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ORIGINAL ARTICLE

Semen Analysis

Association of handgrip strength with semen characteristics: a study with repeated measurements among healthy Chinese men

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Accumulating epidemiological evidence shows that handgrip strength provides predictive potential in physical, mental, and reproductive health status. However, the associations between handgrip strength and semen characteristics have not been explored. We recruited 1382 eligible men at the Hubei Province Human Sperm Bank (Wuhan, China) who had their handgrip strength measured at recruitment and provided 6458 repeated semen specimens within a 6-month period. Semen characteristics, including semen volume, sperm motility parameters (immotility, nonprogressive motility, and progressive motility), and sperm concentration, were assessed. Mixed-effect models and restricted cubic spline functions were applied to investigate the relationship of handgrip strength with repeated measurements of semen characteristics. After adjusting for confounding factors, the mixed-effect models revealed that handgrip strength was positively associated with semen volume, sperm concentration, progressive motility, total motility, and total count (all *P* for trend < 0.05). Compared to men in the lowest quartile, those in the highest quartile of handgrip strength had higher semen volume, sperm concentration, progressive motility, total motility, and total count, with measurements of 14.2% (95% confidence interval [CI]: 5.9%–23.2%), 19.5% (95% CI: 7.3%–33.1%), 9.5% (95% CI: 3.4%–15.9%), 8.8% (95% CI: 3.2%–14.6%), and 36.4% (95% CI: 18.9%–56.5%), respectively. These positive dose-response relationships were further confirmed in restricted cubic splines, where handgrip strength was modeled as a continuous variable. Handgrip strength, as an indicator of muscular function and strength, was positively associated with semen characteristics in a dose-dependent manner.

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INTRODUCTION

Handgrip strength is a feasible and validated marker of muscular function and strength, which makes it attractive for providing valuable information on overall health status for both men and women.[1] Recent studies have also suggested that handgrip strength is an attractive and objective marker of upper extremity strength, which makes it tempting to employ handgrip strength as a screening tool for monitoring and detecting changes in nutritional status, especially among younger adults.[2,3] Accumulating epidemiological evidence shows that low handgrip strength is associated with greater all-cause mortality and cardiovascular outcomes,[4,5] diabetes prevalence,[2] cognitive decline,[6] and functional disability,[7] suggesting that lower handgrip strength may have predictive potential for vulnerability to diseases.[8] Furthermore, Atkinson and colleagues revealed a positive association between handgrip strength and self-reported reproductive success.[9] A more recent study conducted among hunter-gatherers showed that male upper extremity strength significantly predicted reproductive success in terms of offspring production.[10] Meanwhile, handgrip strength was strongly related to higher serum testosterone concentrations among 7064 healthy adults from the National Health and Nutrition Examination Survey,[11] suggesting a potential influence on spermatogenesis,[12–14] given the strong association between testosterone concentrations and semen characteristics.[15,16] However, the relationship between handgrip strength and semen characteristics remains unclear.

To fill the data gap, we explored the associations between handgrip strength and repeated semen characteristics among 1382 healthy Chinese men screened as potential sperm donors. Our findings will provide more useful information on the utility of a handgrip dynamometer as a potentially useful predictor of human semen characteristics.

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PARTICIPANTS AND METHODS

Study design

A total of 1487 healthy men were recruited from potential sperm donors at the Hubei Province Human Sperm Bank (Wuhan, China) during the period from April 2017 to July 2018, as described previously.[17,18] The protocol of this study was approved by the Ethics Committee of the Center for Reproductive Medicine, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China (approval No. 2017-01). After providing written informed consent, each participant underwent a physical examination, completed a baseline questionnaire, and provided a semen specimen at enrolment. The questionnaire collected various information regarding demographic characteristics (*e.g.*, age, height, weight, education level, income level, and marital status), lifestyle factors (*e.g.*, abstinence time, and drinking and smoking habits), medical history, and reproductive health conditions (*e.g.*, testis injury, vasectomy, and varicocele).

Participants were required to fulfill the screening standards for inclusion in the current study: (1) had a high school degree or above; (2) were aged between 22 years and 45 years; (3) were in good health without genetic diseases or sexually transmitted diseases (*e.g.*, thalassemia, karyotype abnormalities, hepatitis, human immunodeficiency virus, syphilis, gonorrhea, and chlamydia); and (4) had no occupational exposure. The donors were asked to provide sufficient quantities of semen samples to impregnate five women in 6 months if they met the following donation standard published by the Chinese Ministry of Health: (1) a fresh sperm concentration $\geq 60 \times 10^6$ ml^{-1}, progressive sperm motility ≥60%, and percentage of normal morphology >30%; and (2) a frozen-thaw survival rate ≥60%, postthaw sperm motility ≥40%, and number of motile sperm per vial $\geq 12 \times 10^6$.[19] Men who failed to meet the screening standard were asked to provide additional amounts of semen samples for further screening at 1–15 days, 16–31 days , 32–63 days, and ≥64 days after recruitment. Semen characteristics were evaluated each time the participants provided specimens regardless of whether the semen characteristics met the donation criteria. We excluded 102 men because of genetic diseases or sexually transmitted diseases (*e.g.*, thalassemia, chromosome abnormalities, and human hepatitis B virus infection) and three men due to missing data on handgrip strength, leaving 1382 eligible men for our current analysis.

Semen collection and analyses

After an abstinence time of more than 48 h, the volunteer collected semen specimens into a sterile polyethylene cup by masturbation. After liquefaction at 37°C, semen characteristics, including semen volume, sperm motility parameters (immotility, nonprogressive motility, and progressive motility), and sperm concentration, were assessed according to the World Health Organization laboratory manual,[20] as described previously.[17,18] Briefly, a weighing method was used to determine semen volume assuming a sperm density of 1.0 g ml^{-1}. After being thoroughly mixed, 10 µl of semen was placed into a sterile Makler chamber (Sefi Medical Instruments, Haifa, Israel) and estimated by an optical microscope (BX53, Olympus Corporation, Tokyo, Japan) to evaluate progressive sperm motility, total motility, and sperm concentration. Then, we calculated total motility (progressive motility + nonprogressive motility) and total sperm count per ejaculate for each sample (sperm concentration × semen volume). The semen sample was analyzed by trained technicians at the Andrology Laboratory of Hubei Province Human Sperm Bank, and the between- and within-day quality control were assessed to ensure variation of less than 10%.[21]

