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Mortality Risk among Older People Who Did vs. Did Not Sustain a Fracture: Baseline Pre-Fracture Strength and Gait Speed as Predictors in a 15-Year Follow-Up

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ABSTRACT

Background

Physiological reserve, as indicated by muscle strength and gait speed, may be especially determinant of survival in people who are exposed to a health stressor. We studied whether the association between strength/speed and mortality risk would be stronger in the time period after a fracture compared to other time periods.

Methods

Participants were population-based sample of 157 men and 325 women aged 75 and 80 years at baseline. Maximal 10-meter gait speed and maximal isometric grip and knee extension strength were tested at the baseline before the fracture. Subsequent fracture incidence and mortality were followed up for 15 years. Cox regression analysis was used to estimate fracture time-stratified effects of gait speed and muscle strength on mortality risk in three states: 1) non-fracture state, 2) the first post-fracture year and 3) after the first post-fracture year until death/end of follow-up.

Results

During the follow-up, 20% of the men and 44% of the women sustained a fracture. In both sexes, lower gait speed and in women lower knee extension strength was associated with increased mortality risk in the non-fracture state. During the first post-fracture year, the mortality risk associated with slower gait and lower strength was increased and higher than in the non-fracture state. After the first post-fracture year, mortality risk associated with lower gait speed and muscle strength attenuated.

Conclusions

Lower gait speed and muscle strength were more strongly associated with mortality risk after fracture than during non-fracture time, which may indicate decreased likelihood of recovery.

Keywords: Physical Function, Epidemiology, Health stressors, Adverse events, Fracture

Introduction

Bone fractures are common health stressors in older age, which, in turn, can lead to loss of function, institutionalization and premature death[1-3]. However, individuals differ considerably in their capability to recover from bone fractures. Understanding the factors that cause differences in post-fracture recovery can help both in identifying individuals at higher risk for health decline when experiencing adverse events and in implementing preventive interventions.

In old age, the increased mortality associated with fractures is a result of several factors. The direct association of a fracture with the events causally related to it, such as complications and infections, explain part of the short-term excess mortality[3,4]. Other factors, such as pain, fear of falling and delay in tissue healing, which are commonly accompanied by inactivity, may further complicate the recovery process. The occurrence of a fracture often triggers progressive functional loss leading to disability[5,6], which may elevate long-term mortality risk. Poor health and reduced physiological reserve may play an important role in explaining the increased risk of post-fracture mortality[7]. However, other studies have reported an increased relative mortality risk after hip fracture even among patients without comorbidities[3,8].

An important factor in assessing the role of pre-fracture health in post-fracture mortality is the severity of the chronic conditions. Measurements of functional status or physiological reserve reflect the burden of diseases and progressive physiological changes in the aging process[9]. The hierarchical model of the metrics of aging, recently introduced by Ferrucci and colleagues, posit that aging occurs in three interrelated domains: biological, phenotypical and functional[10]. According to their hypothesis, functional aging occurs when the reserve mechanisms of biological and phenotypical aging have been enervated.

Measures of muscle strength and gait speed are widely used indicators of functional status and physiological reserve, especially among older people[11]. It is known that lower gait speed and muscle strength are associated with higher risk for bone fractures and higher mortality risk[12-16]. However, little is known about how prospectively assessed pre-fracture functional status predicts the recovery and consequences of fracture. In most studies, functional status has been assessed retrospectively after fracture and thus may be confounded by situational factors. To our knowledge, only a few studies have investigated the association between objectively measured pre-fracture muscle strength and subsequent survival. According to two earlier studies, participants with higher knee extension strength before a bone fracture had lower post-fracture mortality risk than those with lower muscle strength[17,18]. However, in those studies, the study population was composed solely of individuals who had sustained a fracture, and hence we do not know whether the predictive power of higher muscle strength on survival is different after fracture compared to time without fracture. Therefore, it is not clear whether the increased post-fracture mortality risk in those with lower muscle strength is a result of low physiological reserve itself (similar situation without fracture) or if it is because of an interaction between low physiological reserve and fracture, thus indicating that physiological reserve has a more pronounced role in terms of survival. Furthermore, pre-fracture gait speed as a predictor of subsequent mortality has not been addressed in earlier studies.

