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Authors

Sin, Mo-Kyung
Lee, Jung Ah
Murphy, Patrick
et al.

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Upper Extremity Weakness: A Novel Risk Factor for Non-Cardiovascular Mortality Among Community-Dwelling Older Adults

Mo-Kyung Sin, PhD, RN, FGSA[1], **Jung-Ah Lee, PhD, RN, FGSA**[2], **Patrick J.M. Murphy, PhD**[1], **Charles Faselis, MD**[3,4,5], **Ali Ahmed, MD, MPH**[3,4,6]

[1]College of Nursing,' Seattle University, Seattle, WA

[2]School of Nursing, University of California, Irvine, CA

[3]Veterans Affairs Medical Center, Washington, DC

[4]School of Medicine, George Washington University, Washington, DC

[5]School of Medicine, Uniformed Services University, Washington, DC

[6]School of Medicine, Georgetown University, Washington, DC

Abstract

Background—Aging-associated upper extremity weakness has been shown to be associated with adverse health outcomes in older adults, but less is known about the association between impaired upper extremity function and cause-specific mortalities.

Methods—Among the 5512 prospective community-based longitudinal Cardiovascular Health Study participants, 1438 had difficulty with one of the three upper extremity functions of lifting, reaching, or gripping. We assembled a propensity score-matched cohort in which 1126 pairs of participants with and without difficulty with upper extremity function, balanced on 62 baseline characteristics including geriatric and functional variables such as physical and cognitive function. Hazard ratios (HRs) and 95% confidence intervals (CIs) for all-cause and cause-specific mortalities associated with upper extremity weakness were estimated in the matched cohort.

Address for correspondence: Mo-Kyung Sin, PhD, RN, FGSA, 901 12th Ave, P.O. BOX 222000, Seattle, WA 98122-1090; Telephone: 1-206-296-5667. sinm@seattleu.edu.

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Study concept and design, data acquisition, data interpretation, manuscript writing: Mo-Kyung Sin and Ali Ahmed. Data analysis and interpretation: Ali Ahmed and Mo-Kyung Sin; Data interpretation and critical review of the manuscript for important intellectual content: Jung-Ah Lee, Patrick Murphy, and Charles Faselis

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Results—Matched participants had a mean age of 73.1 years, 72.5% were women, and 17.0% African American. During 23 years of follow-up, all-cause mortality occurred in 83.7% (942/1126) and 81.2% (914/1126) of participants with and without upper extremity weakness, respectively (HR, 1.11; 95% CI, 1.01–1.22; p=0.023). Upper extremity weakness was associated with a higher risk of non-cardiovascular mortality, occurring in 595 (52.8%) and 553 (49.1%) of participants, respectively (HR, 1.17; 95% CI, 1.04–1.31; p=0.010), but had no association with cardiovascular mortality (30.8% vs 32.1% in those with and without upper extremity weakness, respectively; HR, 1.03; 95% CI, 0.89-1.19; p=0.70).

Conclusion—Among community-dwelling older adults, upper extremity weakness had a weak, albeit independent, significant association with all-cause mortality, which was primarily driven by a higher risk of non-cardiovascular mortality. Future studies need to replicate these findings and understand the underlying reasons for the observed associations.

Keywords

Cardiovascular disease; mortality; older Americans; propensity score matching; upper extremity weakness

Aging is associated with loss of muscle mass and strength in both upper and lower extremities (Cheng, Yang, Cheng, Chen, & Wang, 2014). Sarcopenia and weakness of lower extremity adversely affect life-space mobility and have been known to be associated with a higher risk of adverse outcomes (e.g., poor physical function, mortality) (Evans, 1997; Newman et al., 2006; Visser et al., 2000). While upper extremity weakness is less directly associated with mobility, it is also known to adversely affect physical function (Calik-Kutukcu et al., 2017; Daly et al., 2013; Kim & Park, 2019). Several studies have demonstrated that weakness in handgrip strength is associated with adverse health outcomes including disability (Lopez-Teros, Gutierrez-Robledo, & Perez-Zepeda, 2014), hospitalization (Simmonds et al., 2015), and a higher risk of death including cardiovascular death (Kim, Sun, Han, Park, & Nam, 2019; Newman et al., 2006; Rantanen et al., 2003; Strand et al., 2016). However, less is known about the association of upper extremity function weakness with all-cause and cause-specific mortalities. The objective of the current study was to examine the association of any upper extremity weaknesses (lifting, reaching, and gripping), with incident of all-cause, CV and non-CV mortalities in community-dwelling older adults during 23 years of follow-up.