Handgrip strength

Handgrip strength was assessed by professional research staff using a Jamar Plus+ hand dynamometer (Sammons Preston, Warrenville, IL, USA). Before each measurement, the grip span of the device was adjusted to fit the participant's hand size. Handgrip strength was assessed while standing; the device was held with the elbow in full extension and the arm was positioned at the side of the body. Then, the participant was required to squeeze the dynamometer as hard as they could for 3 s. The test was measured twice more at intervals of >30 s, and the value was recorded with a precision of 0.1 kg. If the participant changed their position during the measurement, a new test was performed. Handgrip strength was measured twice for each hand, with intraclass correlation coefficients (ICCs) of 0.86 and 0.87 for left and right handgrip strength, respectively. Because the left and right handgrip measurements were significantly correlated ($r_{spearman} = 0.84$, $P < 0.0001$), we used the average values of handgrip strength from both hands in all subsequent analyses.[4,22] The handgrip measurements were expressed as absolute units (kg).[2,4]

Statistical analyses

Descriptive analyses were conducted for participants' demographics, lifestyle factors, and semen characteristics according to handgrip strength (kg). The Kruskal–Wallis test or Chi-square tests were applied to assess the differences in demographic characteristics across the quartiles of handgrip strength. Semen volume, sperm concentration, progressive motility, total motility, and total count were transformed by natural logarithmic transformation to normalize the distribution. Then, linear mixed-effects models with a subject-specific random intercept, which provide researchers with powerful and flexible analytical tools for repeated-measures data,[23,24] were applied to evaluate the relationships of handgrip strength (expressed in quartiles and per standard deviation [s.d.] difference) with repeated measures of semen characteristics. Tests for trends across the quartiles of handgrip strength were evaluated by using a median value within each quartile as a continuous value. Restricted cubic spline functions based on linear mixed-effects models were used to characterize the dose-response relationship between continuous handgrip strength and semen characteristics and visually check the linearity of these associations.[25] Potential confounders were selected *a priori* and were then retained in the multivariable models if the *P* value was less than 0.2 in the bivariate analyses in terms of their association with exposure or at least one outcome measure; covariates with a $P > 0.15$ for all tested semen characteristics were further removed from the final models.[26] Finally, the full models were adjusted for abstinence period (day), body mass index (BMI, kg m^{-2}), age (year), smoking status (never, former, or current), alcohol consumption (never, occasional, former, or current), tea consumption (yes or no), marital status (married, unmarried, or divorced), monthly income (<4000 Chinese Yuan, 4000–8000 Chinese Yuan, or >8000 Chinese Yuan), education level (less than undergraduate, or undergraduate or above), and sampling season (winter, spring, summer, or autumn). For data with missing values (<0.5% for all covariates), missing indicator variables were used in the data analyses.

Stratified analyses were conducted to assess whether the relationships were modified by BMI (underweight [<18.5 kg m^{-2}], normal weight [18.5–23.9 kg m^{-2}], and overweight/obesity [≥24.0 kg m^{-2}])[27] and age (<28 years *vs* ≥28 years). A cross-product term was added to the final model to evaluate multiplicative interactions.[28] Additionally, several sensitivity analyses were conducted to test the robustness of our results. First, we used handgrip strength relative to body weight (kg kg^{-1}, per s.d. difference) to assess the influence of body size. Second, we used the within-subject average measurements to reflect individual semen characteristics. Third, we assessed the cross-sectional associations between handgrip strength and semen characteristics that were both measured at baseline enrolment. Fourth, we filled out the missing data with median values. Fifth, we separately assessed the associations for the average values of left and right handgrip strength. Finally, to evaluate the potential influence of physical activity and body fat, we additionally adjusted for these two variables by restricting our analysis to 535 men who had complete information on physical activity (evaluated by the long-form International Physical Activity Questionnaire[29]) and body fat percentage (assessed by a bioelectrical impedance analyzer; TBF-400, Tanita, Tokyo, Japan). SAS version 9.4 (SAS Institute, Cary, NC, USA) and R version 3.5.1 (https://www.rproject.org/) were used for all data analyses. $P < 0.05$ was considered statistically significant.

RESULTS

The demographic characteristics of the study population stratified by quartiles of handgrip strength are presented in **Table 1**. The mean (s.d.) abstinence time, age, and BMI were 6.2 (3.4) days, 28.0 (5.2) years, and 22.8 (3.3) kg m^{-2}, respectively. The majority of the participants were unmarried (66.9%), had less than a bachelor's degree (64.4%), and had a self-reported household income level of ≥4000 Chinese Yuan per month (71.0%). Among the participants, 742 (53.7%) were nonsmokers and 352 (25.5%) did not drink alcohol over the past 3 months. Compared to men in the lowest quartile of handgrip strength, men in the highest quartiles had a greater BMI (23.7 ± 3.2 kg m^{-2} *vs* 22.3 ± 3.3 kg m^{-2}) and shorter abstinence time (6.0 ± 3.3 days *vs* 6.4 ± 3.6 days) and were also more likely to get married (37.6% *vs* 23.1%). The median (interquartile range [IQR]) within-subject average measurements of semen volume, sperm concentration, progressive motility, total motility, and total count were 2.9 (1.5) ml, 48.3 × 10^6 (31.9 × 10^6) ml^{-1}, 57.5% (13.2%), 60.8% (13.2%), and 138.6 × 10^6 (109.3 × 10^6), respectively.

A total of 6458 semen specimens (mean frequency: 4.7) were collected from 1382 men. The association between handgrip strength and repeated semen characteristics is presented in **Table 2**. The crude and fully adjusted mixed-effects models both revealed increasing semen volume, sperm concentration, sperm motility (progressive and total), and total count across the quartiles of handgrip strength (all *P* for trend < 0.05). In the fully adjusted models, men in the highest versus men in the lowest quartile of handgrip strength had higher semen volume, sperm concentration, progressive sperm motility, total motility, and total count, with measurements of 14.2% (95% confidence interval [CI]: 5.9%–23.2%), 19.5% (95% CI: 7.3%–33.1%), 9.5% (95% CI: 3.4%–15.9%), 8.8% (95% CI: 3.2%–14.6%), and 36.4% (95% CI: 18.9%–56.5%), respectively. The associations remained when handgrip strength was modeled as a continuous variable.