In this study, the aim was to investigate whether the associations of gait speed and muscle strength with mortality risk were higher after fracture compared to time without a fracture. Pronounced associations after fracture would suggest that lower muscle strength and gait speed measured prior to fracture are important predictors of post-fracture health decline and mortality.

Methods

Study Design

The Evergreen Study was conducted in 1989-1990[19]. All the community-living 75- and 80-year-old residents (N=679) of Jyväskylä formed the target group. In total, 617 persons took part in interviews and laboratory examinations on functioning. Of these, 482 took part in maximal isometric strength and maximal gait speed tests and formed the study group for the present analyses.

Of the interviewed participants, 22% did not take part in laboratory examinations. The participants in our study group had better mobility and were more physically active compared to dropouts. 66% of the participants and 83% of the dropouts did not achieve the recommended level of physical activity[20]. Participants had less difficulty in independent walking outdoors than dropouts (6% vs. 38%).

Ascertainment of fractures and death

The participants were followed up from the beginning of 1990 until the end of April 2005 for fractures and mortality. The information on bone fractures was acquired from patient records from the Health Centers in the area and the Central Hospital of Central Finland. Records include ICD-10 diagnosis code, date and scene of fractures. Death dates were obtained from the population register of Finland.

All fracture types, except fractures of toes and fingers, were included in the analysis. Fracture location was categorized into proximal (hip, pelvis and lumbar spine) and distal (thoracic and cervical spine, upper extremity, lower leg and foot, head and collar bone). We constructed the fracture event variable as follows. For those who sustained at least one proximal fracture, we chose the date of the first proximal fracture. For those who only sustained distal fractures, we chose the date of the first distal fracture. We opted for this approach, as earlier studies did not provide any evidence-based examples on the optimal way to categorize different fractures. Some studies have also reported associations of non-hip and non-vertebral fractures with increased mortality risk[21,22] and clinically important functional decline[5,5,6], while others have reported no increase in mortality following non-hip and non-vertebral fractures[23].

Assessment of muscle strength and gait speed

Ten-meter maximal gait speed, maximal isometric hand grip strength and maximal isometric knee extension strength were assessed at the research center at baseline prior to potential fracture events. Maximal gait speed was measured in the laboratory corridor using a hand-held stopwatch. Two to three meters were allowed for acceleration and deceleration[24]. Maximal isometric hand grip strength and maximal isometric knee extension strength were measured using an adjustable dynamometer chair (Faculty of Sport and Health Sciences, University of Jyväskylä, Jyväskylä, Finland)[25]. The measurements were performed on the side of the dominant hand in a sitting position with lower back supported. Hand grip strength was measured using a dynamometer fixed to the arm of the chair. Maximal isometric knee extension strength was measured at an angle of 60 degrees from the fully extended leg towards flexion. The results were expressed in Newtons (N), and the best result of three trials was used in the analyses. The reproducibility of the maximal isometric strength tests has been studied with repeated measures two weeks apart in a subsample of 12 subjects aged 80 years. The Pearson correlation coefficients were excellent (hand grip strength r= .967 and knee extension strength r= .965)[25].

Covariates

Potential confounders were selected because of their possible association with gait speed and muscle strength or mortality risk. Data on age, body size (weight and height), smoking status (ever vs. never), years of education, physical activity (low vs. high) and chronic conditions were collected at baseline prior to potential fractures. Physical activity was considered low when the self-reported amount of weekly physical activity did not meet the level of national guidelines[20]. Number of chronic conditions was calculated based on responses to a questionnaire and subsequent clinical examination by a physician.

Statistical analysis

The baseline characteristics of the participants were compared using one-way ANOVA between non-fractured participants and two groups of fracture participants, one comprising those who survived and the other comprising those who died during the first year after fracture.

