

# Weakened Grip Strength Over 40 Years in a Community-Dwelling Cohort in Tanushimaru, Japan

TAKAHIRO YOSHIKAWA\*, KEN-ICHIRO SASAKI\*, HISASHI ADACHI\*, TATSUYUKI KAKUMA \*\*, SACHIKO HATADA-KATAKABE\*, YUUKI TAKATA\* AND YOSHIHIRO FUKUMOTO\*

\* Division of Cardiovascular Medicine, Department of Internal Medicine, Kurume University School of Medicine,

\*\* Biostatistics Center, Kurume University, Kurume 830-0011, Japan

Received 8 February 2021, accepted 17 August 2021

J-STAGE advance publication 14 June 2023

Edited by NAOTO SHIBA

**Summary: Background:** An epidemiological survey has been periodically performed since 1977 among the adult population in Tanushimaru, a typical farming town in Japan. We aimed in this study to retrospectively investigate changes of grip strength (GS) and its correlates over 40 years in the same cohort of community-dwelling adults. We used pooled data from the survey to deduce essential correlates of GS in community-dwelling adults.

**Methods:** We retrospectively compared serial correlates of GS in the adult population in Tanushimaru between a population tested in 1977 and 1979 (Cohort A, n=2,452) and another population tested in 2016 and 2018 (Cohort B, n=1,505), to identify essential correlates of GS for investigating changes in GS during the past 40 years in community-dwelling adults.

**Results:** Age, height, weight, and the occupation of the subjects remained as correlates of GS in both genders during the past 40 years. In males, abdominal circumference also remained as a correlate of GS. Serum albumin levels in males and systolic blood pressure in females were identified as new correlates. GS after adjustment for the above correlates weakened in both genders, and the serial change in GS was particularly remarkable in subjects whose occupations were Class-1 and Class-2, which were defined as moderately hard work.

**Conclusions:** From a periodically-performed epidemiological survey of a community-dwelling cohort in a Japanese typical farming town, age, height, weight, and occupation were deduced as essential correlates of GS. GS in the community dwelling cohort weakened in both genders over 40 years, possibly affected by their occupation.

**Keywords** epidemiology, health check-up, Japanese population, correlates

## INTRODUCTION

Grip strength (GS) is often used as an indicator of skeletal muscle strength in the whole body. Skeletal muscle volume and strength decrease and weaken with aging, and sarcopenia and dynapenia are defined as the age-related loss of muscle mass and strength. A loss of GS is included in the diagnostic criteria of sarcopenia in Asia and Europe, suggesting that age is an essential correlate of GS. In addition, although weakened GS was reported to be associated with loss of

physical functionality, fractures by falls, cognitive impairment, all-cause mortality [1], and nutritional status [2] in epidemiological studies, there has been no report regarding serial changes in GS and its correlates over several decades in adults in an epidemiological study. If the correlates can be clarified, GS-related adverse events, such as fractures by falls, cognitive impairment, cardiovascular disease, respiratory disease, and cancer [1,3,4], may be prevented more effectively.

Changes in lifestyle components, such as the kind

Corresponding Author: Ken-ichiro Sasaki, M.D., Ph.D., Division of Cardiovascular Medicine, Department of Internal Medicine, Kurume University School of Medicine, 67 Asahi-machi, Kurume, Fukuoka 830-0011, Japan. Tel: +81-942-31-7562, Fax: +81-942-33-6509, E-mail: sasaken@med.kurume-u.ac.jp

Abbreviations: AC, abdominal circumference; BMI, body mass index; DBP, diastolic blood pressure; GS, grip strength; MBP, mean blood pressure; PP, pulse pressure; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; TP, total protein; UA, uric acid.

of occupation [5], smoking [6], and alcohol drinking [7] habits, and nutrition status [2], may influence GS and its correlates over a long period. Therefore, serially epidemiological surveys among adults who have lived in the same communities for several decades may help to resolve the issue by identifying changes in the correlates of GS over time. We have periodically performed an epidemiological survey for the adult population in Tanushimaru, a typical farming town in Japan, since 1958 [8]. The demographic characteristics of the population have been comparable to those of a general Japanese population so far [8,9]. Accordingly, we retrospectively compared correlates of GS in the population in Tanushimaru between a cohort in 1977 and 1979 and another cohort in 2016 and 2018. The aim of this study was to investigate changes in the correlates of GS over 40 years in community-dwelling adults in Tanushimaru, Japan, to deduce essential correlates of GS in such community-dwelling adults, and finally to compare GS after adjustment for the essential correlates between the two cohorts.

## MATERIALS AND METHODS

### *Subjects*

We enrolled subjects from 4 surveys of the Tanushimaru study in 1977, 1979, 2016, and 2018. The subjects provided written informed consent to use their data for retrospective cohort studies in the future. This study conformed to the principles outlined in the Declaration of Helsinki and was approved by the Committees on the Ethics Review Board of the Kurume University School of Medicine.