Figure 1 shows the associations between continuous handgrip strength and semen characteristics based on the restricted cubic spline functions. Consistent with the trend observed in mixed-effect models, handgrip strength was positively associated with semen volume, sperm concentration, progressive motility, total motility, and total count in a monotonical manner. Similar results were observed when we used handgrip strength relative to body weight (kg kg^{-1}) in the mixed-effect models (**Supplementary Table 1**) and cubic spline analysis (**Supplementary Figure 1**).

No evidence of an interaction between handgrip strength and age was determined. However, the associations between handgrip strength and sperm concentration, progressive motility, and total motility were stronger among men who were overweight or obese (BMI ≥24.0 kg m^{-2}; *P*-interaction = 0.02, 0.001, and 0.001, respectively; **Table 3**). The sensitivity analyses showed that the positive dose-response relationships of handgrip strength with semen volume, sperm concentration, and total count persisted when we replaced the missing data with median values, when we used the within-individual average semen characteristics or baseline measurements (**Supplementary Table 2**), and when we separately assessed the associations for the average values of left and right handgrip strength (**Supplementary Table 3**). These associations were also essentially unchanged when we additionally adjusted for physical activity and body fat percentage after excluding men who did not have complete data for these two variables (**Supplementary Table 4**), although men in the highest versus those in the lowest quartile of handgrip strength had a greater body fat percentage (16.6% ± 4.9% *vs* 13.7% ± 5.7%) and higher BMI (24.3 ± 2.8 kg m^{-2} *vs* 22.4 ± 3.3 kg m^{-2}; **Supplementary Table 5**).

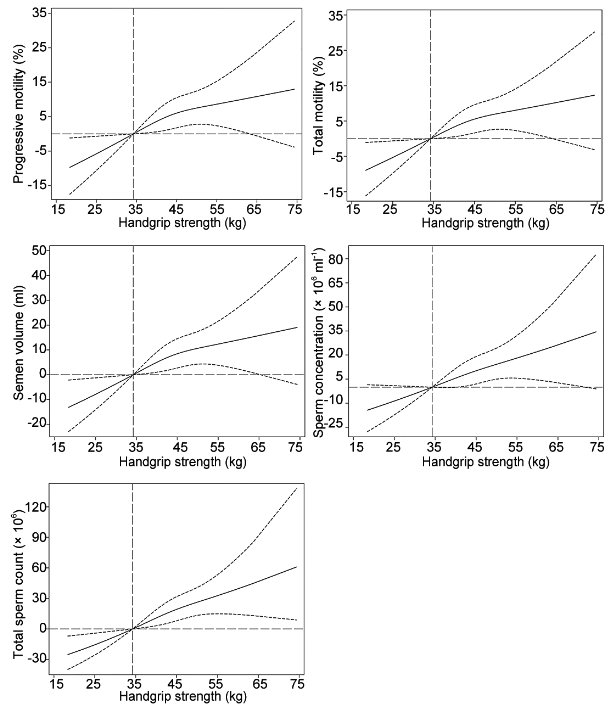

Figure 1: Dose-response relationships of handgrip strength (kg) with repeated semen characteristics based on restricted cubic spline models (*n*=6458). The reference values (*i.e.*, the gray vertical dotted lines) were set to 10% of handgrip strength. All models were adjusted for age, body mass index, abstinence period, marital status, smoking, drinking, tea consumption, monthly income, education level, and sampling season.

DISCUSSION

Across 1382 potential sperm donors, we found that higher handgrip strength was positively associated with semen volume, sperm concentration, motility, and total count. There was no evidence of an interaction between handgrip strength and age. However, the associations of handgrip strength and progressive sperm motility, total motility, and sperm concentration were stronger among men who were overweight or obese.

To the best of our knowledge, studies focusing on the associations of handgrip strength with semen characteristics are rare. In support of our findings, previous studies have reported that handgrip strength is related to masculine features and serum testosterone concentrations,

Table 1: Demographic characteristics and semen characteristics of participants by quartiles of handgrip strength

Characteristic	*Participants included in the analysis[a] (n=1382)*	*Quartile of handgrip strength*				*P[b]*
		Q1 (n=342)	*Q2 (n=347)*	*Q3 (n=347)*	*Q4 (n=346)*	
Handgrip strength (kg), mean±s.d.	43.1±7.3	34.0±3.9	40.7±1.3	45.4±1.4	52.3±3.8	<0.001
Handgrip strength/body weight (kg kg^{-1}), mean±s.d.	0.6±0.1	0.5±0.1	0.6±0.1	0.7±0.1	0.7±0.1	<0.001
Age (year), mean±s.d.	28.0±5.2	28.0±5.5	27.8±5.3	28.1±5.2	28.1±4.9	0.49
BMI (kg m^{-2}), mean±s.d.	22.8±3.3	22.3±3.3	22.3±3.1	23.0±3.2	23.7±3.2	<0.001
Abstinence time (day), mean±s.d.	6.2±3.4	6.4±3.6	6.4±3.2	6.1±3.3	6.0±3.3	0.003
Marital status, *n* (%)						<0.001
Married	419 (30.3)	79 (23.1)	98 (28.2)	112 (32.3)	130 (37.6)	
Unmarried	924 (66.9)	245 (71.6)	239 (68.9)	232 (66.9)	208 (60.1)	
Divorced	39 (2.8)	18 (5.3)	10 (2.9)	3 (0.9)	8 (2.3)	
Smoking, *n* (%)						0.62
Current smoker	541 (39.1)	142 (41.5)	123 (35.5)	139 (40.1)	137 (39.6)	
Former smoker	99 (7.2)	29 (8.5)	24 (6.9)	23 (6.6)	23 (6.7)	
Nonsmoker	742 (53.7)	171 (50.0)	200 (57.6)	185 (53.3)	186 (53.8)	
Drinking, *n* (%)						0.09
Current drinker	169 (12.2)	34 (9.9)	36 (10.4)	49 (14.1)	50 (14.5)	
Former drinker	15 (1.1)	4 (1.2)	3 (0.9)	3 (0.9)	5 (1.5)	
Occasional drinker	846 (61.2)	221 (64.6)	218 (62.8)	211 (60.8)	196 (56.7)	
Nondrinker	352 (25.5)	83 (24.3)	90 (25.9)	84 (24.2)	95 (27.5)	
Tea, *n* (%)						0.51
Yes	388 (28.1)	97 (28.4)	89 (25.7)	99 (28.5)	103 (29.8)	
No	994 (71.9)	245 (71.6)	258 (74.4)	248 (71.5)	243 (70.2)	
Income (Chinese Yuan per month)						0.77
<4000, *n* (%)	400 (29.0)	99 (29.0)	110 (31.7)	94 (27.2)	97 (28.0)	
4000–8000, *n* (%)	527 (38.2)	130 (38.1)	127 (36.6)	133 (38.4)	137 (39.6)	
>8000, *n* (%)	453 (32.8)	112 (32.8)	110 (31.7)	119 (34.4)	112 (32.4)	
Education levels, *n* (%)						0.72
Less than undergraduate	890 (64.4)	225 (65.8)	214 (61.7)	221 (63.7)	230 (66.5)	
Undergraduate or above	492 (35.6)	117 (34.2)	133 (38.3)	126 (36.3)	116 (33.5)	
Season, *n* (%)						0.09
Spring	1582 (24.5)	376 (25.0)	362 (23.3)	429 (26.6)	415 (23.2)	
Summer	2242 (34.7)	477 (31.7)	557 (35.9)	557 (34.5)	651 (36.4)	
Autumn	1738 (26.9)	419 (27.9)	429 (27.7)	400 (24.8)	490 (27.4)	
Winter	896 (13.9)	231 (15.4)	203 (13.1)	230 (14.2)	232 (13.0)	
Average semen characteristics[c]						
Progressive motility (%), median (IQR)	57.5 (13.2)	56.7 (13.9)	56.8 (13.8)	58.0 (13.6)	58.4 (12.0)	0.31
Total motility (%), median (IQR)	60.8 (13.2)	60.1 (13.3)	60.0 (12.9)	61.3 (12.8)	61.5 (12.4)	0.37
Semen volume (ml), median (IQR)	2.9 (1.5)	2.7 (1.5)	2.9 (1.5)	2.8 (1.5)	2.9 (1.6)	0.07
Sperm concentration (×10^6 ml^{-1}), median (IQR)	48.3 (31.9)	44.0 (32.0)	48.0 (32.0)	50.5 (32.0)	51.3 (31.3)	0.01
Total sperm count (×10^6), median (IQR)	138.6 (109.3)	125.7 (112.8)	135.2 (107.0)	139.3 (111.7)	148.7 (109.7)	0.001

