) (Ohkawara et al., 2011). For this measurement, the participants were asked to wear the device all day (except for sleeping and water activities) for 7 days. The PAEE was determined only for those wearing the device for at least 10 hours a day on two or more days (mean \pm standard deviation or SD of wearing period in the present participants: 6.8 ± 1.8 days). Body weight (kg) and height (m) were measured using conventional scales, and body mass index (BMI) was calculated by dividing the body weight by height squared (kg/m^2). Instrumental activities of daily living (IADL) were measured as part of the questionnaire using the five-item scale for instrumental self-maintenance of the Tokyo Metropolitan Institute of Gerontology Index of Competence (Koyano et al., 1991). The five items asked about the abilities of using public transportation, shopping for commodities, preparing meals, paying bills, and handling bank accounts in binary forms (able or unable). The participants answering "able" for all of the five items were regarded as independent in IADL and others as dependent in IADL. In the present study, the number of items answered with "able" was used as the index of IADL in regression analyses while the dependency in IADL was reported in demographic description. The psychological distress was measured by the Japanese version of the Kessler 6 psychological distress scale (K6) in the questionnaire (Sakurai et al., 2011). This is a 6-item and 24-point scale, and participants who scored 5 points or more on the scale were classified as having depressive status. In the present study, the K6 scores were used in regression analyses while the depressive status was reported in demographic description. Comorbidities of hypertension, heart disease, and diabetes and history of stroke were asked on the questionnaire in binary forms (presence or absence).

Statistical analysis

Mean \pm SD or median (25th-75th percentiles) was calculated for continuous variables, appropriately, and frequency (%) for categorical variables. To confirm similarities between the present participants and the baseline subjects, the Wilcoxon rank-sum test and the chi-square test were conducted for continuous and categorical variables, respectively. To examine associations between physical fitness and cognitive function, multiple linear regression analyses were conducted for each of the five

physical fitness measures in the following three models: Model 1: entered each physical fitness measure as an independent variable, MoCA as a dependent variable, and age and sex as covariates, Model 2: Model 1 plus years of formal education and BMI as covariates, Model 3: Model 2 plus economic status, PAEE, IADL, K6, comorbidities of hypertension, heart disease, and diabetes, and history of stroke as covariates. A significance level was set at two-sided $\alpha = 0.05$. All statistical analyses were performed using the SAS version 9.3 (SAS Institute Inc., Cary, NC, USA).

Results

The median age (25th-75th percentiles) for the present participants was 72 (68-77) years and 40.1% of the participants were men ($n = 623$). The mean \pm SD or median (25th-75th percentiles) of the MoCA and the physical fitness measures in the present participants were as follows: MoCA ($n = 1,552$): 22.4 ± 3.4 point, HS ($n = 1,529$): 27.2 ± 8.0 kg, LS ($n = 1,473$): 27.0 ± 10.3 kg, SR ($n = 1,488$): 0.60 ± 0.19 reps/sec, GS ($n = 1,540$): 1.72 ± 0.43 m/sec, OT ($n = 1,525$): 45.7 (15.1-120) sec. Table 1 shows characteristics of the present participants on these and other variables.

Results of the regression analyses were summarized in Table 2. Each of the five physical fitness scores was significantly associated with the MoCA score after adjusting for age and sex (Model 1: $p < 0.001$). After additional adjustment for years of formal education and body mass index, each physical fitness score remained associated with the MoCA score (Model 2: $p < 0.001$). After further adjustment for the other confounding factors (economic status, PAEE, IADL, K6, hypertension, heart disease, diabetes, and stroke), the association between each physical fitness score and MoCA was almost unchanged (Model 3: $p < 0.001$).

Discussion

The present study examined associations between five physical fitness measures and global cognitive function evaluated by the MoCA in Japanese community-dwelling older adults without apparent cognitive problems. The primary finding of the present study is that each of the five physical fitness measures was linearly and positively associated with the MoCA score. These associations were independent of age, sex, years of formal education, BMI, and other confounding factors.

Examining lifestyle-related markers of pre-dementia cognitive functioning is expected to be of value to promote early detection of subtle cognitive impairment in community-based settings. Despite the promise of physical fitness measures as markers of low cognitive function in the pre-dementia stage, research evidence is still limited. To our knowledge, only two studies have examined the potential role of physical fitness as a marker of low cognitive function in the stage by showing association between gait speed and global cognition in non-demented older people living in the United States (Fitzpatrick et al., 2007; Mielke et al., 2013). In one study

Table 1. Characteristics of the present participants.