### *Measurements and calculations*

Body mass index (BMI) was calculated as the body weight in kilograms divided by the square of the height of each person in meters. Blood pressure was measured twice with participants in the supine position. The second blood pressure measurement was taken after 5 deep breaths and the 5th-phase diastolic pressure was used for statistical analyses. The mean blood pressure (MBP), which reflects a reduction in arteriolar caliber [10], was calculated with a standard formula as follows:  $MBP = \text{diastolic blood pressure (DBP)} + 1/3 [\text{systolic blood pressure (SBP)} - \text{DBP}]$ . Pulse pressure (PP), which reflects increased large artery stiffness and a risk factor for cardiovascular and cerebrovascular events [11], was calculated as the difference between SBP and DBP. In order to measure the abdominal circumference (AC), we placed a tape measure in a horizontal plane around the abdomen at

the level of the iliac crest, and read the length at the end of a normal expiration. Maximum voluntary isometric GS was measured with a Smedley-type handheld dynamometer (Matsumiya Ika Seiki Seisakusho Co., Ltd., Tokyo, Japan). Subjects maintained upright standing positions, held the dynamometer in a comfortable grip size adjusted to their hands, and squeezed it as hard as possible two times with each hand. The highest value in measured values for the left and right hands was adopted for statistical analyses. Blood was drawn from the antecubital vein after a half day of fasting. The serum total cholesterol (TC), triglycerides (TG), uric acid (UA), total protein (TP), and albumin levels were measured according to standard methods in a commercial laboratory (Kyodo Igaku Laboratories, Inc., Fukuoka, Japan).

### *Classification of occupations*

We classified the occupations of the subjects into 4 groups based on the grade of work as follows; (Class-0) no occupation, (Class-1) office worker, chief priest, monk, teacher, nursery school teacher, hotel manager, barber, beautician, doctor, nurse, midwife, radiologist, dentist, pharmacist, massager, physical therapist, care worker, industrial artist, dressmaker, housemaker, and garbage person, (Class-2) transporter, electric worker, mechanic, industrial worker, server, cook, butcher, surveyor, painter, and news dealer, (class-3) farmer, builder, masonry, fisherman, Self-Defense Forces personnel, and railway employee [12]. Class-3 was defined as the hardest type of work in the 4 classes.

### *Statistical analysis*

We divided all data into two cohorts defined as subjects in 1977 and 1979 (Cohort A) and in 2016 and 2018 (Cohort B). Comparisons of baseline characteristics between the two groups were performed by the Wilcoxon signed-rank tests. Regarding SBP, DBP, TC, TG, UA, TP, and albumin in the baseline characteristics, comparisons of the characteristics between the two cohorts were performed by the logistic regression analysis, in which the statistical significance was adjusted for age. The chi-square test was used to perform univariate analysis for categorical variables. The univariate analyses were also performed to examine an association between GS and other baseline characteristics excluding BMI, MBP, and PP, which are calculated with other baseline characteristics such as height, weight, SBP, and DBP. Then, the multivariate analyses were performed to adopt essential correlates of GS in Cohorts A and B for adjusting the following com-

parison of least square means of GS between Cohort A and Cohort B in the logistic regression analysis. The comparison of least square means of GS between Cohort A and Cohort B by the occupation class was performed in the logistic analysis including the interaction between the change of time and the occupation class. Normal distribution of measured values was checked using the Shapiro-Wilk test. Statistical significance was assumed at a value of  $p < 0.05$ . Data were analyzed using JMP Pro 13.0 (SAS Institute, Cary, NC, USA).

## RESULTS

### *Differences in the subjects' baseline characteristics between Cohort A and Cohort B*

The baseline characteristics of all subjects are shown by gender in Table 1. The median values of age, height, weight, AC, SBP, DBP, MBP, and PP were greater in both genders in order of Cohort B to Cohort

A. Similarly, the frequency of subjects with hypertension were higher in both genders in order of Cohort B to Cohort A. Despite remaining in normal range, the serum TC and TP levels in both genders and the serum UA levels in males were higher in order of Cohort B to Cohort A, whereas the serum albumin levels in both genders and the serum TG and UA levels in females were lower in order of Cohort B to Cohort A.

The frequency of daily smokers was significantly higher in male subjects in order of Cohort A to Cohort B (the left panel in Figure 1). The frequency of daily alcohol drinkers was significantly higher in female subjects in order of Cohort B to Cohort A (the center panel in Figure 1). The frequencies of both genders in the occupation class-3 markedly decreased in Cohort B compared with those in Cohort A (the right panel in Figure 1).