[a]A total of 2 men had missing information on income, 1 man had missing information on BMI. [b]Demographic characteristics across quartiles of handgrip strength were compared using Kruskal–Wallis analyses or χ^2 tests where appropriate. [c]Each participant provided multiple semen samples and had multiple values of semen characteristics during the study period; therefore, the average value of the semen characteristics of each participant was used here. BMI: body mass index; IQR: interquartile range; s.d.: standard deviation; Q1: the first quartile; Q2: the second quartile; Q3: the third quartile; Q4: the fourth quartile

as well as self-reported reproductive success in men.[9,14,30] Testosterone is responsible for spermatogenesis and provides feedback for the hypothalamic-pituitary-gonadal axis;[15] therefore, a positive association between testosterone and sperm motility has also been revealed.[16] In a recent study conducted among 7064 healthy adults from the National Health and Nutrition Examination Survey, Chiu and colleagues found a positive association between grip strength and serum testosterone concentrations[11] that had been strongly associated with total sperm count and concentration.[31] In addition, many studies have indicated that handgrip strength can serve as an indicator of nutritional status.[32,33] Since muscle morphology and function are affected by undernutrition earlier, alterations in muscle physiology may result in lower handgrip strength.[3] Some sex hormones, such as luteinizing hormone (LH) and follicle-stimulating hormone (FSH), are sensitive to malnutrition, which may impact the onset of spermatogenesis, the development of sexual characteristics, and muscle development.[34]

In our stratified analyses, the associations of handgrip strength with several semen characteristics were stronger among men who were overweight or obese. Compared with leaner men (BMI <24.0 kg m^{-2}), we noted a wider interquartile range of handgrip strength among overweight or obese men (10.4 kg *vs* 8.7 kg), and more people were in the third and fourth quartiles of handgrip strength (60.6% *vs* 45.0%). Therefore, the different distribution of handgrip strength across BMI categories may partly explain the different associations in men with different BMI. Therefore, we further employed handgrip strength relative to body weight to reduce the influence of body size. While the positive trends persisted robustly, we did not observe any evidence

Table 2: Associations between handgrip strength (kg) and repeated semen characteristics (*n*=6458) based on linear mixed-effects models

Parameter	*Quartile of handgrip strength[a], percent change (95% CI)*					*Per standard deviation change*
	Q1	*Q2*	*Q3*	*Q4*	*P for trend[b]*	
Progressive motility (%)						
Crude model	0	7.0 (1.0–13.3)	7.5 (1.5–13.9)	9.6 (3.5–16.0)	0.002	3.2 (1.1–5.3)
Adjusted model	0	6.8 (0.9–13.0)	7.5 (1.6–13.8)	9.5 (3.4–15.9)	0.002	3.2 (1.1–5.4)
Total motility (%)						
Crude model	0	6.2 (0.7–11.9)	6.5 (1.0–12.3)	8.7 (3.2–14.6)	0.002	2.9 (1.0–4.8)
Adjusted model	0	6.1 (0.7–11.7)	6.5 (1.1–12.2)	8.8 (3.2–14.6)	0.002	3.0 (1.1–4.9)
Semen volume (ml)						
Crude model	0	6.8 (−1.0–15.2)	7.2 (−0.6–15.7)	11.5 (3.4–20.2)	0.006	3.5 (0.8–6.3)
Adjusted model	0	5.8 (−1.8–14.0)	7.9 (0.1–16.3)	14.2 (5.9–23.2)	0.001	4.6 (1.8–7.4)
Sperm concentration ($\times 10^6$ ml^{-1})						
Crude model	0	10.1 (−1.1–22.5)	12.2 (0.9–24.9)	20.1 (8.0–33.6)	0.001	6.3 (2.3–10.4)
Adjusted model	0	7.9 (−2.9–20.0)	11.5 (0.2–24.1)	19.5 (7.3–33.1)	0.001	6.3 (2.3–10.5)
Total sperm count ($\times 10^6$)						
Crude model	0	17.3 (2.2–34.5)	20.0 (4.5–37.7)	33.8 (16.7–53.4)	<0.001	10.0 (4.7–15.5)
Adjusted model	0	13.9 (−0.5–30.5)	19.9 (4.6–37.4)	36.4 (18.9–56.5)	<0.001	11.1 (5.7–16.7)

