Handgrip Strength Weakness and Asymmetry Together are Associated with Cardiovascular Outcomes in Elderly Outpatients: A Prospective Cohort Study

Siyang Lin
Shengli Clinical Medical College of Fujian Medical University
Fang Wang
Department of Geriatric Medicine, Fujian Provincial Hospital
Yanjie Huang
Shengli Clinical Medical College of Fujian Medical University
Yin Yuan
Shengli Clinical Medical College of Fujian Medical University
Feng Huang
Shengli Clinical Medical College of Fujian Medical University
Pengli Zhu (zpl7755@hotmail.com)
Shengli Clinical Medical College of Fujian Medical University

Research Article

Keywords: Elderly outpatients, Handgrip strength weakness, Handgrip strength asymmetry, Cardiovascular outcomes

Posted Date: January 3rd, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1161358/v1

Abstract

Background: The evaluations of handgrip strength (HGS) weakness and asymmetry have implications for the comprehensive geriatric assessment. The aim of this study was to investigate the association of HGS weakness and asymmetry on cardiovascular outcomes in elderly outpatients.

Methods: This was a prospective observational cohort study of 364 geriatrics outpatients aged ≥ 60 years, in which all participants performed HGS tests at baseline. Patients with HGS < 28 kg for men and < 18 kg for women were diagnosed as HGS weakness, and HGS ratio < 0.90 or > 1.10 were diagnosed as HGS asymmetry. Primary outcomes defined as the major adverse cardiovascular event (MACE) and composite endpoints were assessed during 21-month median follow-up.

Results: Among 364 participants, 155 (42.6%) demonstrated HGS weakness, and 160 (44.0%) demonstrated HGS asymmetry. HGS weakness was associated with MACE (HR: 2.763, 95%CI: 1.217-6.272) and composite endpoints (HR: 2.842, 95%CI: 1.399-5.774). However, no significant correlation between HGS asymmetry and cardiovascular outcomes was observed. Compared with the normal and symmetric HGS group, older adults with HGS weakness and asymmetry together had a higher risk of MACE (HR: 5.229, 95%CI: 1.559-17.542) and composite endpoints (HR: 4.002, 95%CI: 1.558-10.277).

Conclusion: HGS weakness and asymmetry together may increase the risk of cardiovascular outcomes in elderly outpatients. HGS asymmetry offers complementary information to HGS weakness when making a comprehensive assessment of HGS.

Background

Handgrip strength (HGS) is a pragmatic measure of physical function for older people, as one of the diagnostic criteria of frailty and sarcopenia, which are common syndromes in the elderly population. HGS is also considered as an assessment of the locomotor dimension in intrinsic capacity for older adults. Several studies have shown that HGS weakness was associated with increased all-cause mortality and death rates due to cardiovascular diseases [1–3]. For instance, Leong DP concluded that a decrease in HGS was positively associated with all-cause mortality, myocardial infarction, stroke, and cardiovascular morbidity in the Prospective Urban Rural Epidemiology (PURE) study [4]. In addition, a 4-year longitudinal study that included 3018 Chinese community-dwelling elders confirmed that HGS decreased with age [5]. Timely evaluation of HGS may be helpful in identifying individuals at increased risk for adverse cardiovascular outcomes and premature mortality, especially for the elderly.

However, HGS measurements mainly focused on HGS weakness only. Maximal HGS value was usually reported in the HGS test, while clinicians rarely took HGS asymmetry between left and right hands seriously. In recent two years, McGrath R's team has done in-depth researches about HGS asymmetry and adverse events in older adults, such as falls, functional limitations, cognitive disorders, and mortality [6–11]. There is uncertainty whether HGS asymmetry is associated with cardiovascular outcomes, which is of great importance in assessing the health of the elderly population.

Atherosclerosis may contribute to the development of HGS weakness [12]. Meanwhile, HGS weakness provides a valid marker of muscle strength weakness [13, 14], nutritional status [15]. These potential mechanisms can be employed as a bridge to correlate HGS weakness with cardiovascular outcomes. Furthermore, HGS asymmetry may indicate deficient brain hemisphere activation and impairment of the neuromuscular system [16]. Adding HGS

asymmetry to the basis of HGS weakness assessment may enhance risk prediction for cardiovascular outcomes in older adults.

We hypothesized that elders with HGS weakness and asymmetry together might have a higher risk of cardiovascular outcomes. Therefore, this study aimed to analyze the association of HGS weakness and asymmetry on cardiovascular outcomes in elderly outpatients.

Methods

Study population

This prospective cohort study was conducted in Fujian Provincial Hospital from December 2015 to July 2017. A total of 408 subjects were recruited from the Geriatrics outpatients. The inclusion criteria were as follows: (1) aged 60 years or older; (2) written informed consent. Participants who met one of the following criteria were excluded: (1) acute, critical or terminal stages of various diseases; (2) diagnosed with malignant tumors; (3) severe neurological or psychiatric disorders; (4) disability or immobility due to severe osteoarthritis or neuromuscular disease; (5) a history of myocardial infarction and stroke; (6) New York Heart Association (NYHA) class III-IV; (7) hospitalization with unstable angina or heart failure in the past six months. The follow-up ended in January 2019, and 44 participants lost to follow-up. 364 subjects were included in the final analysis. Approval for the study was obtained from the Fujian Provincial Hospital research ethics committee (KY2015-09-01).