| Indexes | Men | | Women | |
|------------------------|------------------|-----------------|-----------------|-----------------|
| | 65-74 years | 75+ years | 65-74 years | 75+ years |
| n | 402 | 221 | 570 | 359 |
| Age, years | 69 (67-71) | 79 (77-82) | 69 (67-71) | 79 (77-82) |
| MoCA, point | 23.3 (3.1) | 21.4 (3.3) | 23.1 (3.2) | 20.8 (3.5) |
| HS, kg | 36.4 (5.6) | 31.4 (5.5) | 23.3 (3.9) | 20.2 (4.1) |
| LS, kg | 36.6 (9.9) | 29.3 (8.6) | 24.1 (6.9) | 18.8 (6.5) |
| SR, reps/sec | .65 (.19) | .55 (.17) | .63 (.18) | .52 (.16) |
| GS, m/sec | 1.93 (.44) | 1.68 (.41) | 1.76 (0.37) | 1.44 (.36) |
| OT, sec | 109.3 (35.0-120) | 22.9 (7.2-47.6) | 80.6 (24.6-120) | 16.7 (5.8-43.4) |
| Education, years | 12 (10-14) | 11 (9-13) | 12 (9-12) | 10 (9-11) |
| Economy*, % | 32.1 | 47.5 | 38.2 | 48.2 |
| PAEE, kcal/day | 557.5 (162.8) | 453.6 (144.7) | 536.3 (134.5) | 405.6 (115.8) |
| BMI, kg/m ² | 23.5 (2.7) | 23.0 (2.8) | 23.3 (3.4) | 22.9 (3.3) |
| IADL†, % | 16.9 | 14.0 | 1.4 | 6.7 |
| K6‡, % | 24.9 | 27.1 | 30.4 | 32.6 |
| Hypertension, % | 38.1 | 37.1 | 33.0 | 46.5 |
| Heart disease, % | 12.9 | 25.8 | 5.8 | 18.7 |
| Diabetes, % | 19.7 | 17.6 | 9.6 | 9.7 |
| Stroke history, % | 4.5 | 5.0 | 1.6 | 3.1 |

Note: continuous variables are represented as mean (SD) or median (25th-75th percentiles). * Percentage of participants answering "comfortable" and "relatively comfortable" in economic status; † percentage of participants regarded as dependent in instrumental activities of daily living (IADL score of <5); ‡ percentage of participants classified as having depressive status (K6 score of ≥5). MoCA: Montreal Cognitive Assessment; HS: handgrip strength; LS: leg strength; SR: sit-to-stand rate; GS: gait speed; OT: one-leg stand time; PAEE: physical activity energy expenditure; BMI: body mass index; IADL: instrumental activities of daily living; K6: Kessler 6 psychological distress scale.

from the Ginkgo Evaluation of Memory study group, the investigators used the Modified MMSE (3MSE) as a global cognitive test and excluded individuals with the test score of <80 from the study participants (Fitzpatrick et al., 2007). They found that the risk of low cognition defined as the 3MSE score of 80 to 85 was almost twice for participants in the slowest quartile of maximal walking speed compared with that for participants in the fastest quartile after adjusting for demographic and comorbid factors. Another study from the Mayo Clinic group also showed an association between usual walking speed and global cognitive function measured as a standard score of a neuropsychological battery covering four cognitive domains in older adults without diagnosed mild cognitive impairment and dementia (Mielke et al., 2013). These associations reasonably support the ability of gait speed as a marker of low cognitive function in the United States older people free from dementia, but comparable observations had not been made in other ethnicities including Japanese. The present study first demonstrated a similar

association between gait speed and global cognition in a Japanese older population without apparent cognitive problems. Moreover, the present study further demonstrated novel association between each of the other four physical fitness measures and global cognition in the Japanese population (Table 2). A notable aspect of the present study is the use of the MoCA as a reasonable neuropsychological instrument to measure global cognitive function among the participants who were free from apparent cognitive problems. MoCA is a relatively new instrument devised to detect early cognitive changes with multiple domains for screening mild cognitive impairment (Nasreddine et al., 2005). This instrument has been reported to have higher sensitivity to subtle cognitive alterations than MMSE and other conventional tools (Nasreddine et al., 2005; Pendlebury et al., 2010), and has been used as a scale of global cognitive status in population-based studies (Donoghue et al., 2012; King et al., 2013).

One possible mechanism underlying the observed

Table 2. Associations between each physical fitness measure and MoCA.

| Independent variables | n | Model 1 | | Model 2 | | Model 3 | |
|-----------------------|-------|------------------------------------|-------|------------------------------------|-------|------------------------------------|-------|
| | | Regression coefficient (95% CI) | p | Regression coefficient (95% CI) | p | Regression coefficient (95% CI) | p |
| HS, kg | 1,529 | .10 (.07-.14) | <.001 | .09 (.06-.13) | <.001 | .08 (.05-.12) | <.001 |
| LS, kg | 1,473 | .07 (.05-.09) | <.001 | .06 (.04-.08) | <.001 | .06 (.04-.08) | <.001 |
| SR, reps/sec | 1,488 | 2.34 (1.42-3.26) | <.001 | 1.95 (1.05-2.85) | <.001 | 1.55 (.64-2.45) | <.001 |
| GS, m/sec | 1,540 | 1.38 (.96-1.80) | <.001 | 1.17 (.76-1.57) | <.001 | 1.01 (.59-1.43) | <.001 |
| OT, sec | 1,525 | .02 (.01-.02) | <.001 | .01 (.01-.02) | <.001 | .01 (.01-.02) | <.001 |