[a]Regression coefficients (95% CI) were converted into percentage change (95% CI) using the following formula: [exp(β) − 1] × 100%. Models were adjusted for age (year), BMI (kg m^{-2}), abstinence period (day), marital status (married, unmarried, or divorced), smoking (never, former, or current), drinking (never, occasional, former, or current), tea consumption (yes or no), monthly income (<4000 Chinese Yuan, 4000–8000 Chinese Yuan, or >8000 Chinese Yuan), education level (less than undergraduate or undergraduate or above), and sampling season (spring, summer, autumn, or winter). [b]Tests for trend across the quartiles of handgrip strength were assessed by modeling median values within each quartile as a continuous value. BMI: body mass index; CI: confidence interval; Q1: the first quartile; Q2: the second quartile; Q3: the third quartile; Q4: the fourth quartile

Table 3: Associations between handgrip strength (kg) and repeated semen characteristics stratified by age and body mass index

Handgrip strength	*Percent change (95% CI)[a]*				
	Progressive motility	*Total motility*	*Semen volume*	*Sperm concentration*	*Total sperm count*
Age <28 years (*n*=746)					
Q1	0	0	0	0	0
Q2	6.7 (−1.6–15.7)	6.0 (−1.6–14.2)	3.2 (−6.8–14.3)	8.3 (−6.5–25.5)	12.0 (−7.5–35.8)
Q3	8.4 (−0.2–17.7)	7.4 (−0.5–15.8)	5.0 (−5.3–16.6)	6.8 (−8.0–24.1)	11.9 (−7.9–36.1)
Q4	5.2 (−3.2–14.3)	5.4 (−2.4–13.8)	11.3 (0.2–14.3)	11.1 (−4.5–29.3)	23.8 (1.5–35.8)
P for trend[b]	0.23	0.18	0.044	0.21	0.043
Age ≥28 years (*n*=636)					
Q1	0	0	0	0	0
Q2	5.8 (−2.0–14.3)	5.2 (−1.9–12.8)	9.0 (−2.3–21.6)	6.7 (−8.4–24.2)	15.7 (−4.3–40.0)
Q3	4.8 (−2.9–13.1)	4.0 (−3.0–11.5)	11.3 (−0.3–24.2)	18.6 (1.8–38.1)	31.0 (8.3–58.4)
Q4	13.7 (5.5–22.6)	12.1 (4.7–20.0)	20.0 (7.7–33.8)	29.5 (11.3–50.6)	54.6 (28.0–86.6)
P for trend[b]	0.001	0.002	0.001	<0.0001	<0.0001
P for interaction[c]	0.32	0.43	0.70	0.46	0.37
BMI <18.5 kg m^{-2} (*n*=94)					
Q1	0	0	0	0	0
Q2	−1.2 (−23.6–27.9)	−1.8 (−22.6–24.6)	21.5 (−5.1–55.5)	−5.2 (−32.2–32.4)	16.0 (−26.7–83.6)
Q3	14.5 (−15.2–54.4)	13.6 (−13.8–49.8)	33.3 (0.0–77.6)	34.6 (−8.9–98.7)	78.1 (4.3–203.9)
Q4	−24.5 (−49.6–13.0)	−23.4 (−47.2–11.3)	29.0 (−12.2–89.6)	−6.1 (−43.5–55.9)	21.1 (−40.0–144.6)
P for trend[b]	0.66	0.65	0.05	0.55	0.14
BMI ≥18.5 kg m^{-2} and <24.0 kg m^{-2} (*n*=831)					
Q1	0	0	0	0	0
Q2	0.0 (−4.8–5.0)	0.1 (−4.2–4.6)	1.7 (−7.1–11.5)	2.6 (−9.1–15.8)	4.4 (−10.5–21.8)
Q3	0.9 (−4.0–6.1)	0.6 (−3.8–5.3)	6.9 (−2.7–17.5)	1.8 (−10.1–15.3)	8.9 (−7.1–27.7)
Q4	1.7 (−3.4–7.1)	1.9 (−2.7–6.8)	12.4 (2.0–23.9)	6.3 (−6.6–20.9)	19.7 (1.6–41.0)
P for trend[b]	0.46	0.40	0.01	0.41	0.03
BMI ≥24.0 kg m^{-2} (*n*=457)					
Q1	0	0	0	0	0
Q2	28.2 (8.9–51.1)	25.4 (7.7–45.9)	10.1 (−5.6–28.4)	28.0 (0.7–62.6)	39.8 (2.7–90.2)
Q3	22.6 (5.2–42.9)	20.1 (4.2–38.5)	3.5 (−10.4–19.5)	38.6 (10.8–73.4)	42.1 (6.6–89.4)
Q4	30.1 (12.5–50.4)	27.4 (11.3–45.8)	13.6 (−0.9–30.2)	54.5 (24.9–91.2)	74.2 (32.6–128.9)
P for trend[b]	0.002	0.003	0.12	<0.0001	<0.0001
P for interaction[c]	0.001	0.001	0.53	0.02	0.10

[a]Regression coefficients (95% CI) were converted into percentage change (95% CI) using the following formula: [exp(β) − 1]×100%. Models were adjusted for age (year), BMI (kg m^{-2}), abstinence period (day), marital status (married, unmarried, or divorced), smoking (never, former, or current), drinking (never, occasional, former, or current), tea consumption (yes or no), monthly income (<4000 Chinese Yuan, 4000–8000 Chinese Yuan, or >8000 Chinese Yuan), education level (less than undergraduate or undergraduate or above), and sampling season (spring, summer, autumn, or winter). [b]Tests for trend across the quartiles of handgrip strength were assessed by modeling median values within each quartile as a continuous value. [c]A cross-product term was added to the final model to evaluate multiplicative interactions. BMI: body mass index; CI: confidence interval; Q1: the first quartile; Q2: the second quartile; Q3: the third quartile; Q4: the fourth quartile

of an interaction between handgrip strength relative to body weight and BMI. Additionally, some previous studies found that BMI was positively associated with muscle strength, and people with higher BMI tended to have a greater performance on handgrip strength tests.[35–37] Moreover, overweight or obesity has been associated with increased fat mass[38] and reduced physical activity, which might, in turn, affect semen characteristics.[39] Previous epidemiological studies have reported a positive association of physical activity with semen characteristics,[40–42] as well as an inverse relationship of body composition with sperm concentration and volume.[43,44] Consistent with previous studies, our data showed that greater handgrip strength was associated with higher BMI and a higher percentage of body fat, but there was no difference in physical activity across the quartiles of handgrip strength. After further adjusting for body fat percentage and physical activity in our mixed-effects models, the positive dose-response relationships of handgrip strength with progressive sperm motility, semen volume, and total count remained robust. Moreover, we found no evidence of an interaction between handgrip strength and age, which may be partly explained by the fact that our recruited individuals were mostly young adults (72.5% were less than 30 years old).