HGS weakness and asymmetry measurement

HGS was assessed using a handheld hydraulic dynamometer (Jamar, USA) in the sitting position with the forearm in the neutral position. There was a familiarization trial before the registered trials. Participants squeezed the dynamometer with the arm elbow bent to a 90 angle as hard as possible. The maximum reading of 3 trials for both hands was taken as HGS value (kg). Every between-trial interval was more than 15 seconds to avoid muscle fatigue [17]. According to the Asian Working Group for Sarcopenia (AWGS) 2019 consensus [18], HGS weakness was defined as an HGS of < 28 kg in men and < 18 kg in women. The highest recorded HGS from both hands were used to calculate HGS ratio (dominant HGS (kg) / non-dominant HGS (kg)) [19]. HGS asymmetry was considered HGS ratio < 0.90 or >1.10, and HGS symmetry was classified as an HGS ratio between 0.90 and 1.10.

Follow-up and outcomes

All subjects were followed up routinely every six months by telephone to obtain their survival data and record the time-to-event endpoints. All records were reviewed by well-trained staff. The death records were obtained from the participant's family and medical records. Cardiovascular diseases and causes of death were codified according to the 10th version of International Classification of Diseases (ICD).

Major adverse cardiovascular event (MACE) was defined as cardiac death (ICD-10: 100-199), acute myocardial infarction (ICD-10: I21), hospitalization for unstable angina (ICD-10: I20), hospitalization for congestive heart failure (ICD-10: I50), and acute stroke (ICD-10: I60-64, I67, I69). Composite endpoints were defined as all-cause mortality, acute myocardial infarction (ICD-10: I21), hospitalization for unstable angina (ICD-10: I20), hospitalization for congestive heart failure (ICD-10: I50), and acute stroke (ICD-10: I60-64, I67, I69). The endpoint of the study was the time to the first recorded adverse event.

Statistical analysis

Statistical analysis was conducted using Statistical Package for the Social Sciences, version 22.0 (SPSS, USA). Figures were drawn using GraphPad Prism 8.0 (GraphPad Software, USA) and MedCalc (MedCalc Software, Belgium). Continuous variables of the normal distribution are presented as the mean and standard deviation (SD). Continuous variables of non-normal distribution are presented as the median and interquartile range (IQR). Categorical variables are presented as frequencies and percentages (%). Homogeneity of variance test and normality analysis were performed before comparing two groups. Independent sample T-test or one-way ANOVA was used for continuous variables of normal distribution, and the non-parametric test was used for continuous variables of non-normal distribution. The differences in categorical variables were evaluated by the chi-square test or Fisher's exact test.

Survival analysis was performed using the Kaplan-Meier method and Cox proportional hazard regression analysis. Kaplan-Meier curves were constructed to evaluate the association of HGS weakness and HGS asymmetry at baseline on MACE or composite endpoints. The log-rank statistic was calculated for each curve. Cox proportional hazard models were employed to estimate HRs and 95% CIs for MACE and composite endpoints, comparing HGS weakness categories (the reference group: normal HGS), HGS asymmetry categories (the reference group: HGS symmetry), HGS weakness and asymmetry categories (grouped into normal and symmetric HGS (the reference group), HGS weakness or asymmetry only, HGS weakness and asymmetry), which were presented as three models. Model 1 was unadjusted for confounders. In Model 2, the analysis was adjusted for age and gender. Model 3 was adjusted as Model 2 with body mass index (BMI), smoking, drinking, hypertension, diabetes, hyperlipidemia, heart failure (HF), and coronary heart disease (CHD). The hypothesis test was conducted by a two-sided test, and statistical significance was set at $P < 0.05$.

Results

After excluding 44 participants lost to follow-up, 364 participants (mean 72.4 ± 8.3 years) were included in the study, nearly half (49.7%) of them were men. Table 1 shows the baseline characteristics of the study participants between the HGS symmetry and HGS asymmetry group. There were 155 (42.6%) older adults with HGS weakness, 160 (44.0%) with HGS asymmetry, and 78 (21.4%) with HGS weakness and asymmetry together. The incidence of cardiovascular outcomes during the follow-up, of which the median observation time was 21.0 months (IQR: 18.5-26.4), is shown in Table 2. 35 (9.6%) older adults developed MACE and 50 (13.7%) presented composite endpoints.