Mortality risks were analyzed with extended Cox's hazard regression. A time-fixed exposure variable of having a fracture does not account for the fact that subjects may enter the study with an initial fracture-free period. Such a covariate does not usually meet the proportional hazard assumption as the risk for death is highest immediately after the fracture and decreases during the following years[26,27,27] and does not account for the "immortal bias" related to the time spent fracture-free[28]. We used an extension of the illness-death model[29] accommodating time-dependent predictors related to the post-fracture recovery process. In this model, fracture states were modeled as a time-dependent variable in a relative risk model based on a counting process formulation. The possible states for study participants are shown in Figure 1. All participants contributed to the non-fracture state until a fracture occurred or until death or end of follow-up if they did not sustain a fracture. For participants who sustained a fracture, separate risks were estimated for the first post-fracture year and after the first post-fracture year until death or end of follow-up if they survived the first post-fracture year.

Interaction terms were used to investigate the associations between fracture state, gait speed and muscle strength on mortality risk. The gait speed and muscle strength variables were centered prior to entry in the model. All models were conducted separately for men and women. The models were adjusted with baseline age, number of chronic conditions and physical activity due to their association with the predictors (gait speed and muscle strength) and the outcome (mortality risk). The results are shown as aggregate risk ratio's (linear combinations) for gait speed and muscle strength in the fracture states. Descriptive statistics were computed in SPSS Statistics 24 for Windows and Cox regression models were constructed using the package 'survival' version 2.44-1.1 in the R environment (version 3.5.1).

Results

During the follow-up, 176 of 482 participants (36% in total, 20% of men and 44% of women) sustained at least one fracture. The accumulation of fractures and deaths during the follow-up is shown under Supplementary Figure 1. The majority (92%) of the fractures occurred owing to a fall and the remainder for other reasons. The average time from the baseline measures to fracture was 5.7 years (SD 3.9) in men and 7.0 years (SD 4.1) in women. Mean age at time of fracture was 83 years (SD 4.5) for men and 84 years (SD 4.7) for women. During the follow-up, 134 men and 252 women died during their respective 1 359 and 3 167 person-years of surveillance. The crude mortality rate was 9.8 deaths per 100 person-years in men and 7.9 deaths per 100 person-years in women. During the first year after fracture, 10 (31%) of the men and 33 (23%) of the women who had sustained a fracture died.

The baseline characteristics of the participants and comparisons between the non-fracture group and two fracture groups are presented in Table 1. In men, those who died during the first year after fracture had lower pre-fracture knee extension strength and were heavier than the first-year post-fracture survivors and non-fractured participants. In women, those who died during the first year after fracture had lower pre-fracture hand grip strength compared to the first-year post-fracture survivors and non-fractured participants, and lower pre-fracture gait speed than the first-year post-fracture survivors. In addition, older women had a higher probability to die during the first year after fracture. The groups showed no differences in physical activity level or smoking status.

The unadjusted Cox regression models revealed associations of higher mortality risk with lower maximal gait speed, lower maximal isometric hand grip and knee extension strength, older age and a higher number of chronic conditions, and in men, a low level of physical activity (Table 2). Therefore, age, physical activity and number of chronic conditions were selected as covariates for the further analyses.

Post-fracture mortality risk

The risk of death during the first post-fracture year compared to non-fracture state was almost four-fold in both men and women (Table 3). After the first post-fracture year, increased mortality risk continued to be observed, although attenuated after the first year.

Table 4 shows the associations of maximal gait speed, maximal isometric muscle strength and fracture state on mortality risk during the non-fracture state and the fracture states. The first fracture state comprised the first post-fracture year and the second the follow-up time after the first post-fracture year until death or end of follow-up. In both sexes, lower gait speed was statistically significantly associated with increased mortality risk in the non-fracture state (RR 1.09, 95% CI 1.04-1.14 in men and RR 1.10, 95% CI 1.05-1.16 in women per 0.1 m/s decrease). The association between lower gait speed and mortality risk was higher during the first post-fracture year compared to the non-fracture state (RR 3.61, 95% CI 1.75-7.46 in men and RR 4.21, 95% CI 2.82-6.28 in women). After the first post-fracture year, the association between gait speed and mortality risk attenuated approximately to the level of non-fracture state (RR 1.75, 95% CI 1.03-2.99 in men and RR 1.76, 95% CI 1.26-2.46 in women).