The strengths of this study included the large number of subjects, repeat-measured semen characteristics at multiple time points, and a relatively homogeneous population (healthy men aged 22–45 years) that reduced potential residual confounders. In addition, we enrolled healthy men from a sperm bank who were more representative than previous study participants enrolled from fertility centers and clinics. The present study also had some limitations. First, handgrip strength was measured at a single time point at recruitment. However, we measured the handgrip strength for both hands twice, and the average value of the two hands was used for analysis, which could reduce the potential measurement error. In addition, we deemed that handgrip strength may not be greatly changed in a short time period (6-month follow-up in the current study) if the individual maintained his lifestyle, particularly physical activity and training. Second, sex hormones (*e.g.*, testosterone, LH, and FSH) were not measured in the current study, although previous studies revealed that testosterone was associated with not only semen characteristics,[31,45] but also handgrip strength.[11,46] However, the potential mechanisms between handgrip strength and semen characteristics need to be demonstrated in further studies. Third, our recruited participants were typically healthy and young (all aged between 22 years and 45 years), and our study results should be extrapolated with caution to other age groups or those with physical diseases. Fourth, given that our study had a cross-sectional design, it did not confirm any causal relationship of handgrip strength with semen characteristics. However, handgrip strength is strongly elated to limb strength and provides an objective index of overall muscle strength,[47] which can benefit from healthy lifestyle habits[48] (*e.g.*, regular physical exercise and a healthy diet). Previous studies have demonstrated that people who have less sedentary time and are more physically active have a higher handgrip strength.[49,50] Finally, residual confounding cannot be fully ruled out.

CONCLUSIONS

In conclusion, our repeated measurements study found that greater handgrip strength was associated with higher semen volume, sperm motility, sperm concentration, and total count in a dose-dependent manner. Our findings suggest that handgrip strength, as an objective, noninvasive marker of muscle strength, may therefore provide more useful information on the utility of a handgrip dynamometer as a potentially useful predictor of human semen characteristics. Further studies are needed to confirm our novel findings and explore the precise mechanisms.

AUTHOR CONTRIBUTIONS

All authors fulfill the criteria for authorship. TQM, CLX, YXW, and AP participated in the study design and conception. BS, HGC, PD, ZZT, and YJC were responsible for data collection and data management. BS drafted the manuscript and YXW and AP reviewed and revised the manuscript. All authors read and approved the final manuscript.

COMPETING INTERESTS

All authors declared no competing interests.

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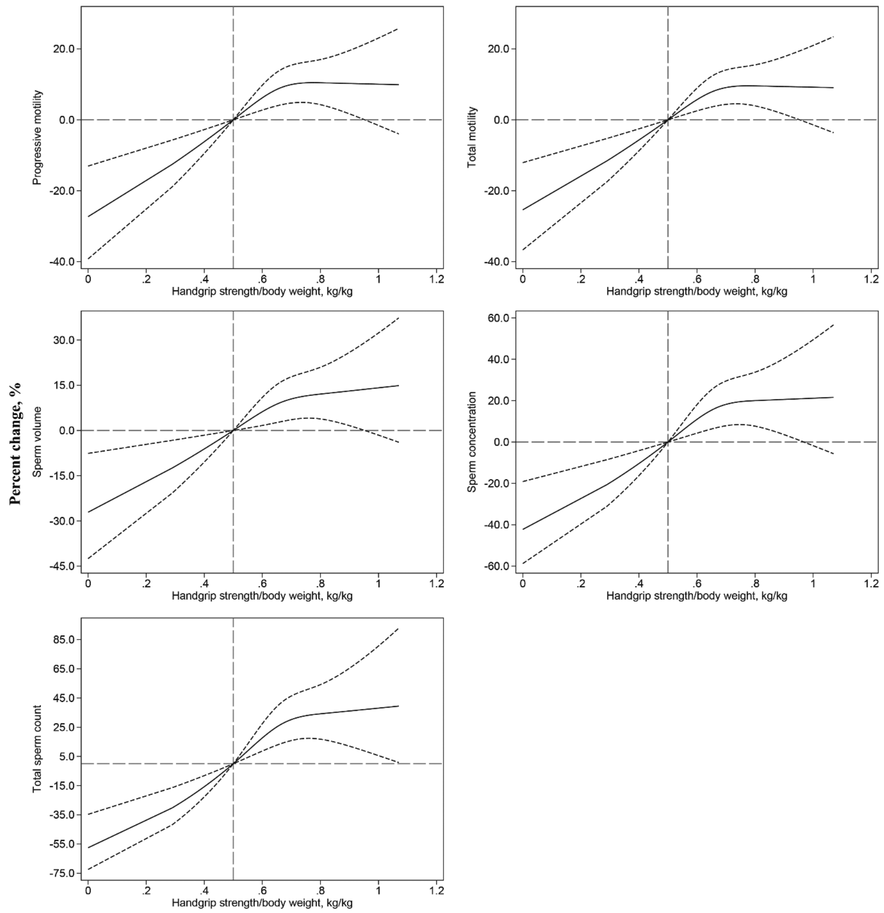

Supplementary Figure 1: Dose-response relationships of handgrip strength/body weight with semen characteristics (percent change, %) based on restricted cubic spline models (*n*=6458)[a]. [a]A total of 2 men had missing information on income, 1 man had missing information on BMI. The reference values (*i.e.*, the grey vertical dotted lines) were set to 10% of handgrip strength/body weight. All models were adjusted for age (years), BMI (kg/ m^{-2}), abstinence period (days), marital status (married, unmarried, or divorced), smoking (never, former or current), drinking (never, occasional, former or current), tea consumption (yes or no), monthly income (<4000, 4000–8000 or >8000 Yuan), education levels (less than undergraduate or undergraduate or above), and sampling season (spring, summer, autumn, or winter). BMI: body mass index.