Table 1

General characteristics of participants at baseline

Characteristics	Total (*n*=364)	HGS symmetry (*n*=204)	HGS asymmetry (*n*=160)
Age (years)	72.4 ± 8.3	70.7 ± 7.6	74.5 ± 8.8
Men, n (%)	181 (49.7)	105 (51.5)	76 (47.5)
BMI (kg/m^2)	23.8 ± 3.5	24.0 ± 3.4	23.5 ± 3.5
Smoking, n (%)	60 (16.5)	38 (18.6)	22 (13.8)
Drinking, n (%)	27 (7.4)	16 (7.8)	11 (6.9)
Hypertension, n (%)	249 (68.4)	150 (73.5)	99 (61.9)
Diabetes, n (%)	150 (41.2)	92 (45.1)	58 (36.3)
Hyperlipidemia, n (%)	96 (26.4)	61 (29.9)	35 (21.9)
HF, n (%)	25 (6.9)	12 (5.9)	13 (8.1)
CHD, n (%)	94 (25.8)	48 (23.5)	46 (28.7)
HGS weakness, n (%)	155 (42.6)	77 (37.7)	78 (48.8)
FBG	6.03 ± 1.66	6.04 ± 1.55	6.02 ± 1.79
TG (mmol/L)	1.30 (0.93, 1.81)	1.33 (0.90, 1.79)	1.24 (0.94, 1.82)
TC (mmol/L)	4.64 ± 1.15	4.78 ± 1.22	4.47 ± 1.04
LDL-C (mmol/L)	2.86 ± 0.89	2.94 ± 0.89	2.76 ± 0.88
HDL-C (mmol/L)	1.30 ± 0.50	1.35 ± 0.58	1.23 ± 0.37

BMI body mass index, *HF* heart failure, *CHD* coronary heart disease, *HGS* handgrip strength, *FBG* Fasting blood glucose, *TG* triglycerides, *TC* total cholesterol, *LDL-C* low-density lipoprotein protein cholesterol, *HDL-C* High-density lipoprotein cholesterol

Table 2

The incidence of major outcomes in elderly outpatients during the follow-up

Outcomes	Total (n=364)
Composite endpoints, n (%)	50 (13.7)
All-cause mortality, n (%)	16 (4.4)
MACE, n (%)	35 (9.6)
Cardiac death, n (%)	1 (0.3)
Acute myocardial infarction, n (%)	7 (1.9)
Unstable angina, n (%)	4 (1.1)
Congestive heart failure, n (%)	18 (4.9)
Acute stroke, n (%)	5 (1.4)
Composite endpoints: a composite of all-cause mortality, acute myocardial infarction, hospitalization for unstable angina, hospitalization for congestive heart failure, and acute stroke. MACE: a composite of cardiac death, acute myocardial infarction, hospitalization for unstable angina, hospitalization for congestive heart failure, and acute stroke.	

Participants with HGS weakness developed more cardiovascular outcomes with a higher incidence of MACE (P for trend = 0.001) and composite endpoints (P for trend < 0.001) than the normal HGS group. Likewise, the incidence of MACE (P for trend = 0.006) and composite endpoints (P for trend = 0.006) in the HGS asymmetry group were higher than that in the HGS symmetry group. Combined with HGS weakness and HGS asymmetry, older adults were classified into three groups: normal and symmetric HGS group (n = 127), HGS weakness or asymmetry only (n = 159), and HGS weakness and asymmetry group (n = 78). Participants with HGS weakness and asymmetry together had the highest incidence of MACE (P for trend < 0.001) and composite endpoints (P for trend < 0.001) between the three groups (Figure 1).

In the survival analysis, MACE-free survival rates and composite endpoints survival rates of the HGS weakness groups (P < 0.001) and HGS asymmetry groups (P = 0.007) were statistically significant according to the log-rank test of the Kaplan–Meier curve. Significant differences also existed among normal and symmetric HGS group, HGS weakness or asymmetry only group, and HGS weakness and asymmetry group (P < 0.001, Figure 2).

HGS handgrip strength. MACE: a composite of cardiac death, acute myocardial infarction, unstable hospitalization for unstable angina, hospitalization for congestive heart failure, and acute stroke. Composite endpoints: a composite of all-cause mortality, acute myocardial infarction, hospitalization for unstable angina, hospitalization for congestive heart failure, and acute stroke.

Cox-regression analysis was performed to assess the association of HGS weakness and HGS asymmetry separately on cardiovascular outcomes in elderly outpatients (Table 3). The hazard ratio (HR) in the fully adjusted (Model 3) model of HGS weakness for predicting MACE was 2.763 (95% CI: 1.217-6.272, P = 0.015) and composite endpoints was 2.842 (95% CI: 1.399-5.774, P = 0.004). However, HGS asymmetry could not predict MACE (HR: 1.944, 95% CI: 0.918-4.116, P = 0.083) and composite endpoints (HR: 1.714, 95% CI: 0.920-3.193, P = 0.089).

In Table 4, participants with HGS weakness and asymmetry had a 5.229 (95%CI: 1.559-17.542) higher HR for MACE and a 4.002 (95%CI: 1.558-10.277) higher HR for composite endpoints, whereas HGS weakness or asymmetry only group had no statistical significance for predicting MACE and composite endpoints (P >0.05).

Table 3

Association of HGS weakness and HGS asymmetry separately on cardiovascular outcomes in elderly outpatients

	HGS weakness		HGS asymmetry	
	HR (95% CI)	P value	HR (95% CI)	P value
MACE				
Model 1	3.386 (1.657-6.919)	0.001	2.509 (1.248-5.042)	0.010
Model 2	2.261 (1.046-4.888)	0.038	2.109 (1.036-4.292)	0.040
Model 3	2.763 (1.217-6.272)	0.015	1.944 (0.918-4.116)	0.083
Composite endpoints				
Model 1	3.965 (2.137-7.356)	<0.001	2.138 (1.208-3.784)	0.009
Model 2	2.588 (1.332-5.027)	0.005	1.796 (1.004-3.213)	0.048
Model 3	2.842 (1.399-5.774)	0.004	1.714 (0.920-3.193)	0.089

HGS handgrip strength. MACE: a composite of cardiac death, acute myocardial infarction, hospitalization for unstable angina, hospitalization for congestive heart failure, and acute stroke. Composite endpoints: a composite of all-cause mortality, acute myocardial infarction, hospitalization for unstable angina, hospitalization for congestive heart failure, and acute stroke. Model 1: unadjusted. Model 2: adjusted for age and gender. Model 3: adjusted as Model 2 with BMI, smoking, drinking, hypertension, diabetes, hyperlipidemia, HF, and CHD.