Methods

Data Source and Study Population

We used de-identified public-use copies of the Cardiovascular Health Study (CHS) data obtained from the Biologic Specimen and Data Repository Information Coordinating Center (BioLINCC) of the National Heart, Lung, and Blood Institute (NHLBI). The CHS was sponsored by the NHLBI and was designed to identify risk factors for the development and progression of cardiovascular disease in older adults who were eligible for Medicare benefits at the time of enrollment (Fried et al., 1991). Starting in 1989 and continuing through 1999, it recruited 5,888 men and women aged 65 or older in four U.S. communities, viz., Sacramento, California; Hagerstown, Maryland; Winston-Salem, North Carolina; and

Pittsburgh, Pennsylvania, conducting annual clinical examinations. The public-use version of the CHS data included data of 5795 participants who consented to be included in the data. After excluding 36 participants with missing data on upper extremity function and 247 participants with baseline stroke because of its cardiovascular influence on upper extremity weakness, the final study cohort consisted of 5512 older adults.

Study Exposure: Upper Extremity Weakness

Information about upper extremity weakness was collected at baseline from all CHS participants during the eligibility phase. According to the CHS Physical Functioning Form, study participants were asked: Do you have any difficulty (1) lifting or carrying something heavy, (2) reaching out, (3) gripping with your hands? The CHS data has a calculated variable called “upper extremity score” that records the number of tasks (0-3) that a participant has difficulty with lifting, reaching, gripping. Of the 5512 participants with data on upper extremity score, 1438 (26.1%) had impairment in one of the three functions of lifting, reaching, or gripping. Of the 1438 with any upper extremity difficulty, 285 (19.9%) had reach difficulty, 806 (56.1%) had grip difficulty, 765 (53.2%) had lifting difficulty, 1090 (75.8%) had difficulty with any of the three, 278 (19.3%) with any two, and 70 (4.9%) with all three upper extremity functions.

Assembly of a Balanced Cohort

As demonstrated in Table 1, there were significant differences in many prognostically important baseline characteristics, including impairments in physical and cognitive function, between participants with difficulty with upper extremity function. Older adults with difficulty with lifting, reaching, gripping, were older, predominantly women and African Americans, and a higher proportion of these individuals had morbidities such as hypertension, coronary heart disease, diabetes mellitus, chronic obstructive pulmonary disease, and arthritis. Importantly, twice as many participants with upper extremity function difficulty had a history of stroke than those without.

To be able to determine an independent association between upper extremity weakness and outcomes, we assembled a propensity score-matched cohort in which these and other measured baseline characteristics would be balanced (Austin, 2008). We began by estimating propensity scores for upper extremity difficulty using a non-parsimonious multivariable logistic regression model, described in detail elsewhere (Ahmed et al., 2008; Arundel et al., 2019; Bayoumi et al., 2019; Faselis et al., 2020; Lam et al., 2017; Tsimploulis et al., 2018; Wahle et al., 2009). In the model, upper extremity difficulty was the dependent variable, and 62 baseline characteristics listed in the Figure 1 were used as covariates. All these variables were collected from CHS participants at baseline and have been previously described (Ekundayo et al., 2009; Ekundayo et al., 2009; Iyer et al., 2010). Using a greedy matching algorithm, we matched 1126 (78.3%) individuals with difficulty in one or more upper extremity function with 1126 individuals without those difficulties. Thus, the matched primary cohort consisted of 2252 participants balanced on 62 baseline characteristics. Because the primary objective of the propensity score models is to assemble a balanced cohort within the study sample, and not use for out-of-sample predictions, traditional metrics of regression models such as fitness and discrimination are less important

in assessing these models' performance (Ahmed et al., 2009; Austin, 2011). Instead, we estimated between-group absolute standardized differences for all 62 baseline characteristics (Austin, 2009; Austin & Stuart, 2017). Values of absolute standardized difference <10% indicates minimal residual bias, and a value of 0% would indicate no residual bias.

Study Outcomes

Our outcomes of interest were time to all-cause, CV and non-CV mortalities. Death was ascertained at annual examination and 6-month telephone interview. If the participant was unavailable, a proxy was interviewed. Then, death was classified by CHS field investigators, which was then centrally adjudicated by CHS outcomes committee. Outcomes were followed up for a total of 22.6 years, with a median follow-up of 13.3 (25 and 75 percentiles, 7.9 and 18.7) years. Individuals who did not die during study follow-up were censored.