### *Changes in the subjects' blood pressure and nutrition during 40 years*

TABLE 1.  
*Baseline characteristics of all subjects*

	Male			Female		
	Cohort A (n=1528)	Cohort B (n=607)	P-value	Cohort A (n=924)	Cohort B (n=898)	P-value
Age (year)	52 (43, 65)	70 (63, 77)	$p < 0.001$	50 (38, 63)	69 (61, 77)	$p < 0.001$
Height (m)	162.4 (158.0, 166.6)	165.5 (161.3, 170)	$p < 0.001$	150.5 (146.4, 154.5)	152.4 (147.8, 156.7)	$p < 0.001$
Weight (Kg)	58 (52.5, 64.9)	64 (57.9, 70.3)	$p < 0.001$	50.2 (45, 56)	51.6 (46.5, 57.5)	$p < 0.001$
BMI	22.0 (20.2, 24.1)	23.5 (21.6, 25.2)	$p < 0.001$	22.2 (20.2, 24.4)	22.2 (20.1, 24.8)	$p = 0.684$
AC (cm)	84 (78.5, 89)	88 (83, 93)	$p < 0.001$	78 (71, 85)	83.5 (77, 90)	$p < 0.001$
Grip strength (Kg)	40 (33, 48)	35.6 (29.8, 40.8)	$p < 0.001$	28 (23, 34)	22.9 (19.8, 25.8)	$p < 0.001$
SBP (mmHg)	136 (122, 150)	146 (131, 161)	$p < 0.001$	128 (116, 150)	144 (129, 159)	$p < 0.001$
DBP (mmHg)	80 (74, 90)	83 (75, 91)	$p < 0.001$	78 (70, 86)	80 (73, 88)	$p < 0.001$
MBP (mmHg)	98.7 (90.7, 108)	104 (94.7, 113)	$p < 0.001$	95.3 (86, 107.3)	102.2 (93, 110.8)	$p < 0.001$
Pulse pressure (mmHg)	54 (46, 68)	61 (51, 74)	$p < 0.001$	52 (42, 64)	63 (52, 75)	$p < 0.001$
Hypertension (%)	55.2	69.9	$p < 0.001$	44.7	67.0	$p < 0.001$
TC (mg/dL)	157 (141, 179)	196 (175, 217)	$p < 0.001$	156 (142, 176)	214 (190, 237)	$p < 0.001$
TG (mg/dL)	108 (82, 152)	106 (74, 152)	$p = 0.131$	111 (83, 157)	99 (71.5, 141.5)	$p < 0.001$
UA (mg/dL)	5.2 (4.5, 5.9)	6.0 (5.1, 6.9)	$p < 0.001$	5.3 (4.5, 6.1)	4.7 (4.1, 5.5)	$p < 0.001$
TP (mg/dL)	7.0 (6.8, 7.3)	7.4 (7.0, 7.6)	$p < 0.001$	7.0 (6.8, 7.3)	7.4 (7.1, 7.6)	$p < 0.001$
Albumin (mg/dL)	4.6 (4.3, 4.8)	4.5 (4.3, 4.6)	$p < 0.001$	4.6 (4.3, 4.8)	4.5 (4.3, 4.7)	$p < 0.001$

Cohort A indicates community-dwelling adults who lived in Tanushimaru in 1977 and 1979. Cohort B indicates those in 2016 and 2018. BMI; body mass index, AC; abdominal circumference, SBP; systolic blood pressure, DBP; diastolic blood pressure, MBP; mean blood pressure, TC; total cholesterol, TG; triglyceride, UA; uric acid, TP; total protein. Values except for the frequency of hypertension are indicated by median (interquartile range). Statistical comparisons were performed by Mann-Whitney U tests.

In males, DBP was elevated over the 40 years from 1977 to 2018 after adjustment for age (Table 2). Their serum TC, TG, UA, and TP levels also increased in that period. In females, SBP or DBP did not change, whereas serum TC and TP levels increased. Meanwhile, the TG, UA, and albumin levels decreased.

*GS-related characteristics in the subjects*

In males in Cohorts A and B, the univariate analysis for correlates of GS showed that age, SBP, and the history of hypertension were inversely associated with GS (Table 3). Meanwhile, height, weight, the serum TG and albumin levels, habits of daily smoking and alcohol intake, and occupation were positively associated with GS. In females in Cohorts A and B, the univariate analysis showed that age, AC, SBP, DBP, the serum TC and TP levels, and the history of hypertension were inversely associated with GS. Meanwhile, height, weight, the serum albumin levels, and the occupation were positively associated.

The multiple stepwise regression analysis for males in Cohort A adopted age, AC, and occupation as inverse correlates of GS. Weight, height, and the se-

rum TC levels were adopted as positive collates of GS (Table 4). Meanwhile, the multiple stepwise regression analysis for males in Cohorts A and B adopted age, AC, and the occupation as inverse correlates of GS. Weight, height, and the serum albumin levels were adopted as positive correlates of GS. Findings in the above multiple stepwise regression analyses indicated that the factors of age, weight, AC, height, and occupation, in that order, were unchanged as the correlates of GS of males over 40 years. Next, the multiple stepwise regression analysis for females in Cohort A adopted age as an inverse correlate of GS. Height, weight, and the occupation were adopted as positive correlates of GS (Table 4). Meanwhile, the multiple stepwise regression analysis for females in Cohorts A and B adopted age as an inverse correlate of GS. Height, weight, the occupation, and SBP were adopted as positive correlates of GS. Findings in the multiple stepwise regression analyses indicated that the factors of age, height, weight, and occupation, in that order, were unchanged as the correlates of GS of females over the 40 years.