Table 4

Association of HGS weakness and asymmetry together on cardiovascular outcomes in elderly outpatients

	Normal and symmetric HGS (n=127)		HGS weakness or asymmetry only (n=159)		HGS weakness and asymmetry (n=78)	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
MACE						
Model 1	1 (control)	-	3.210 (1.065-9.675)	0.038	7.562 (2.527-22.629)	<0.001
Model 2	1 (control)	-	2.863 (0.945-8.671)	0.063	4.737 (1.491-15.052)	0.008
Model 3	1 (control)	-	3.179 (0.994-10.172)	0.051	5.229 (1.559-17.542)	0.007
Composite endpoints						
Model 1	1 (control)	-	2.308 (0.970-5.491)	0.059	6.458 (2.782-14.995)	<0.001
Model 2	1 (control)	-	2.021 (0.845-4.833)	0.114	3.927 (1.604-9.614)	0.003
Model 3	1 (control)	-	1.944 (0.774-4.883)	0.157	4.002 (1.558-10.277)	0.004

HGS handgrip strength; MACE: a composite of cardiac death, acute myocardial infarction, hospitalization for unstable angina, hospitalization for congestive heart failure, and acute stroke. Composite endpoints: a composite of all-cause mortality, acute myocardial infarction, hospitalization for unstable angina, hospitalization for congestive heart failure, and acute stroke. Model 1: unadjusted. Model 2: adjusted for age and gender. Model 3: adjusted as Model 2 with BMI, smoking, drinking, hypertension, diabetes, hyperlipidemia, HF, and CHD.

Discussion

This study explored the association of HGS weakness and HGS asymmetry on cardiovascular outcomes represented by MACE and composite endpoints in elderly outpatients. The results indicated that HGS weakness was associated with MACE and composite endpoints, whereas HGS asymmetry alone was not. Compared with the normal and symmetric group, older adults with HGS weakness and asymmetry together had a higher risk of MACE and composite endpoints, which demonstrated the predictive value of HGS weakness and HGS asymmetry in combination for cardiovascular outcomes.

The epidemiological data of HGS asymmetry was limited, and there was also no unified diagnostic criterion for HGS asymmetry. Our study applied the “10% rule” because it has been used for HGS asymmetry in most studies. In this study, the prevalence of HGS asymmetry was 44.0%, consistent with epidemiological information (44.3%) in older Americans for the same age range [10]. Secondary analyses of data from the English Longitudinal Study of Ageing

(ELSA) showed the prevalence of HGS asymmetry was 46.2% in the elderly population aged ≥50 years [20]. 15.9% of elderly Koreans were diagnosed with HGS asymmetry (20% rule) in a nationwide population-based cross-sectional study [21]. To date, no studies have reported HGS asymmetry data in the Chinese elderly population.

The association between HGS weakness and cardiovascular outcomes was similar to previous studies. Some large epidemiological cohorts from different countries focused on HGS and cardiovascular outcomes. The PURE study done in 17 countries with a median follow-up of 4 years suggested that measurement of HGS was an effective risk-stratifying method for all-cause mortality, cardiac death, and cardiovascular disease [4]. In the prospective cohort study of half a million UK Biobank participants, HGS weakness was associated with all-cause and cardiovascular mortality [1]. The Korean Longitudinal Study of Aging (KLoSA) found that HGS was longitudinally related to the occurrence of cardiovascular diseases such as heart disease (angina, myocardial infarction, congestive heart failure) and stroke [3]. Another study from KLoSA demonstrated that lower HGS was an independent predictor of all-cause and cardiovascular mortality [2]. Several meta-analyses also confirmed the correlation between HGS and cardiac adverse events [22–25]. Rita Pavasini et al. made a meta-analysis of patients with cardiac disorders (ischemic heart disease, HF, cardiomyopathies, valvulopathies, arrhythmias), which concluded that HGS emerged as a predictor of all-cause death, cardiac death and hospital admission for HF. But they didn't find any relationship between HGS and the occurrence of cerebrovascular accidents or myocardial infarction [22].

Arterial stiffness, physical activity, and nutrition may mediate the association between HGS weakness and cardiovascular outcomes. Firstly, a prospective study of older Dutch men in the community reported higher baseline carotid intima media thickness (CIMT) associated with low HGS after 4-year follow-up [26]. In people with muscle strength weakness, chronic inflammation increases [27] to reduce the bioavailability of nitric oxide, aggravate endothelial dysfunction, and accelerate atherosclerosis and arterial plaque formation by autocrine and paracrine mechanisms [28, 29]. Meanwhile, insufficient levels of physical activity influence muscle weakness, which in turn exhibits HGS weakness [25, 30]. In addition, HGS is a useful functional measure when added to a clinical nutrition assessment [31], and it can reflect the dietary intake in older adults [32]. As a result of these factors, older people with HGS weakness are more likely to develop cardiovascular events.