Statistical Analyses

Baseline characteristics of the pre-match and post-match cohorts were compared using Pearson's Chi-Square for categorical variables and Student's t-test for continuous variables. All outcome analyses were conducted in the matched cohort. Kaplan-Meier survival curves were used to compare the time to death between the two upper extremity weakness groups. We used Cox regression models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for outcomes associated with upper extremity weakness. Despite some indication of non-proportionality, we used the Cox model as the HR estimates from Cox models are weighted average of the time-varying HRs which is a convenient summary of the treatment effect during the follow-up (Stensrud & Hernan, 2020). Subgroup analyses were conducted to determine the homogeneity of the association of upper extremity weakness and outcomes. SPSS for Windows (IBM Version 28) was used for data analyses.

Results

Baseline Characteristics

The 2252 participants in the matched primary cohort had a mean age of 73.1 (±5.75) years; 72.5% were women, and 17.0% were African American. Of the 1126 matched individuals with upper extremity function difficulty, 199 (17.7%) had reach difficulty; 635 (56.4%) had grip difficulty; 526 (46.7%) had lifting difficulty, and 922 (81.9%) had difficulty with any of three, 174 (15.5%) with any two, and 30 (2.7%) had difficulty in all three upper extremity functions. Absolute standardized differences in the pre- and post-match cohorts are displayed in Figure 2. Absolute standardized differences for all 62 baseline characteristics were <10% suggesting adequate balance. Balances in the proportions (%) and means (SD) of key baseline characteristics in the matched cohort are displayed in Table 1.

Mortality

All-cause mortality occurred in 942 (83.7%) and 914 (81.2%) matched participants with and without difficulty with upper extremity function, respectively (HR associated with upper extremity function difficulty, 1.11; 95% CI, 1.10-1.22; p=0.023; Table 2, Figure 3). Findings from the Kaplan-Meier curves suggest that this association did not become apparent until after the first 5 years of follow-up (Figure 3). The association between upper extremity

weakness and total death was primarily driven by non-CV death (HR associated with upper extremity function difficulty, 1.17; 95% CI, 1.04-1.31, p=0.010; Table 2, Figure 3). Findings from our subgroup analyses demonstrate that except for by diabetes, there is no evidence of heterogeneity in the association of upper extremity weakness with non-CV death across various clinically important subgroups (Supplementary Figure). Difficulty with upper extremity function had no association with CV death (HR, 1.03; 95% CI, 0.89-1.19; p=0.701; Table 2, Figure 3).

Discussion

The findings from our analyses of the CHS data demonstrate that difficulty in upper extremity function is common in community-dwelling older adults without stroke and is associated with a delayed higher risk of all-cause and non-CV deaths, but not with CV death. To the best of our knowledge this is the first report of an association between various upper extremity function weakness and non-CV death in older adults balanced on various baseline characteristics including physical and cognitive impairment. These findings suggest impairment in upper extremity function may occur in isolation from impairment of other physical function and provide insights into characteristics and prognosis of upper extremity weakness in community-dwelling older adults.

As in any observational studies, there are three possible explanations for significant associations observed in our study: chance, confounding, and true association. The significant association between upper extremity weakness and total mortality observed in our study is unlikely a chance finding considering that over 80% of 2156 older adults died during over two decades of follow-up. Taken together with the fact that prior studies have observed associations of handgrip weakness with death, the observed association is unlikely to be a chance finding. This association is also unlikely to be confounding by the 62 measured baseline characteristics that were balanced in our matched cohort. However, bias due to residual confounding is possible. While matching may balance the prevalence of morbidities such as diabetes or chronic obstructive pulmonary disease, matching may not balance severity of these conditions. For example, diabetes and COPD are associated with sarcopenia and higher risk of death (Chung et al., 2021; Limpawattana et al., 2018). Although the prevalence of both conditions was balanced in our matched cohort, if upper extremity weakness was a complication of diabetes and COPD of longer duration and/or greater severity, that may in part explain the observed higher risk of death. Thus, the upper extremity weakness was likely a marker of more severe or advanced disease. Similar imbalances in duration and/or severity of other morbidities that may lead to loss of muscle mass and function may explain the small but significantly higher risk of death associated with upper extremity weakness. This is likely a more plausible explanation as unlike smoking, high blood pressure, or high serum cholesterol, upper extremity weakness is not mechanistically or pathophysiologically associated with a higher risk of mortality. It is unclear why upper extremity weakness would preferentially be associated with a higher risk of non-CV death but not of CV death. One possible explanation is that a higher proportion of death was due to non-CV causes than CV causes, and that sarcopenia associated with isolated upper extremity weakness may increase the risk of dysphagia, albuminuria, malnutrition, falls, fractures, depression, and cognitive impairment, all potentially leading to

non-CV hospitalization and non-CV death (Xia et al., 2020). Finally, although the observed association with non-CV death was insensitive to unmeasured confounders, it was weak, reflecting the weak association and the possibility that this association may be potentially explained away by small change in the exposure-confounder relationship.