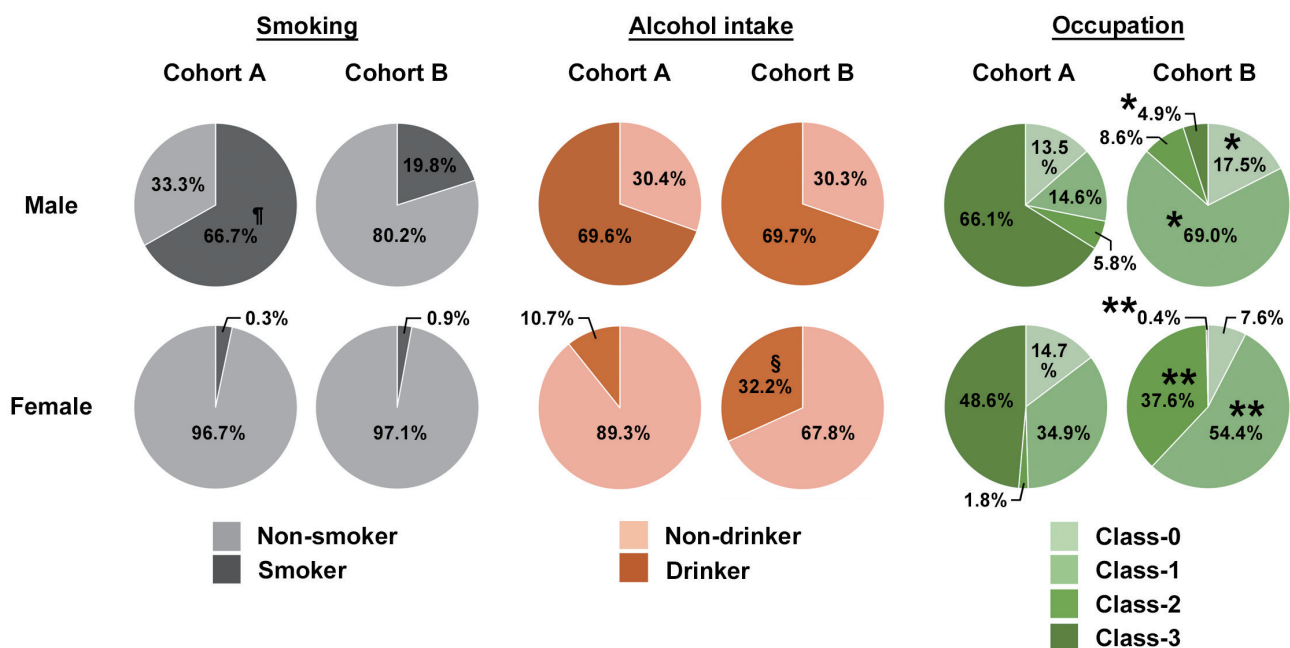


Fig. 1. The frequencies of smokers, alcohol drinkers, and workers classified into four different occupations in both genders in Cohorts A and B. Cohort A indicates community-dwelling adults who lived in Tanushimaru in 1977 and 1979. Cohort B indicates those in 2016 and 2018. Smoking and alcohol intake were classified as current habitual use or not. The content of the four different classes of the occupations is described in the Material and Methods section. Subjects in Class-0 indicates subjects who do not work daily. The work levels of Class-1, Class-2, and Class-3 were classified into comparatively light, moderate, and hard, respectively. †: p<0.001 vs. the percentage of the male smokers in Cohort B, §: p<0.001 vs. the percentage of the female alcohol drinkers in Cohort A, \*: p<0.001 vs. the percentage of the male workers corresponding to the same occupation class in Cohort A, \*\*: p<0.001 vs. the percentage of the female workers corresponding to the same occupation class in Cohort A.

TABLE 2.  
Comparison of several baseline characteristics estimated after adjustment for age

	Male			Female		
	Cohort A (n=1528)	Cohort B (n=607)	P-value	Cohort A (n=924)	Cohort B (n=898)	P-value
AC (cm)	84.0±0.2	87.6±0.4	p<0.001	79.3±0.3	82.3±0.3	p<0.001
SBP (mmHg)	140.1±0.9	142.5±1.0	p=0.116	143.1±1.3	142.1±0.7	p=0.512
DBP (mmHg)	80.9±0.5	84.5±0.6	p<0.001	79.7±0.7	80.7±0.4	p=0.264
TC (mg/dL)	158.0±1.4	201.6±1.5	p<0.001	156.8±2.1	216.7±1.2	p<0.001
TG (mg/dL)	120.5±3.4	141.6±4.1	p<0.001	131.8±4.1	114.6±2.4	p<0.001
UA (mg/dL)	5.23±0.05	6.12±0.06	p<0.001	5.43±0.07	4.81±0.04	p<0.001
TP (mg/dL)	7.01±0.02	7.37±0.02	p<0.001	7.04±0.03	7.39±0.01	p<0.001
Albumin (mg/dL)	4.52±0.01	4.56±0.02	P=0.119	4.55±0.02	4.50±0.01	P=0.014

Cohort A indicates community-dwelling adults who lived in Tanushimaru in 1977 and 1979. Cohort B indicates those in 2016 and 2018. AC; abdominal circumference, SBP; systolic blood pressure, DBP; diastolic blood pressure, TC; total cholesterol, TG; triglyceride, UA; uric acid, TP; total protein. P values are adjusted by age. Other values are indicated by least squares mean ± standard error.

TABLE 3.  
Univariate analysis for correlates of grip strength in all subjects by gender

	Male			Female		
	$\beta$	SE	P-value	$\beta$	SE	P-value
Age, years	-0.720	0.010	<0.001	-0.709	0.007	<0.001
Height, cm	0.472	0.031	<0.001	0.444	0.022	<0.001
Weight, Kg	0.387	0.020	<0.001	0.270	0.018	<0.001
AC, cm	-0.014	0.028	0.536	-0.110	0.017	<0.001
SBP, mmHg	-0.187	0.010	<0.001	-0.287	0.007	<0.001
DBP, mmHg	0.029	0.020	0.184	-0.076	0.014	0.001
TC, mg/dL	-0.010	0.006	0.712	-0.120	0.004	<0.001
TG, mg/dL	0.144	0.003	<0.001	0.020	0.002	0.483
UA, mg/dL	0.015	0.181	0.576	-0.010	0.145	0.720
TP, mg/dL	-0.021	0.507	0.440	-0.101	0.370	<0.001
Albumin, mg/dL	0.241	0.712	<0.001	0.138	0.561	<0.001
Smoking	0.158	0.232	<0.001	0.035	0.464	0.136
Alcohol drinking	0.145	0.255	<0.001	0.002	0.204	0.943
Hypertension	-0.106	0.238	<0.001	-0.272	0.157	<0.001
Occupation	0.297	0.185	<0.001	0.340	0.147	<0.001

AC; abdominal circumference, SBP; systolic blood pressure, DBP; diastolic blood pressure, TC; total cholesterol, TG; triglyceride, UA; uric acid, TP; total protein.  $\beta$  and SE indicate standardized regression coefficients and standard error, respectively.