Supplementary Table 1: Associations between handgrip strength/body weight and repeated semen characteristics (*n*=6458) based on mixed-effect models[a]

	Quartile of handgrip strength/body weight, percent change (95%CI)					*Per s.d. change*
	Q1	*Q2*	*Q3*	*Q4*	*P for trend[b]*	
Progressive motility (%)						
Crude model	0	7.1 (1.2–13.4)	8.9 (2.8–15.4)	8.0 (2.0–14.3)	0.008	3.1 (1.1–5.1)
Adjusted model	0	8.3 (2.2–14.7)	10.9 (4.4–17.8)	10.1 (3.1–17.5)	0.004	3.9 (1.5–6.3)
Total motility (%)						
Crude model	0	7.0 (1.6–12.8)	8.3 (2.7–14.2)	7.6 (2.2–13.4)	0.006	2.9 (1.0–4.8)
Adjusted model	0	7.9 (2.4–13.8)	10.0 (4.1–16.3)	9.4 (3.1–16.1)	0.004	3.5 (1.4–5.8)
Semen volume (ml)						
Crude model	0	3.8 (–3.7–11.8)	13.9 (5.5–22.9)	10.4 (2.4–19.0)	0.002	3.9 (1.2–6.6)
Adjusted model	0	3.7 (–3.9–12.0)	13.4 (4.6–22.9)	11.9 (2.6–22.1)	0.003	4.5 (1.4–7.8)
Sperm concentration (10^6 ml^{-1})						
Crude model	0	3.4 (–7.0–14.9)	13.9 (2.2–26.9)	7.5 (–3.4–19.6)	0.08	3.6 (–0.2–7.5)
Adjusted model	0	7.1 (–3.9–19.4)	18.2 (5.4–32.6)	17.7 (4.0–33.1)	0.004	7.3 (2.7–12.0)
Total sperm count (10^6)						
Crude model	0	7.2 (–6.5–22.8)	29.6 (12.8–49.0)	18.5 (3.3–35.9)	0.002	7.5 (2.5–12.7)
Adjusted model	0	11.2 (–3.3–27.7)	34.0 (15.7–55.2)	31.5 (12.3–53.9)	<0.001	12.0 (5.9–18.4)

Regression coefficients (95% CI) were converted into percentage change (95% CI) using the following formula: [exp (β) − 1] × 100%. [a]A total of 2 men had missing information on income, 1 man had missing information on BMI. Models were adjusted for age (year), BMI (kg m^{-2}), abstinence period (days), marital status (married, unmarried or divorced), smoking (never, former, or current), drinking (never, occasional, former or current), tea consumption (yes or no), monthly income (<4000, 4000–8000 or >8000 Yuan), education level (less than undergraduate or undergraduate or above), and sampling season (spring, summer, autumn, or winter); [b]Tests for trend across the quartiles of handgrip strength were assessed by modeling median values within each quartile as a continuous value. s.d.: standard deviation; Q1: the first quartile; Q2: the second quartile; Q3: the third quartile; Q4: the fourth quartile; CI: confidence interval; BMI: body mass index

Supplementary Table 2: Estimated percent change (95% confidence intervals) of semen characteristics in relation to handgrip strength (kg)[a]

Handgrip strength	*Q1*	*Q2*	*Q3*	*Q4*	*P for trend[b]*
Average semen characteristics[c]					
Progressive motility	0	6.8 (0.6–13.4)	7.2 (0.9–13.9)	7.7 (1.3–14.4)	0.02
Total motility	0	6.0 (0.3–12.0)	6.2 (0.5–12.2)	7.2 (1.3–13.4)	0.02
Semen volume	0	5.5 (–2.5–14.2)	6.9 (–1.3–15.8)	14.5 (5.6–24.1)	0.001
Sperm concentration	0	8.3 (–2.7–20.5)	12.0 (0.5–24.8)	18.5 (6.2–32.2)	0.002
Total sperm count	0	14.7 (–0.3–32.0)	20.0 (4.2–38.3)	35.4 (17.3–56.2)	<0.0001
Semen characteristics at enrolment[d]					
Progressive motility	0	5.1 (–4.0–15.0)	9.4 (–0.2–19.8)	6.4 (–2.9–16.7)	0.14
Total motility	0	4.5 (–3.9–13.6)	8.8 (0.0–18.4)	6.6 (–2.1–16.1)	0.10
Semen volume	0	8.0 (–1.7–18.8)	11.2 (1.0–22.4)	15.3 (4.7–27.1)	0.004
Sperm concentration	0	6.8 (–6.6–22.0)	11.7 (–2.4–27.8)	13.9 (–0.6–30.5)	0.05
Total sperm count	0	15.4 (–3.5–37.9)	24.1 (3.7–48.6)	31.4 (9.5–57.6)	0.003
Repeated semen characteristics[e]					
Progressive motility	0	6.7 (0.8–12.8)	7.5 (1.5–13.7)	9.3 (3.3–15.7)	0.003
Total motility	0	6.0 (0.6–11.6)	6.5 (1.1–12.2)	8.6 (3.1–14.4)	0.002
Semen volume	0	5.6 (–1.9–13.8)	7.9 (0.1–16.3)	14.1 (5.8–23.0)	0.001
Sperm concentration	0	8.4 (–2.5–20.5)	12.0 (0.7–24.6)	20.2 (7.9–33.8)	0.001
Total sperm count	0	14.2 (–0.2–30.8)	20.3 (5.0–37.9)	36.9 (19.4–57.1)	<0.0001

[a]Models were adjusted for age, BMI, abstinence period, marital status, smoking, drinking, tea consumption, monthly income, education level, and sampling season; [b]Tests for trend across the quartiles of handgrip strength were assessed by modeling median values within each quartile as a continuous value; [c]Associations between quartiles of handgrip strength and the average sperm parameters based on general linear models; [d]Associations between quartiles of handgrip strength and sperm parameters at enrolment based on general linear models; [e]Associations between quartiles of handgrip strength and repeated sperm parameters based on mixed-effects models after median imputation for missing values. Q1: the first quartile; Q2: the second quartile; Q3: the third quartile; Q4: the fourth quartile; BMI: body mass index

Supplementary Table 3: Estimated percent change (95% confidence intervals) of semen characteristics in relation to left or right handgrip strength[a]