The skeletal muscle is an endocrine organ (Pedersen & Fischer, 2007) and muscle fibers from skeletal muscle contractions produce myokines (e.g., interleukin (IL)-6, IL-8, Il-15), which modulates the metabolic and immunological response to exercise in several tissues (Pedersen et al., 2007; Pedersen & Febbraio, 2008). IL-6, for example, stimulates anti-inflammatory cytokine production and suppresses tumor necrosis factor (TNF)-α production. Muscle-derived IL-6 was found to have a protective effect against TNF-induced insulin resistance. The nervous, endocrine, and immune systems all contribute to the maintenance of homeostasis. Sarcopenia related to the natural aging process, lack of physical activity/exercise, sedentary lifestyle, and poor nutrition, and chronic illness all can influence muscle weakness in older adults. It is not clear, however, why a systemic sarcopenia would lead to isolated upper extremity weakness. One possible explanation is that most older adults may retain lower extremity strength longer through mobility and ambulation while a relative lack of use of upper extremity function may lead to a preferential upper extremity weakness. Future studies need to examine whether strengthening upper extremity would prevent early mortality in older adults.

Several studies have examined the relationship of muscle strength and mortality in older adults (Kim et al., 2019; Metter et al., 2002; Newman et al., 2006; Strand et al., 2016). Muscle strength is fundamental for maintenance of functional abilities and positive health outcomes in later life. In the Health, Aging and Body Composition (Health ABC) Study, muscle strength, but not muscle mass, in both quadriceps and grip strength were strongly related to mortality (Newman et al., 2006). The Baltimore Longitudinal Study of Aging reported cardiovascular disease and cancer accounted for 60% of the mortality from low grip strength (Metter et al., 2002). In a population-based longitudinal sample of Korean older adults, handgrip strength had a significant association with all-cause mortality and cardiovascular disease mortality (Strand et al., 2016). In a 17-year longitudinal study of Norwegians aged 50–80 years, weaker handgrip had significant association with higher all-cause mortality and mortality due to cardiovascular disease and respiratory diseases (Strand et al., 2016). In a population-based longitudinal sample of Korean older adults, handgrip strength had a significant association with all-cause mortality and cardiovascular disease mortality (Kim et al., 2019). Our study is distinguished by its larger sample size, longer follow-up, centrally-adjudicated events, propensity score matching, other clinically-relevant measures of upper extremity function (lifting, reaching) and the observation of a previously unreported association with non-CV death.

Limitations

There are several limitations to our study. Despite our use of propensity score matching to achieve baseline balance, biases due to residual and unmeasured confounding are possible. The upper extremity weakness score was based on self-report, and we did not have access to upper extremity muscle strength during follow-up. It is possible that those with normal

upper extremity strength developed weakness during follow-up. However, it is likely to have underestimation of the association observed in our study. CHS participants were volunteers, which may limit generalizability. However, CHS participants have been shown to be comparable to national and regional Medicare cohorts. Because data on upper extremity muscle strength was not available as a continuous variable, we were not able to perform a spline regression analysis to determine the muscle weakness threshold at which the risk of poor outcomes became significant.

Conclusions

Among community-dwelling older adults, upper extremity weakness is common, may exist in isolation from impairment of other physical function, and is a marker of a significantly higher, albeit small and delayed, risk of all-cause and non-CV mortality. Future studies need to examine the underlying reason for the association with non-CV but not with CV death, and whether a physical activity or exercise program dedicated to improving upper extremity strength would improve outcomes in older adults with upper extremity weakness who are at a higher risk of death.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Assessment and preservation of physical function is at the core of geriatrics.
- Upper extremity weakness (UEW) is common in community-dwelling older adults.
- UEW may exist in isolation from other weaknesses.
- UEW has a significant association with non-cardiovascular death.