In our study, HGS asymmetry was not associated with MACE and composite endpoints after being fully adjusted in Model 3, which illustrated that HGS asymmetry was not as effective as HGS weakness in predicting cardiovascular outcomes. One of the explanations may be the disuse of the non-dominant limb [33]. Lack of exercise in the non-dominant hand generates a gap in HGS with the dominant hand. On the other hand, HGS asymmetry can be explained by the asymmetry of the primary somatosensory cortex in each hemisphere of the brain [34] and cerebellar-related neurologic dysfunction [8]. The complex correlation between HGS asymmetry and the nervous system exactly supported that the aging people with HGS asymmetry might have a higher risk of falls and functional limitations discussed in several studies [6, 9–11]. Nonetheless, further research is required to identify whether HGS asymmetry can be an independent predictor for other adverse events, such as cardiovascular outcomes.

After consideration for both HGS weakness and asymmetry, an important conclusion can be obtained that HGS weakness and asymmetry together were associated with cardiovascular outcomes in older adults compared with those with normal and symmetric HGS. HGS asymmetry offers complementary information to HGS weakness when making a complete evaluation of HGS, implying the dysfunction of the neuromuscular system and cardiovascular system. The combination of HGS weakness and HGS asymmetry may improve the prediction ability of HGS assessment in cardiovascular outcomes, which have implications for comprehensive geriatric assessment.

Implementing HGS asymmetry measurement in clinical practice merits greater attention, and more geriatricians and clinicians should target appropriate interventions for elderly patients with both HGS weakness and asymmetry.

The study includes some strengths that need to be acknowledged. Our study is one of the first studies adding HGS asymmetry to the assessment of HGS. Additionally, the study is the first to explore the longitudinal association of HGS weakness and asymmetry together on cardiovascular outcomes in older adults. The study also had some limitations that should be considered. First, the current sample size may not be sufficient, and the included population was geriatric outpatients rather than community-based elderly population. The results may not be considered relevant to the population at large. Second, the primary endpoint of this study was cardiovascular outcomes, and the baseline population was not fully excluded patients with CHD and HF. However, efforts were made to exclude patients with poor cardiac function and hospitalization for myocardial infarction and HF in the recent six months to reduce potential bias. Third, although we choose the “10% rule” as the threshold of HGS asymmetry, there still exist differences in HGS between hands. The underlying mechanism of HGS asymmetry needs to be confirmed in future biological or large longitudinal studies.

Conclusions

In conclusion, this study identified the association of HGS weakness and asymmetry on cardiovascular outcomes. Elderly outpatients with HGS weakness and asymmetry together had a higher risk of cardiovascular outcomes. The findings suggested that HGS asymmetry in combination with HGS weakness could improve the predictive value of cardiovascular outcomes. It is necessary to conduct developed research on the mechanism and interventions of HGS asymmetry in the future.

Abbreviations

BMI: body mass index; HF: heart failure, CHD: coronary heart disease, HGS: handgrip strength; FBG: Fasting blood glucose; TG: triglycerides; TC: total cholesterol; LDL-C: low-density lipoprotein protein cholesterol; HDL-C: High-density lipoprotein cholesterol.; MACE: major adverse cardiovascular event.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Fujian Provincial Hospital. The design and procedure of the study were performed in accordance with the principles of the Declaration of Helsinki. The manuscript complies with the Ethical Rules for publication. Informed consent was obtained from all participants.

Consent for publication

All of the authors approved the manuscript’s submission for publication.

Availability of data and materials

All data generated or analysed during this study are included in this published article [and its supplementary information files].

Competing interests

Upon manuscript submission, all the authors declare that they have no competing interests.

Funding

Not applicable.

Authors' contributions

LSY, WF, and HYJ managed the study concept and design. LSY, WF, HYJ, and YY completed the acquisition of subjects, which was directed by HF and ZPL. LSY and WF analyzed and interpreted the data. LSY drafted the manuscript. All authors reviewed and revised the manuscript, read and approved the final manuscript.

Acknowledgments

We are grateful for the support from Fujian Provincial Center for Geriatrics and Fujian Provincial Institute of Clinical Geriatrics. We would like to thank the technical assistance of the Institute of Fujian Provincial Key Laboratory of Geriatrics. This study was supported by the Fujian Major Project Foundation (2016YZ01010016) and Fujian Science and Technology Innovation Joint Major Project (2019Y9027).