TABLE 4.  
Multiple stepwise regression analysis for correlates of grip strength in part of or all of subjects by gender

Cohort A	$\beta$	SE	P-value	Cohort A and Cohort B	$\beta$	SE	P-value
Male				Male			
Age, years	-0.493	0.024	<0.001	Age, years	-0.577	0.015	<0.001
Weight, Kg	0.427	0.047	<0.001	Weight, Kg	0.406	0.035	<0.001
AC, cm	-0.253	0.048	<0.001	AC	-0.234	0.037	<0.001
Height, cm	0.113	0.047	<0.001	Height, cm	0.148	0.034	<0.001
Occupation	-0.089	0.224	<0.001	Occupation	-0.063	0.173	0.005
TC, mg/dL	0.072	0.007	0.006	Albumin, mg/dL	0.054	0.518	0.005
Female				Female			
Age, years	-0.466	0.016	<0.001	Age, years	-0.492	0.011	<0.001
Height, cm	0.227	0.037	<0.001	Height, cm	0.206	0.023	<0.001
Weight, Kg	0.172	0.039	<0.001	Weight, Kg	0.144	0.024	<0.001
Occupation	0.127	0.150	<0.001	Occupation	0.092	0.114	<0.001
				SBP, mmHg	0.064	0.007	0.012

Cohort A indicates community-dwelling adults who lived in Tanushimaru in 1977 and 1979. Cohort B indicates those in 2016 and 2018. AC; abdominal circumference, TC; total cholesterol, SBP; systolic blood pressure.  $\beta$  and SE indicate standardized regression coefficients and standard error, respectively.

#### Changes in GS of the subjects during 40 years

In males, GS in Cohort B was weaker than that in Cohort A after adjustment for age, height, weight, AC, the serum albumin levels, and occupation ( $39.6 \pm 0.4$  Kg vs.  $37.9 \pm 0.4$  Kg) (Figure 2). Also, in females, GS in Cohort B was weaker than that in Cohort A after adjustment for age, height, weight, SBP, and occupation ( $26.8 \pm 0.3$  Kg vs.  $25.7 \pm 0.3$  Kg). Moreover, in the comparison of GS between Cohort A and Cohort B by the occupation class (Figure 3), GS in males whose occupations were graded into Class-2 weakened from  $41.5 \pm 0.9$  Kg in Cohort A to  $36.9 \pm 0.9$  Kg in Cohort B. GS in females whose occupations were graded into Class-1 and Class-2 weakened from  $26.3 \pm 0.3$  Kg in Cohort A to  $24.7 \pm 0.2$  Kg in Cohort B and from  $27.6 \pm 1.1$  Kg in Cohort A to  $24.1 \pm 0.3$  Kg in Cohort B, respectively.

## DISCUSSION

This retrospective and cross-sectional cohort study is the first report to evaluate serial changes in GS and its correlates over a period of 40 years from 1977 to 2018 in the same community-dwelling cohort in Japan. This major findings of this study were as follows: (1) age, weight, AC, height, and occupation remained as the correlates of GS of males over 40 years, (2) se-

rum albumin levels became a new correlate of GS in males over 40 years, replacing serum TC levels, (3) age, height, weight, and occupation remained as the correlates of GS of females over the 40 year period, (4) SBP became a new correlate of GS of females during the 40 years, (5) GS after adjustment for the above correlates weakened in both genders, and (6) the weakened GS was prominent in the occupation class-2 group in males and in the occupation class-1 and class-2 groups in females.

#### Changes in the subjects' physiques and nutritional status during 40 years

According to the national nutrition survey in Japan [13], the average per-capita daily calories in Japanese adults decreased from 2,131 Kcal in 1977 and 1979 to 1,904 Kcal in 2016 and 2018. The average per-capita daily intake of animal protein in adults also decreased from 39.0 g in 1977 and 1979 to 38.4 g in 2016 and 2018. However, the numerical values of height, weight, AC, and the serum concentrations of TC and TP in both genders in this study increased in Cohort B as compared with those in Cohort A, indicating that the physiques of the subjects got bigger without showing overnutrition but with an increase in obesity during the period. It is unclear why this discrepancy occurred. Meanwhile, the average per-capita daily intake

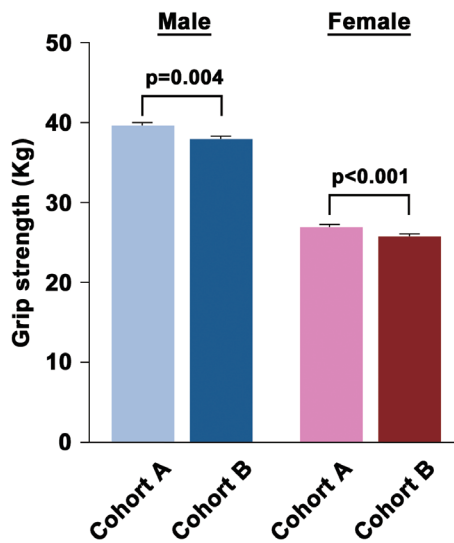


Fig. 2. Comparisons of grip strength between Cohort A and Cohort B by gender. Cohort A indicates community-dwelling adults who lived in Tanushimaru in 1977 and 1979. Cohort B indicates those in 2016 and 2018. The comparisons were performed by statistical analyses adjusted for confounding factors described in the Results section. Grip strength in both genders weakened toward 2018.

of animal fat in Japanese adults increased from 28.4 g in 1977 and 1979 to 30.1 g in 2016 and 2018 [13]. The increase in the daily intake of animal fat from 1977 to 2018 might have contributed to increases in the numerical values of weight, AC, and the serum concentrations of TC in both genders in Cohort B. However, such a speculation must be tempered by the fact that the increase in daily intake of animal fat was very small.