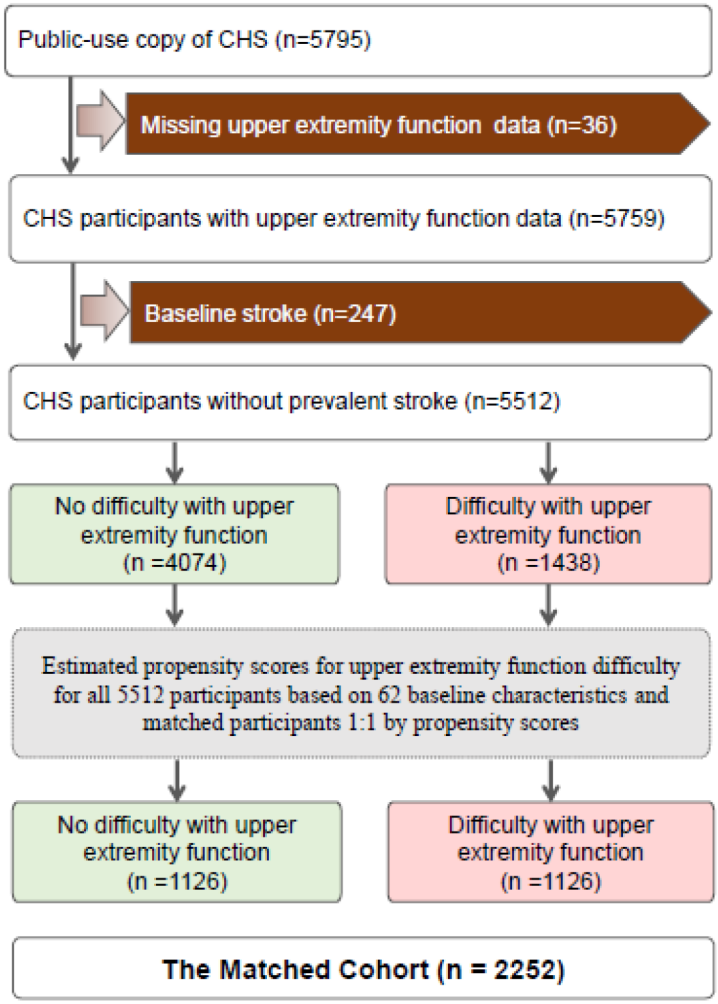

FIGURE 1.

Flow chart displaying assembly of the matched cohort of older adults without stroke with and without baseline upper extremity difficulty in the Cardiovascular Health Study (CHS).

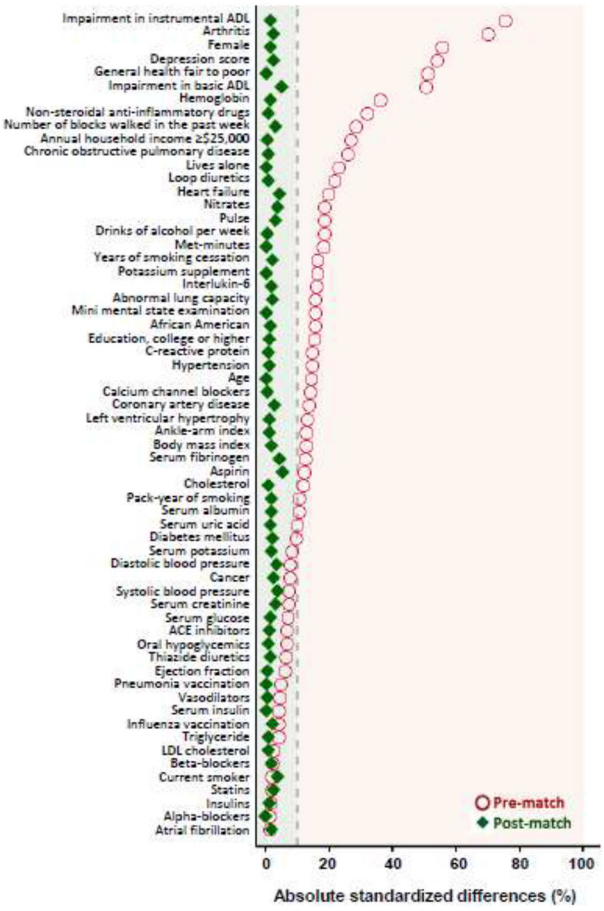

FIGURE 2.

Love plot displaying absolute standardized differences for 62 baseline characteristics between older adults with vs. without upper extremity difficulty, before and after propensity score matching. A standardized difference of 0% indicates no residual bias and values <10% indicate inconsequential bias.