Note: Model 1: association between each physical fitness measure as an independent variable and MoCA as a dependent variable, with age and sex as covariates; Model 2: Model 1 plus years of education and BMI as covariates; Model 3: Model 2 plus other confounding factors (economic status, PAEE, IADL, K6, hypertension, heart disease, diabetes, and stroke) as covariates. MoCA: Montreal Cognitive Assessment; HS: handgrip strength; LS: leg strength; SR: sit-to-stand rate; GS: gait speed; OT: one-leg stand time; BMI: body mass index; PAEE: physical activity energy expenditure; IADL: instrumental activities of daily living; K6: Kessler 6 psychological distress scale. 95% CI denotes 95% confidential interval of regression coefficient. Coefficients of determination (adjusted R-squared) in the regression analyses are as follows: Model 1: 0.145, 0.138, 0.132, 0.148, 0.157; Model 2: 0.197, 0.192, 0.183, 0.198, 0.205; Model 3: 0.210, 0.206, 0.196, 0.209, 0.217 (for HS, LS, SR, GS, and OT, in respective models).

associations is the concurrent deterioration of the brain regions responsible for cognitive and physical performance in the pre-dementia stage of aging. Small to relatively large deterioration of overall brain structures is observed by magnetic resonance imaging even in healthy older adults (Resnick et al., 2003). Such deterioration may lead to concurrent alterations in cognitive and physical performance in the pre-dementia stage. Because all the physical fitness tests used in the present study require refined brain control for initiation of the tasks, recruitment of muscles, and motor coordination in given constraints, it can be plausible that the deterioration of the brain affects not only cognitive function but also the quality of physical performance objectified by the physical fitness measures.

Based on the observed results, the present study offers a practical value of the physical fitness measures as objective means to assist identifying and monitoring early cognitive impairment in community-based regular checkups. Virtually, all the physical fitness tests used in the present study are simple and require no clinical resources or sophisticated devices. For example, the gait test, sit-to-stand test, and one-leg stand test need only a stopwatch and can be self-performed even at home. In addition, considering the significant association for each physical fitness measure, the five tests may not necessarily have to be performed all together. Rather, any one or a few tests can be selected in the regular checkups, depending on the physical functional status of individuals being tested. Incorporating the physical fitness measures into community-based regular checkups may add information to help earlier detection of cognitive impairment which can allow potential patients to receive effective medical treatments to prevent or slow the onset of dementia sooner. If this will be the case in the near future, it could bring a positive economic impact to society. Indeed, an estimation showed that if new treatment delaying the onset of Alzheimer's disease (AD) by 5 years will be available in 2015, it could result in the reduction of the projected Medicare costs of AD by 45.1% (from \$627 billion to \$344 billion) in 2050 in the United States (Sperling et al., 2011).

The strengths of the present study are the relatively large population-based samples, the choice of the cognitive instrument (i.e., MoCA) suitable for examining the differences in cognitive function in the participants free from apparent cognitive problems, the use of multiple objective measures of physical fitness, and the variety of confounding measures including the accelerometer-derived PAEE and other health-related scales such as the IADL and K6. In contrast, the present report has several limitations which are worth noting here. First, the sample of the present study might be biased to some extent by the exclusion of subjects (Figure 1). Specifically, subjects excluded due to the refusal or incompleteness of the cognitive tests were younger and had a higher proportion of men than the remaining subjects (median age: 72 vs. 73 years, $p < 0.01$; percentage of men: 50.8 vs. 41.8%, $p < 0.001$). However, since the excluded subjects are considered to have relatively good status on both physical and cognitive functions, the influence of the exclusion on the observed associations may not be considerable. Also,

subjects excluded due to the refusal of the physical fitness tests and the other incomplete measures had a higher proportion of men and lower MoCA scores than the present participants (percentage of men: 48.2 vs. 40.1%, $p < 0.005$; mean MoCA score: 21.8 vs. 22.4 years, $p < 0.001$). Nevertheless, the influence of this exclusion may also not be sizable because the excluded subjects presumably had relatively lower physical functioning than the present participants besides the lower cognitive function. Second, the relatively large samples of the present study did not allow us to perform neurological examination to determine older individuals with clinical cognitive impairment. Instead, we used the MMSE cut-off score of <24 which has been widely used to screen dementia in clinical and population-based studies (Holsinger et al., 2007). Finally, because the present study was performed in a single Japanese town, generalizability of the results to other regions is limited. Therefore, further community-based studies in other populations should be performed to overcome this limitation.

Conclusion

In summary, the present study first demonstrated the associations between five physical fitness measures and global cognitive function in Japanese community-dwelling older people without apparent cognitive problems, independent of age, sex, years of formal education, body mass index, and other confounding factors. The present results suggest that each of the five physical fitness measures has a potential ability as a single lifestyle-related marker of low cognitive function in older populations free from dementia and thereby can be used to help earlier detection of cognitive impairment in community-based preventive care of dementia. Future studies will be conducted to develop a specific screening method for early cognitive impairment in the pre-dementia stage with using these physical fitness measures.

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