#### Changes in the subject's GS and its correlates during 40 years

A multiple stepwise regression analysis adopted age, height, weight, and occupation as common correlates of GS in both genders in Cohorts A and B, suggesting that these four correlates, which were unchanged as the correlates of GS over 40 years from 1977 to 2018, may be essential correlates of GS in both genders. There were previous reports regarding a strong correlation between age and GS in healthy adults [14,15]. There were also reports that height and weight were correlated with GS in adults [16]. The absolute values of the standardized regression coefficients of age were comparable with those of weight in males in Cohort A and Cohort B, suggesting that age and weight may be generally high-powered correlates in the community-dwelling adult males. Nevertheless, the increase of weight, which is a positive correlate of

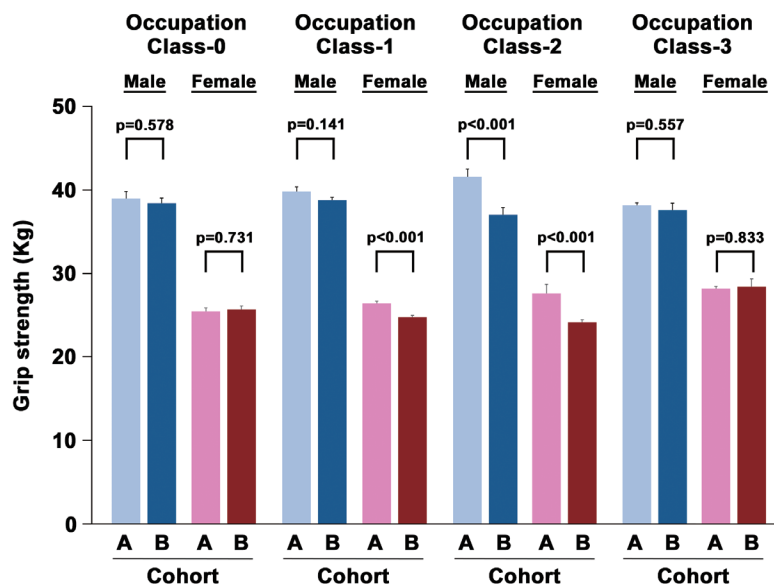


Fig. 3. Comparisons of grip strength between Cohort A and Cohort B by gender and the occupation class of the subjects. Cohort A indicates community-dwelling adults who lived in Tanushimaru in 1977 and 1979. Cohort B indicates those in 2016 and 2018. Grip strength weakened toward 2018 in males in the group of the occupation class-2 and in females in the groups of the occupation class-1 and class-2.

GS, in both genders in Cohort B over 40 years did not influence the weakness of GS in either gender in Cohort B.

AC, which is an inverse correlate of GS in males in Cohorts A and B, elongated in Cohort B as compared with that in Cohort A, suggesting that it might be a considerable correlate as an influencer to weaken GS in males. There was a report that AC was inversely associated with GS in elderly men [17], possibly supporting the above speculation. It will be necessary to monitor similar reports going forward. Although GS was reported to be associated with metabolic syndrome [18], it was impossible in this study to diagnose metabolic syndrome in Cohort A, because we had no data regarding serum high-density lipoprotein levels and fasting glucose levels. We would like to study serial changes in the coexistence of metabolic syndrome as a correlate of GS in the future.

The multiple stepwise regression analysis additionally adopted serum albumin as a correlate of GS in males and SBP in females. Although the serum albumin levels were correlated with GS in patients with heart failure, in which the correlation coefficient was 0.034 [19], the relationship might not apply to the community-dwelling cohort as reported in this study. Meanwhile, a longitudinal study of older adults in the Netherlands reported that low serum albumin level was independently associated with weaker GS and future decline in GS [20]. The roles of low-grade inflammation and protein synthesis degradation were speculated as potential mechanisms of the association between serum albumin levels and GS in the longitudinal study, in which inflammatory markers, such as serum C-reactive protein and interleukin-6 which were measured; however, we did not examine any inflammatory markers in our study. Another longitudinal study of older adults in the Netherlands reported that arterial stiffness, which is a factor regulating SBP [21], was not associated with GS [22]. Nevertheless, several reports indicated a positive correlation between serum albumin levels and GS in 1,750 adults in Netherlands [19] and 273 adults in Spain [23], and another positive correlation between blood pressure and GS in 420 adults in the United States [24]. Although those studies were conducted in different races and age groups from our study, their findings may support our results. The age-adjusted values of the serum albumin in males or those of SBP in females did not change in Cohort B as compared with those in Cohort A, suggesting that the two correlates might not influence changes in GS in either gender in Cohort B. Nevertheless, it will be necessary to monitor whether the two

correlates remain as essential correlates of GS in the community-dwelling cohort during the next several decades.