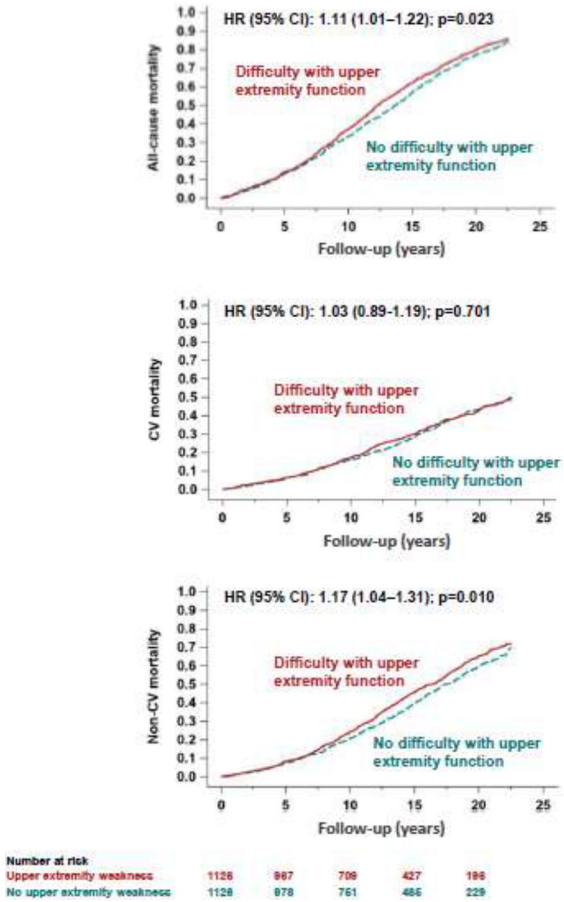

FIGURE 3.

Kaplan-Meier plots for all-cause, CV and non-CV death during 23 years of follow up by upper extremity difficulty in 1126 pairs of propensity score-matched older adults free of stroke (HR = hazard ratio; CI = confidence interval). The numbers at risk are same for both all-cause and cause-specific mortalities, and as such presented only once.

Table 1.

Baseline characteristics by difficulty in one or more upper extremity function, before and after propensity score matching based on 62 baseline characteristics