References

1. Celis-Morales CA, Welsh P, Lyall DM, 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.
2. Kim GR, Sun J, Han M, Park S, Nam CM. Impact of handgrip strength on cardiovascular, cancer and all-cause mortality in the Korean longitudinal study of ageing. BMJ Open. 2019;9(5):e027019.
3. Jang SK, Kim JH, Lee Y. Effect of relative handgrip strength on cardiovascular disease among Korean adults aged 45 years and older: Results from the Korean Longitudinal Study of Aging (2006-2016). Arch Gerontol Geriatr. 2020;86:103937.
4. Leong DP, Teo KK, Rangarajan S, et al. Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. Lancet. 2015;386(9990):266-73.
5. Auyeung TW, Lee SW, Leung J, Kwok T, Woo J. Age-associated decline of muscle mass, grip strength and gait speed: a 4-year longitudinal study of 3018 community-dwelling older Chinese. Geriatr Gerontol Int. 2014;14 Suppl 1:76-84.
6. McGrath R, Clark BC, Cesari M, Johnson C, Jurivich DA. Handgrip strength asymmetry is associated with future falls in older Americans. Aging Clin Exp Res. 2021;33(9):2461-9.
7. McGrath R, Cawthon PM, Cesari M, Al Snih S, Clark BC. Handgrip Strength Asymmetry and Weakness Are Associated with Lower Cognitive Function: A Panel Study. J Am Geriatr Soc. 2020;68(9):2051-8.
8. McGrath R, Tomkinson GR, LaRoche DP, Vincent BM, Bond CW, Hackney KJ. Handgrip Strength Asymmetry and Weakness May Accelerate Time to Mortality in Aging Americans. J Am Med Dir Assoc. 2020;21(12):2003-7.e1.

9. Parker K, Rhee Y, Tomkinson GR, Vincent BM, O&#39, Connor ML, McGrath R. Handgrip Weakness and Asymmetry Independently Predict the Development of New Activity Limitations: Results from Analyses of Longitudinal Data from the US Health and Retirement Study. J Am Med Dir Assoc. 2021;22(4):821-6.e1.
10. Collins K, Johnson N, Klawitter L, Waldera R, Stastny S, Kraemer WJ, Christensen B, McGrath R. Handgrip Strength Asymmetry and Weakness are Differentially Associated with Functional Limitations in Older Americans. Int J Environ Res Public Health. 2020;17(9).
11. McGrath R, Vincent BM, Jurivich DA, Hackney KJ, Tomkinson GR, Dahl LJ, Clark BC. Handgrip Strength Asymmetry and Weakness Together Are Associated With Functional Disability in Aging Americans. J Gerontol A Biol Sci Med Sci. 2021;76(2):291-6.
12. den Ouden ME, Schuurmans MJ, Arts IE, Grobbee DE, Bots ML, van den Beld AW, Lamberts SW, van der Schouw YT. Atherosclerosis and physical functioning in older men, a longitudinal study. J Nutr Health Aging. 2013;17(1):97-104.
13. Bohannon RW, Magasi SR, Bubela DJ, Wang YC, Gershon RC. Grip and knee extension muscle strength reflect a common construct among adults. Muscle Nerve. 2012;46(4):555-8.
14. Volaklis KA, Halle M, Koenig W, et al. Association between muscular strength and inflammatory markers among elderly persons with cardiac disease: results from the KORA-Age study. Clin Res Cardiol. 2015;104(11):982-9.
15. Norman K, Stobäus N, Gonzalez MC, Schulzke JD, Pirlich M. Hand grip strength: outcome predictor and marker of nutritional status. Clin Nutr. 2011;30(2):135-42.
16. Mitchell M, Martin BJ, Adamo DE. Upper Limb Asymmetry in the Sense of Effort Is Dependent on Force Level. Front Psychol. 2017;8:643.
17. Reijnierse EM, de Jong N, Trappenburg MC, et al. Assessment of maximal handgrip strength: how many attempts are needed. J Cachexia Sarcopenia Muscle. 2017;8(3):466-74.
18. Chen LK, Woo J, Assantachai P, et al. Asian Working Group for Sarcopenia: 2019 Consensus Update on Sarcopenia Diagnosis and Treatment. J Am Med Dir Assoc. 2020;21(3):300-7.e2.
19. Armstrong CA, Oldham JA. A comparison of dominant and non-dominant hand strengths. J Hand Surg Br. 1999;24(4):421-5.
20. Liu M, Liu S, Sun S, Tian H, Li S, Wu Y. Sex Differences in the Associations of Handgrip Strength and Asymmetry With Multimorbidity: Evidence From the English Longitudinal Study of Ageing. J Am Med Dir Assoc. 2021.
21. Go YJ, Lee DC, Lee HJ. Association between handgrip strength asymmetry and falls in elderly Koreans: A nationwide population-based cross-sectional study. Arch Gerontol Geriatr. 2021;96:104470.
22. Pavasini R, Serenelli M, Celis-Morales CA, et al. Grip strength predicts cardiac adverse events in patients with cardiac disorders: an individual patient pooled meta-analysis. Heart. 2019;105(11):834-41.
23. Rijk JM, Roos PR, Deckx L, van den Akker M, Buntinx F. Prognostic value of handgrip strength in people aged 60 years and older: A systematic review and meta-analysis. Geriatr Gerontol Int. 2016;16(1):5-20.
24. Wu Y, Wang W, Liu T, Zhang D. Association of Grip Strength With Risk of All-Cause Mortality, Cardiovascular Diseases, and Cancer in Community-Dwelling Populations: A Meta-analysis of Prospective Cohort Studies. J Am Med Dir Assoc. 2017;18(6):551.e17-551.e35.
25. Soysal P, Hurst C, Demurtas J, et al. Handgrip strength and health outcomes: Umbrella review of systematic reviews with meta-analyses of observational studies. J Sport Health Sci. 2021;10(3):290-5.