Although a European survey of 27,351 adults reported that occupational class based on current or last occupation did not predict GS of the subjects [5], weakened GS in Cohort B was particularly shown in the subjects whose occupations' classes were Class-1 and Class-2. The reason remains unclear. The frequencies of both genders whose occupations were graded into Class-1 and Class-2 were increased in Cohort B. Workers whose occupations graded into Class-1 and Class-2 might not use their hands and fingers as forcefully and frequently in general as before, possibly due to improvement of working tools and/or mechanization of work. If so, we should advise workers graded into Class-1 and Class-2 to use their hands and fingers actively in daily life to avoid any loss of GS. Although a British cohort study reported that greater time spent sitting was associated with weaker GS in 4,726 adults [25], it was unclear in our study if the workers graded into Class-1 and Class-2 were sitting for a comparatively long time in the working, and if the workers had a risk of low occupational physical activity and high sedentary time [26]. Nevertheless, it is undoubtable that there are other correlates of GS, which we could not examine in this study, such as daily medications, exercise habits, leisure activities, and circumstances of livelihood support. According to a study examining the longitudinal interactions between occupational physical activity levels and leisure time exercise in 12,969 Swedish working people, people changing from physically active to sedentary occupations seemed to compensate by increasing leisure time exercise [27]. Despite the lack of data, weakened GS in the subjects whose occupations' classes were Class-1 and Class-2 in Cohort B might be partly due to the contents of leisure time exercise.

The least square means of GS in both genders aged 65-74 years in Cohort B were  $36.0 \pm 0.5$  Kg in males and  $23.6 \pm 0.3$  Kg in females (data not shown). Meanwhile, in a national survey of GS for Japanese in 2018, the averages of GS in both genders aged in 65-74 years were 38.8 Kg in males and 24.6 Kg in females [28]. Thus, in adults aged 65-74 years, GS in both genders in Tanushimaru in 2016 and 2018 seemed to be weaker than that in both genders in the Japanese survey in 2018. GS was reported to be positively associated with physical function [1], suggesting that the physical functionality of both genders in Cohort B might have become lower during the past 40 years.



### Study limitations

This study had several limitations. First, this study was not a longitudinal study. It was possible that a not insignificant number of subjects may have changed their occupations during 40 years. Second, activities of daily living, cognitive functioning, and social and leisure activities were not assessed. These were reported as correlates to GS in older people [29]. Some males in occupation Class-0 (i.e., subjects who do not work daily) might have a high leisure activity, resulting in a comparatively strong grip strength in the males. Third, the nutritional status in the subjects was not assessed in detail. Muscle function may react to nutritional deprivation [30]; however, we do not have appropriate methods or indices to assess the nutrition of healthy subjects in detail at present. Fourth, whole-body protein and muscle mass, which are correlated with muscle strength [30], were not measured in the subjects. Therefore, it is unclear whether a weakened GS in females in Cohort B was involved in a decrease in the whole-body protein and/or muscle mass in the females. Fifth, the classification of occupations in the subjects might not precisely reflect their work levels.

### CONCLUSIONS

Age, height, weight, and occupation may be essential correlates of GS in community-dwelling adults. For future clinical studies, our findings suggest that we should adjust measured values of GS with at least these four correlates. GS after adjustment for the correlates which were adopted in this study weakened over 40 years from 1977 to 2018 in both genders in Tanushimaru, which is a typical farming town in Japan. Although this result might be attributed in part to the kind of occupation during the observational period, longitudinal studies to validate that hypothesis and to examine other correlates of GS are needed.

**ACKNOWLEDGEMENTS:** We would like to thank Motoki Sasaki, Yuta Ishizaki, Miki Biwa, Naoko Yuuda, Mika Enomoto, Ako Fukami, Eita Kumagai, Sachiko Nakamura, Yume Nohara, Shoko Kono, Erika Nakao, Akiko Sakaue, Hitoshi Hamamura, and Kenta Toyomasu in the Division of Cardiovascular Medicine, Department of Internal Medicine, Kurume University School of Medicine, Jiahui Sun and Mai Yamamoto in the Cardiovascular Research Institute, Kurume University, Chiharu Sasaki, Manami Iwasa, and Yuuka Inoue in Chikushi Jogakuen Senior High School for their excellent performance to collect and enter the data in the surveys in Tanushimaru in 2016 and 2018.

**FUNDING:** This work was in part supported by Japan Society for the Promotion of Science KAKENHI [grant number

15K08757] and the Fukuoka Medical Research award from MEDICAL CARE EDUCATION RESEARCH FOUNDATION.