Variables n (%) or mean (±SD)	Before propensity score matching (n=5512)			After propensity score matching (n=2252)		
	Difficulty in one or more upper extremity function			Difficulty in one or more upper extremity function		
	No (n=4074)	Yes (n=1438)	P value	No (n=1126)	Yes (n=1126)	P value
Age in years	72.6 (±5.46)	73.4 (±5.96)	<0.001	73.1 (±5.73)	73.1 (±5.76)	0.959
Female	2096 (51%)	1109 (77%)	<0.001	815 (72%)	822 (73%)	0.741
African American	555 (14%)	278 (19%)	<0.001	191 (17%)	197 (17%)	0.738
Lives alone	439 (11%)	272 (19%)	<0.001	182 (16%)	181 (16%)	0.954
Education, ≥college	1823 (45%)	535 (37%)	<0.001	447 (40%)	441 (39%)	0.796
Annual household income, ≥$25,000	1594 (39%)	383 (27%)	<0.001	331 (29%)	333 (30%)	0.926
Pack-years of smoking	17.7 (±26.6)	15.1 (±24.8)	<0.001	15.1 (±24.7)	15.5 (±24.7)	0.685
Years of smoking cessation	9.05 (±14.0)	6.92 (±12.5)	<0.001	7.04 (±12.5)	7.30 (±12.8)	0.629
Current smoker	484 (12%)	180 (13%)	0.523	126 (11%)	139 (12%)	0.395
Alcohol, drinks per week	2.74 (±6.85)	1.66 (±4.75)	<0.001	1.94 (±5.31)	1.92 (±5.04)	0.919
Influenza vaccination	1770 (43%)	653 (45%)	0.197	521 (46%)	510 (45%)	0.642
Pneumococcal vaccination	1030 (25%)	393 (27%)	0.127	300 (27%)	301 (27%)	0.962
Impairment in basic ADL	0.04 (±0.24)	0.34 (±0.81)	<0.001	0.11 (±0.40)	0.13 (±0.46)	0.242
Impairment in instrumental ADL	0.19 (±0.48)	0.79 (±1.02)	<0.001	0.47 (±0.73)	0.49 (±0.69)	0.699
Number of blocks walked last week	42.8 (±57.2)	28.3 (±43.7)	<0.001	30.7 (±43.5)	32.0 (±45.7)	0.471
Met-minutes	1411.7 (±1502.1)	1136.6 (±1528.6)	<0.001	1246.4 (±1496.3)	1240.9 (±1586.3)	0.932
Mini mental state examination score	27.7 (±2.61)	27.2 (±2.92)	<0.001	27.5 (±2.78)	27.4 (±2.77)	0.933
Depression score	4.00 (±4.06)	6.55 (±5.32)	<0.001	5.76 (±4.98)	5.64 (±4.74)	0.564
General health, fair to poor	754 (19%)	591 (41%)	<0.001	374 (33%)	373 (33%)	0.964
Hypertension	1813 (45%)	744 (52%)	<0.001	551 (49%)	544 (48%)	0.768
Coronary artery disease	718 (18%)	333 (23%)	<0.001	242 (21%)	229 (20%)	0.501
Heart failure	130 (3%)	110 (8%)	<0.001	70 (6%)	59 (5%)	0.319
Diabetes mellitus	608 (15%)	265 (18%)	0.002	194 (17%)	185 (16%)	0.612
Atrial fibrillation	98 (2%)	37 (3%)	0.724	27 (2%)	24 (2%)	0.671
Chronic obstructive pulmonary disease	418 (10%)	278 (19%)	<0.001	192 (17%)	195 (17%)	0.867
Arthritis	1745 (43%)	1083 (75%)	<0.001	807 (72%)	795 (71%)	0.577
Cancer	559 (14%)	236 (16%)	0.013	182 (16%)	172 (15%)	0.563
ACE inhibitors	275 (7%)	122 (8%)	0.029	91 (8%)	87 (8%)	0.755
Beta-blockers	520 (13%)	174 (12%)	0.514	142 (13%)	135 (12%)	0.653
Alpha-blockers	71 (2%)	23 (2%)	0.718	18 (2%)	18 (2%)	1.000
Calcium channel blockers	483 (12%)	241 (17%)	<0.001	168 (15%)	166 (15%)	0.906
Vasodilators	290 (7%)	119 (8%)	0.150	87 (8%)	89 (8%)	0.875
Thiazide diuretics	428 (11%)	180 (13%)	0.036	126 (11%)	131 (12%)	0.740
Oral hypoglycemics	240 (6%)	108 (8%)	0.030	71 (6%)	73 (6%)	0.863
Insulin injections	100 (2%)	39 (3%)	0.592	28 (2%)	26 (2%)	0.783