The associations of lower grip strength and knee extension strength with mortality risk were also higher after fracture than in the non-fracture state (Table 4). In the non-fracture state, lower muscle strength was associated statistically significantly with mortality risk only in women for knee extension strength (RR 1.03, 95% CI 1.01-1.06). During the first post-fracture year, mortality risk was three- to four-fold per 100N decrease in muscle strength in both sexes (grip strength in men RR 3.51, 95% CI 1.72-7.14 and in women RR 3.62, 95% CI 2.39-5.49; knee extension strength in men RR 2.85, 95% CI 1.28-6.31 and in women RR 3.80, 95% CI 2.54-5.67). After the first post-fracture year, the mortality risk was still elevated compared to non-fracture time but it attenuated to being almost two-fold (grip strength in men RR 1.76, 95% CI 1.28-6.31 and in women RR 3.80, 95% CI 2.54-5.67; knee extension strength in men RR 1.75, 95% CI 1.06-2.91 and in women RR 1.74, 95% CI 1.27-2.38).

Sensitivity analysis using weight as an additional time-dependent covariate indicated that among women, weight was not associated with fracture and mortality risk and hence it did not change the results materially. Among men, post fracture estimates for gait speed and strength were attenuated slightly, but the only risk ratio affected was the state after the first post-fracture year, which was no longer statistically significant.

Finally, we repeated the analyses separately for subjects with distal and proximal fractures to ensure that the results were not driven by the higher mortality risk after proximal fractures. This did not materially change the results, but the separate analyses by fracture location lacked sufficient statistical power (data not shown).

Discussion

In the current study, participants with lower pre-fracture gait speed and muscle strength had pronounced mortality risk during the first post-fracture year compared to time without fracture exposure. The current results extend earlier findings on the role of pre-fracture muscle strength in post-fracture survival[17,18,18] by including non-fracture time (no fracture during the follow-up and time before fracture occurrence of the participants sustaining a fracture) in the analyses. To our knowledge, this was the first study to assess the association between pre-fracture gait speed and post-fracture mortality risk.

The association of gait speed and muscle strength with mortality risk has been reported several times[30-32]. However, it is unclear, what underlies these associations[31]. In this study, comparing the different event states with and without fracture exposure revealed that lower gait speed and muscle strength were associated more strongly with increased mortality risk in the first post-fracture year compared to non-fracture state. However, after the first post-fracture year, for gait speed the mortality risk attenuated to approximately the non-fracture state level whereas for muscle strength although the mortality risk attenuated it remained elevated compared to non-fracture time (as indicated by non-overlapping confidence intervals). Comparison of the mortality risks associated with gait speed and muscle strength at different fracture event states suggest that people with low physiological reserve measured with pre-fracture gait speed and muscle strength may be especially vulnerable to health decline during the first year after fracture. The risk may not be that high at other times although even in the absence of catastrophic events, gradual progressive physiological changes will increase vulnerability to health decline in older age.

Measuring maximal functional capacity can reveal the underlying state of biological and phenotypical aging-related changes and the system's capacity for resilient responses. In older age, maximal gait speed and muscle strength may reflect physical resilience, possibly due to their associations with underlying individual biological aging processes[10,33]. Age-related biological changes reduce the capacity to produce resilient responses after stressors, which complicates recovery, accelerates functional decline and increases mortality risk. Blood-based biomarkers of aging, such as higher serum levels of inflammatory markers are associated with both age-related decline in physical function and mortality risk[34-36], and thus may be an important pathway between the functional status and physical resilience of the organism. Functional measures have also been linked with age-related changes at the molecular and DNA level[37,38], although the longitudinal evidence remains limited. In addition, earlier studies have demonstrated that age-related neurological changes are associated with alterations in physical function[39]. Both grip strength and gait speed measurements require regulation of the central nervous system (CNS) and thus may reflect variations in the function of the CNS, which plays an important role in the aging processes.