26. den Ouden ME, Schuurmans MJ, Arts IE, Grobbee DE, Bots ML, van den Beld AW, Lamberts SW, van der Schouw YT. Atherosclerosis and physical functioning in older men, a longitudinal study. J Nutr Health Aging. 2013;17(1):97-104.
27. Strasser B, Keinrad M, Haber P, Schobersberger W. Efficacy of systematic endurance and resistance training on muscle strength and endurance performance in elderly adults–a randomized controlled trial. Wien Klin Wochenschr. 2009;121(23-24):757-64.
28. Asano RY, Sales MM, Browne RA, Moraes JF, Coelho Júnior HJ, Moraes MR, Simões HG. Acute effects of physical exercise in type 2 diabetes: A review. World J Diabetes. 2014;5(5):659-65.
29. Guizoni DM, Dorighello GG, Oliveira HC, Delbin MA, Krieger MH, Davel AP. Aerobic exercise training protects against endothelial dysfunction by increasing nitric oxide and hydrogen peroxide production in LDL receptor-deficient mice. J Transl Med. 2016;14(1):213.
30. Caillouet KA, Cosio-Lima L. Association of health empowerment and handgrip strength with intention to participate in physical activity among community-dwelling older adults. Exp Gerontol. 2019;121:99-105.
31. McNicholl T, Dubin JA, Curtis L, Mourtzakis M, Nasser R, Laporte M, Keller H. Handgrip Strength, but Not 5-Meter Walk, Adds Value to a Clinical Nutrition Assessment. Nutr Clin Pract. 2019;34(3):428-35.
32. Tak YJ, Lee JG, Yi YH, Kim YJ, Lee S, Cho BM, Cho YH. Association of Handgrip Strength with Dietary Intake in the Korean Population: Findings Based on the Seventh Korea National Health and Nutrition Examination Survey (KNHANES VII-1), 2016. Nutrients. 2018;10(9).
33. Straight CR, Brady AO, Evans EM. Asymmetry in leg extension power impacts physical function in community-dwelling older women. Menopause. 2016;23(4):410-6.
34. Jung P, Baumgärtner U, Bauermann T, Magerl W, Gawehn J, Stoeter P, Treede RD. Asymmetry in the human primary somatosensory cortex and handedness. Neuroimage. 2003;19(3):913-23.