Variables n (%) or mean (±SD)	Before propensity score matching (n=5512)			After propensity score matching (n=2252)		
	Difficulty in one or more upper extremity function			Difficulty in one or more upper extremity function		
	No (n=4074)	Yes (n=1438)	P value	No (n=1126)	Yes (n=1126)	P value
Loop diuretics	215 (5%)	161 (11%)	<0.001	107 (10%)	104 (9%)	0.828
Potassium supplements	239 (6%)	147 (10%)	<0.001	93 (8%)	92 (8%)	0.939
Aspirin	100 (2%)	67 (5%)	<0.001	52 (5%)	40 (4%)	0.201
Nitrates	295 (7%)	184 (13%)	<0.001	130 (12%)	117 (10%)	0.381
Statins	86 (2%)	34 (2%)	0.571	23 (2%)	27 (2%)	0.567
Non-steroidal antiinflammatory drugs	389 (10%)	300 (21%)	<0.001	206 (18%)	203 (18%)	0.870
Body mass index	26.4 (±3.94)	27.0 (±4.46)	<0.001	26.9 (±4.34)	26.8 (±4.32)	0.678
Pulse, beats/min	67.4 (±11.0)	69.5 (±11.5)	<0.001	68.9 (±11.0)	68.5 (±10.8)	0.457
Systolic BP, mmHg	136.0 (±21.8)	137.6 (±21.7)	0.017	137.7 (±21.8)	136.9 (±21.0)	0.385
Diastolic BP, mmHg	71.0 (±11.3)	70.1 (±11.6)	0.013	70.5 (±11.4)	70.1 (±11.7)	0.433
Ankle-arm index	1.07 (±0.17)	1.05 (±0.17)	<0.001	1.06 (±0.17)	1.06 (±0.16)	0.764
Abnormal lung capacity	197 (5%)	126 (9%)	<0.001	88 (8%)	95 (8%)	0.589
Left ventricular hypertrophy	158 (4%)	98 (7%)	<0.001	70 (6%)	67 (6%)	0.791
Ejection fraction, reduced	326 (8%)	140 (10%)	0.042	100 (9%)	98 (9%)	0.882
Serum glucose, mg/dL	110.4 (±34.4)	113.1 (±42.0)	0.017	112.1 (±35.3)	111.5 (±39.5)	0.713
Serum creatinine, mg/dL	0.97 (±0.34)	0.93 (±0.50)	0.009	0.94 (±0.38)	0.92 (±0.47)	0.460
Serum potassium, mEq/L	4.17 (±0.38)	4.14 (±0.38)	0.008	4.16 (±0.38)	4.15 (±0.37)	0.688
Serum uric acid, mg/dL	5.70 (±1.48)	5.55 (±1.60)	0.001	5.57 (±1.58)	5.55 (±1.56)	0.708
Hemoglobin, gm/L	14.1 (±1.34)	13.6 (±1.35)	<0.001	13.8 (±1.29)	13.8 (±1.29)	0.701
Serum cholesterol, mg/dL	210.1 (±38.9)	214.6 (±39.3)	<0.001	213.9 (±39.3)	214.3 (±39.0)	0.822
Serum LDL cholesterol, mg/dL	129.6 (±34.7)	130.5 (±36.5)	0.435	130.4 (±35.6)	130.7 (±36.1)	0.854
Serum triglyceride, mg/dL	138.3 (±75.1)	141.2 (±73.6)	0.203	139.7 (±70.9)	139.0 (±72.6)	0.817
Serum albumin, mg/dL	4.00 (±0.28)	3.97 (±0.30)	<0.001	3.99 (±0.28)	3.98 (±0.30)	0.645
Serum fibrinogen1	321.2 (±65.6)	329.4 (±67.5)	<0.001	324.7 (±67.2)	327.8 (±67.3)	0.285
Serum interlukin6_1	2.13 (±1.73)	2.42 (±1.97)	<0.001	2.32 (±2.18)	2.28 (±1.80)	0.657
Serum C-reactive protein	4.39 (±7.54)	5.61 (±8.99)	<0.001	5.08 (±8.37)	5.15 (±8.70)	0.850
Serum insulin	16.6 (±25.0)	17.7 (±28.0)	0.167	17.0 (±24.2)	17.1 (±25.5)	0.977

*Abbreviations: TIA=Transient ischemic attack; COPD=Chronic obstructive pulmonary disease; LVH=Left ventricular hypertrophy; LVEF=Left ventricular ejection fraction; BADL=Basic activities of daily living; IADL=Instrumental activities of daily living; CES=Center for Epidemiologic Studies; BP= Blood pressure

Table 2.

Mortality during 23 years of follow-up by difficulty in one or more upper extremity function, in a propensity score-matched cohort of 2156 older adults, balanced on 62 baseline characteristics

	Events (%)		Hazard ratio (95% CI)
	Difficulty in one or more upper extremity function		
	No (n=1126)	Yes (n=1126)	
All-cause mortality *	914 (81.2%)	942 (83.7%)	1.11 (1.01–1.22)
Cardiovascular mortality **	361 (32.1%)	347 (30.8%)	1.03 (0.89-1.19)
Non-cardiovascular mortality ***	553 (49.1%)	595 (52.8%)	1.17 (1.04–1.31)

Hazard ratios are estimated for the group with difficulty in one or more upper extremity function, using those without as reference

* In 1088 of the 1126 matched pairs, we were able to determine which patient of the pair clearly survived longer, and in 52.9% (576/1,088) of those pairs, these patients belonged to the group with no difficulty in upper extremity function, which was of borderline significance (sign-score test P=0.0523).

** In 419 of the 1126 matched pairs, we were able to determine which patient of the pair clearly survived longer before death due to cardiovascular causes, and in 50.1% (210/419) of those pairs, these patients belonged to the group with no difficulty in upper extremity function, which was not statistically significant (sign-score test P=0.9610).

*** In 669 of the 1126 matched pairs, we were able to determine which patient of the pair clearly survived longer before death due to non-cardiovascular causes, and in 54.7% (366/669) of those pairs, these patients belonged to the group with no difficulty in upper extremity function, a difference that was statistically significant (sign-score test P=0.0149). However, a hidden confounder that is a near-perfect predictor of non-CV mortality and was not strongly correlated with any of the 62 balanced baseline characteristics in our matched cohort could explain away this association if it could increase the odds of having upper extremity difficulty by 3.61%.