	Quartile of handgrip strength, percent change (95%CI)					*Per s.d. change*
	Q1	*Q2*	*Q3*	*Q4*	*P for trend[b]*	
The average value of left handgrip strength (kg)						
Progressive motility	0	3.8 (–1.4–9.2)	1.4 (–3.9–6.9)	9.2 (3.4–15.4)	0.003	2.7 (0.6–4.8)
Total motility	0	3.8 (–1.0–8.8)	1.4 (–3.4–6.5)	8.7 (3.3–14.3)	0.003	2.5 (0.6–4.4)
Semen volume	0	5.9 (–0.6–12.8)	7.7 (0.7–15.2)	13.2 (5.5–21.5)	0.001	4.2 (1.4–7.0)
Sperm concentration	0	5.1 (–3.2–14.3)	5.7 (–3.5–15.8)	23.3 (11.8–35.9)	0.001	5.4 (1.4–9.5)
Total sperm count	0	12.2 (0.2–25.6)	14.6 (1.5–29.3)	38.1 (21.5–57.0)	<0.001	9.8 (4.5–15.3)
The average value of right handgrip strength (kg)						
Progressive motility	0	5.4 (0.0–11.0)	7.0 (1.5–12.9)	8.1 (2.3–14.2)	0.002	3.4 (1.3–5.5)
Total motility	0	5.2 (0.3–10.3)	6.4 (1.3–11.7)	7.7 (2.4–13.2)	0.002	3.1 (1.3–5.1)
Semen volume	0	7.0 (0.3–14.2)	7.3 (0.3–14.7)	10.6 (3.0–18.7)	0.001	4.4 (1.7–7.2)
Sperm concentration	0	7.3 (–1.5–16.9)	10.6 (1.1–21.2)	15.7 (4.9–27.5)	0.005	6.4 (2.5–10.6)
Total sperm count	0	14.4 (1.9–28.4)	18.4 (4.9–33.6)	27.2 (11.9–44.5)	<0.001	11.1 (5.8–16.6)

[a]Models were adjusted for age (year), BMI (kg m^{-2}), abstinence period (days), marital status (married, unmarried or divorced), smoking (never, former or current), drinking (never, occasional, former or current), tea consumption (yes or no), monthly income (<4000, 4000–8000 or >8000 Yuan), education level (less than undergraduate or undergraduate or above), and sampling season (spring, summer, autumn, or winter); [b]Tests for trend across the quartiles of handgrip strength were assessed by modeling median values within each quartile as a continuous value. s.d.: standard deviation; Q1: the first quartile; Q2: the second quartile; Q3: the third quartile; Q4: the fourth quartile; BMI: body mass index

Supplementary Table 4: Estimated percent change (95% confidence intervals) of semen characteristics in relation to handgrip strength limited to 535 men who had the completed physical activity and body fat percentage information[a]

	Quartile of handgrip strength, percent change (95%CI)					*Per s.d. change*
	Q1	*Q2*	*Q3*	*Q4*	*P for trend[b]*	
Progressive motility[c]						
Crude model	0	1.1 (–3.3–5.8)	1.7 (–2.8–6.4)	5.3 (0.7–10.1)	0.02	2.2 (0.6–3.8)
Adjusted model	0	0.6 (–3.8–5.1)	1.2 (–3.2–5.9)	4.6 (0.0–9.5)	0.0496	1.8 (0.2–3.5)
Total motility[c]						
Crude model	0	1.2 (–2.9–5.4)	1.3 (–2.8–5.6)	4.7 (0.5–9.1)	0.03	2.0 (0.5–3.5)
Adjusted model	0	0.7 (–3.3–4.9)	1.0 (–3.1–5.2)	4.2 (0.0–8.7)	0.054	1.7 (0.2–3.2)
Semen volume[c]						
Crude model	0	8.2 (–1.4–18.7)	12.2 (2.3–23.1)	9.6 (–0.01–20.2)	0.04	3.5 (0.2–7.0)
Adjusted model	0	6.8 (–2.4–16.8)	12.7 (2.8–23.5)	11.5 (1.6–22.4)	0.01	4.0 (0.6–7.5)
Sperm concentration[c]						
Crude model	0	3.4 (–8.7–17.2)	4.3 (–7.9–18.3)	13.8 (0.4–28.9)	0.04	4.6 (0.1–9.3)
Adjusted model	0	2.2 (–9.7–15.5)	5.1 (–7.2–19.1)	12.9 (–0.6–28.3)	0.056	4.4 (–0.2–9.2)
Total sperm count[c]						
Crude model	0	11.8 (–4.2–30.6)	16.9 (0.1–36.6)	24.4 (6.6–45.2)	0.005	8.2 (2.4–14.3)
Adjusted model	0	9.0 (–6.3–26.8)	18.3 (1.5–37.9)	25.6 (7.4–46.8)	0.003	8.5 (2.6–14.7)

[a]Models were adjusted for age (year), BMI (kg m^{-2}), abstinence period (days), body fat (%), total physical activity (MET-min $week^{-1}$), marital status (married, unmarried, or divorced), smoking (never, former, or current), drinking (never, occasional, former, or current), tea consumption (yes or no), monthly income (<4000, 4000–8000, or >8000 Yuan), education level (less than undergraduate or undergraduate or above), and sampling season (spring, summer, autumn, or winter); [b]Tests for trend across the quartiles of hand-grip strength were assessed by modeling median values within each quartile as a continuous value; [c]A total of 4131 semen specimens were collected among 535 men. s.d.: standard deviation; Q1: the first quartile; Q2: the second quartile; Q3: the third quartile; Q4: the fourth quartile; BMI: body mass index

Supplementary Table 5: Demographic characteristics of participants by quartile of handgrip strength[a]

	Included in the analysis	*Quartile of handgrip strength*				*P*
		Q1	*Q2*	*Q3*	*Q4*	
	n=535	*n=133*	*n=135*	*n=133*	*n=134*	
Handgrip strength (kg), mean±s.d.	43.3±7.1	34.4±3.9	41.0±1.3	45.6±1.5	52.4±3.3	<0.001
BMI (kg m^{-1}), mean±s.d.	23.0±3.2	22.4±3.3	22.3±3.0	23.0±3.1	24.3±2.8	<0.001
Body fat (%), mean±s.d.	14.6±5.2	13.7±5.7	13.6±4.8	14.6±4.9	16.6±4.9	<0.001
Total physical activity (MET-min $week^{-1}$), mean±s.d.	3477.5±4176.1	3469.1±4028.4	3107.5±4342.1	3700.3±4572.1	3517.6±3739.8	0.70

[a]535 men who had the completed information of physical activity and body fat. Demographic characteristics across quartiles of handgrip strength were compared using Kruskal–Wallis analyses. s.d.: standard deviation; Q1: the first quartile; Q2: the second quartile; Q3: the third quartile; Q4: the fourth quartile