Figures

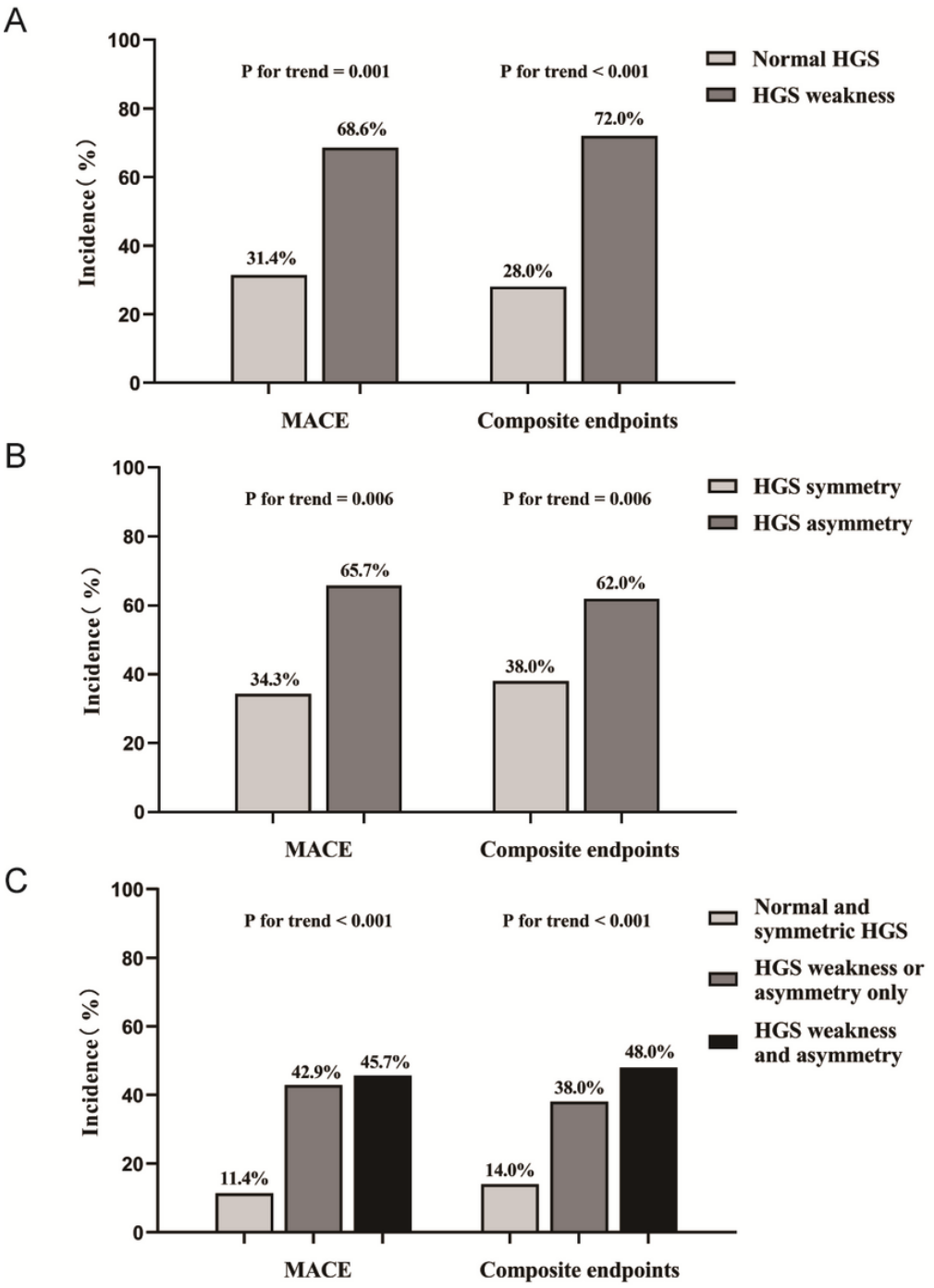

Figure 1

Incidence of cardiovascular outcomes in elderly outpatients by different HGS weakness and HGS asymmetry groups

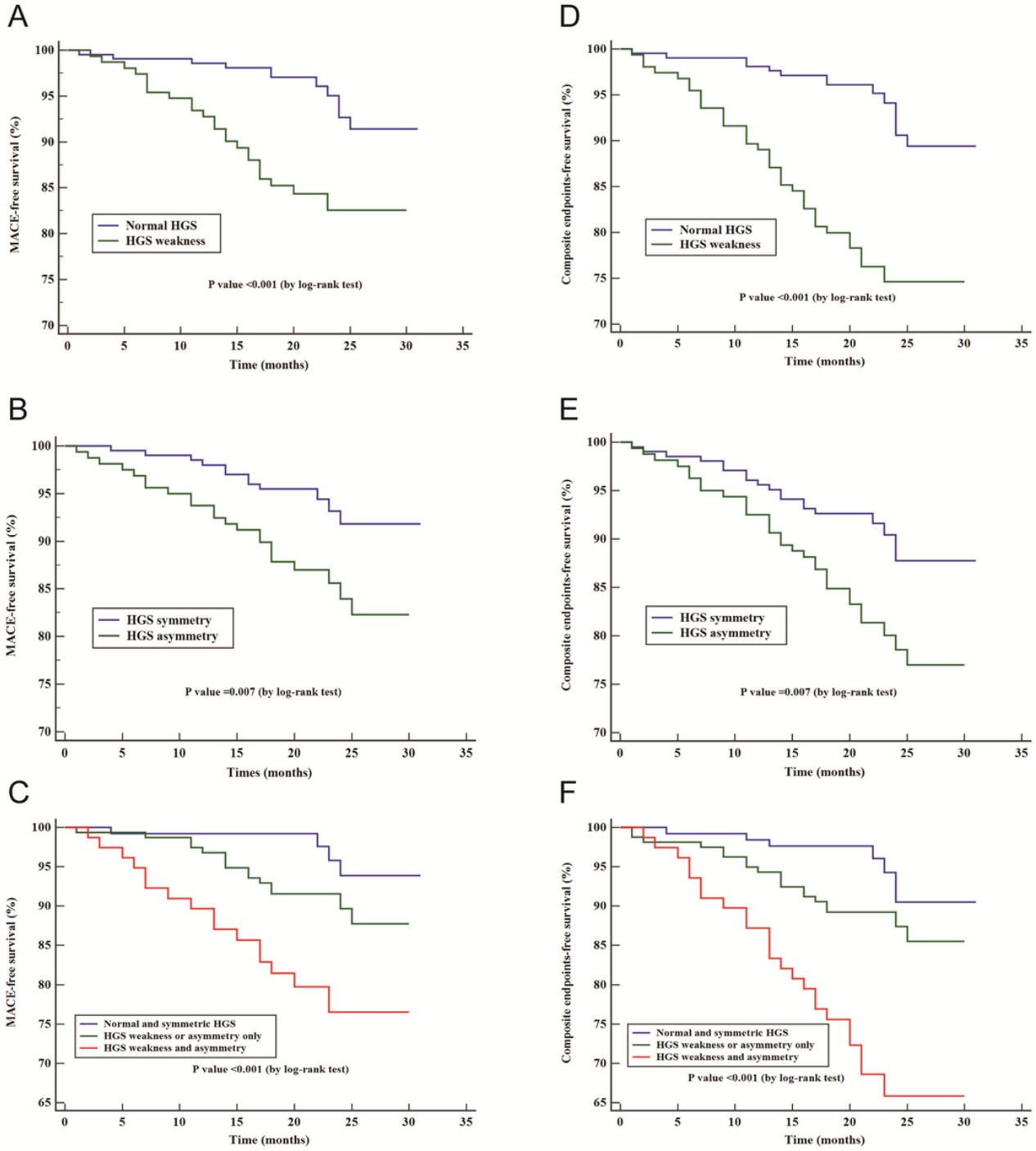

Figure 2

Kaplan–Meier survival curve of cardiovascular outcomes in elderly outpatients by different HGS weakness and HGS asymmetry groups

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- 364casesBMCgeriatrics.xlsx