**CONFLICT OF INTEREST:** The authors declare that there is no conflict of interest.

### REFERENCES

1. Bohannon RW. Muscle strength: clinical and prognostic value of hand-grip dynamometry. *Curr Opin Clin Nutr Metab Care* 2015; 18:465-470.
2. Vaz M, Thangam S, Prabhu A, and Shetty PS. Maximal voluntary contraction as a functional indicator of adult chronic undernutrition. *Br J Nutr* 1996; 76:9-15.
3. McGrath R, Vincent BM, Hackney KJ, Robinson-Lane SG, Downer B et al. The Longitudinal Associations of Handgrip Strength and Cognitive Function in Aging Americans. *J Am Med Dir Assoc* 2020; 21:634-639.
4. Celis-Morales CA, Welsh P, Lyall DM, Steell L, Petermann F et al. Associations of grip strength with cardiovascular, respiratory, and cancer outcomes and all cause mortality: prospective cohort study of half a million UK Biobank participants. *BMJ* 2018; 361:k1651.
5. Mohd Hairi F, Mackenbach JP, Andersen-Ranberg K, and Avendano M. Does socio-economic status predict grip strength in older Europeans? Results from the SHARE study in non-institutionalised men and women aged 50+. *J Epidemiol Community Health* 2010; 64:829-837.
6. Saito T, Miyatake N, Sakano N, Oda K, Katayama A et al. Relationship between cigarette smoking and muscle strength in Japanese men. *J Prev Med Public Health* 2012; 45:381-386.
7. Wang T, Sun S, Li S, Sun Y, Sun Y et al. Alcohol Consumption and Functional Limitations in Older Men: Does Muscle Strength Mediate Them? *J Am Geriatr Soc* 2019; 67:2331-2337.
8. Adachi H, Enomoto M, Fukami A, Nakamura S, Nohara Y et al. Trends in nutritional intake and coronary risk factors over 60 years among Japanese men in Tanushimaru. *Heart Vessels* 2020; 35:901-908.
9. Hirai Y, Geleijnse JM, Adachi H, Imaizumi T, and Kromhout D. Systolic blood pressure predicts cardiovascular mortality in a farming but not in a fishing community. *Circ J* 2011; 75:1890-1896.
10. Bennett PC, Silverman S, and Gill P. Hypertension and peripheral arterial disease. *J Hum Hypertens* 2009; 23:213-215.
11. Glynn RJ, Chae CU, Guralnik JM, Taylor JO, and Hennekens CH. Pulse pressure and mortality in older people. *Arch Intern Med* 2000; 160:2765-2772.
12. Keys A. Seven Countries Study. A multivariate analysis of death and coronary artery disease. Cambridge: Harvard University Press; 1980.
13. National Health and Nutrition Survey. List of Statistical Surveys conducted by Ministry of Health, Labour and Welfare.
14. Mendes J, Amaral TF, Borges N, Santos A, Padrão P et al. Handgrip strength values of Portuguese older adults: a pop-

- ulation based study. *BMC Geriatr* 2017; 17:191.
15. Wearing J, Konings P, Stokes M, and de Bruin ED. Handgrip strength in old and oldest old Swiss adults - a cross-sectional study. *BMC Geriatr* 2018; 18:266.
  16. Keevil V, Mazzuini Razali R, Chin AV, Jameson K, Sayer AA et al. Grip strength in a cohort of older medical inpatients in Malaysia: a pilot study to describe the range, determinants and association with length of hospital stay. *Arch Gerontol Geriatr* 2013; 56:155-159.
  17. de Carvalho DHT, Scholes S, Santos JLF, de Oliveira C, and Alexandre TDS. Does Abdominal Obesity Accelerate Muscle Strength Decline in Older Adults? Evidence From the English Longitudinal Study of Ageing. *J Gerontol A Biol Sci Med Sci* 2019; 74:1105-1111.
  18. Kawamoto R, Ninomiya D, Kasai Y, Kusunoki T, Ohtsuka N et al. Handgrip strength is associated with metabolic syndrome among middle-aged and elderly community-dwelling persons. *Clin Exp Hypertens* 2016; 38:245-251.
  19. Chung CJ, Wu C, Jones M, Kato TS, Dam TT et al. Reduced handgrip strength as a marker of frailty predicts clinical outcomes in patients with heart failure undergoing ventricular assist device placement. *J Card Fail* 2014; 20:310-315.
  20. Schalk BW, Deeg DJ, Penninx BW, Bouter LM, and Visser M. Serum albumin and muscle strength: a longitudinal study in older men and women. *J Am Geriatr Soc* 2005; 53:1331-1338.
  21. O'Rourke M. Arterial stiffness, systolic blood pressure, and logical treatment of arterial hypertension. *Hypertension* 1990; 15:339-347.
  22. Blanchard AR, Taylor BA, Thompson PD, Lepley LK, White CM et al. The influence of resting blood pressure on muscle strength in healthy adults. *Blood Press Monit* 2018; 23:185-190.
  23. Verde Z, Giaquinta A, Sainz CM, Ondina MD, and Araque AF. Bone Mineral Metabolism Status, Quality of Life, and Muscle Strength in Older People. *Nutrients* 2019; 11:2748.
  24. van Dijk SC, Swart KM, Ham AC, Enneman AW, van Wijngaarden JP et al. Physical Fitness, Activity and Hand-Grip Strength Are Not Associated with Arterial Stiffness in Older Individuals. *J Nutr Health Aging* 2015; 19:779-784.
  25. Cooper R, Stamatakis E, and Hamer M. Associations of sitting and physical activity with grip strength and balance in mid-life: 1970 British Cohort Study. *Scand J Med Sci Sports* 2020; 30:2371-2381.
  26. Smith L, McCourt O, Sawyer A, Ucci M, Marmot A et al. A review of occupational physical activity and sedentary behaviour correlates. *Occup Med (Lond)* 2016; 66:185-192.
  27. Nooijen CFJ, Del Pozo-Cruz B, Nyberg G, Sanders T, Galanti MR et al. Are changes in occupational physical activity level compensated by changes in exercise behavior?. *Eur J Public Health* 2018; 28:940-943.
  28. Sports physical examination survey conducted by Japan Sports Agency, 2019. [https://www.mext.go.jp/prev\\_sports/comp/b\\_menu/other/\\_icsFiles/afieldfile/2019/10/15/1421922\\_4.pdf](https://www.mext.go.jp/prev_sports/comp/b_menu/other/_icsFiles/afieldfile/2019/10/15/1421922_4.pdf)
  29. Taekema DG, Gussekloo J, Maier AB, Westendorp RGJ, and de Craen A. Handgrip strength as a predictor of functional, psychological and social health. A prospective population-based study among the oldest old. *Age and Ageing* 2010; 39:331-337.
  30. Norman K, Stobäus N, Gonzalez MC, Schulzke JD, and Pirllich M. Hand grip strength: outcome predictor and marker of nutritional status. *Clin Nutr* 2011; 30:135-142.