Mortality provides indirect information of failure of recovery and therefore in itself may not provide a complete picture of physical resilience. However, mortality is a powerful indicator of the burden of diseases and health decline and can lead to insight into resilient or non-resilient responses of the system after experiencing chronic or acute health stressors. Linking epidemiological data with clinical information on bone fractures and survival allowed us to take both the situation without fracture exposure and the time-varying character of mortality risk after fracture into account. This in turn enabled us to investigate whether the associations of lower gait speed and muscle strength with mortality risk were more pronounced after fracture exposure, and therefore predict responses of the organism after experience of a health stressor.

Our results are in line with those of earlier studies showing that catastrophic events such as fractures in older age are followed by higher mortality incidences that gradually attenuate over the ensuing years[4,26]. This attenuation may be explained by variation in individual mortality risk after a health stressor. In other words, people who are more vulnerable die more likely during the first year whereas the survivors with lower susceptibility may recover from the fracture. According to this study, measures of pre-fracture gait speed and muscle strength before a fracture seem to be important aspects predicting this susceptibility to mortality after a fracture. However, especially in older populations, the attenuation of post-fracture mortality risk over time may be a result of the occurrence of other mortality risk factors among non-fractured individuals. Unfortunately, data were not available on other catastrophic events, such as strokes, cardiac infarctions or recurrent fractures.

This study has some limitations. The time to fracture varied and it was not possible to capture changes in muscle strength and gait speed after the baseline measures. For people who sustained a fracture early on during the follow-up, their pre-fracture strength and gait speed reflect more accurately their condition at the time of fracture. In addition, the rate of change is known to be associated with mortality risk[40,41]. However, strength decline without external stressors seem to be rather stable in old age. A previous study found that those with stronger grip strength in midlife were also at the top of the distribution in old age even though strength had declined[42]. Consequently, we believe that it was justified to study the baseline physical performance as a predictor of mortality, even though time-varying measurements of predictors were not available for adjustment. Another limitation is the small sample size that resulted in low analytical power especially for men. The small number of specific types of fracture did not allow examination of the associations by fracture type. When interpreting the results we need to take into account that treatment and rehabilitation protocols used today differ from those at the time of the study. In addition, more recent age cohorts may have better functional status than earlier cohorts[43], and therefore their mortality risk following a fracture may be lower.

The strengths of our study are the long follow-up time and the availability of laboratory-based measures of functional status performed before a bone fracture, meaning that the tests were not confounded by situational factors caused by injury or treatment. In Finland, data on deaths are recorded in a national register and the data quality of patient records is good. A novel feature of this study is that the association of pre-fracture gait speed and muscle strength on mortality rirk was examined with time-varying coefficients, which allowed taking into account the immortal time bias[28] and comparing the mortality risks of lower gait speed and muscle strength between the non-fracture and fracture states. The occurrence of fractures cannot be anticipated and thus in clinical practice objective measures of physical functioning cannot be performed immediately before injury. Consequently, the possibility to link epidemiological data with fracture dates and mortality records provided a unique opportunity to conduct analyses of the kind reported here.

In conclusion, higher pre-fracture gait speed and muscle strength may indicate higher resources for recovery and survival after acute health events, such as bone fractures. Further investigation on the biological and psychosocial processes that help people resist health decline and assist in recovery is needed.

Conflict of Interest

T.R. serves on the Journal of Gerontology: Medical Sciences editorial board. Otherwise, the authors declare no conflicts of interest.

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Author contribution

K. Koivunen: Conception and design of the study, drafting the manuscript, data analysis and interpretation. E. Sillanpää: Contribution to the design of the study, critical revision for important intellectual content. M. von Bonsdorff: critical revision for important intellectual content. R. Sakari: Data collection, critical revision for important intellectual content. T. Törmäkangas: data analysis and interpretation, critical revision for important intellectual content. T. Rantanen: Conception and design of the study, acquiring the funding for conducting the research, and critical revision for important intellectual content.

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Table 1. Baseline Characteristics of the Participants Stratified into Those Who Did Not Sustain a Fracture, Those Who Had a Fracture and Either Survived the First Post-fracture Year or Died during the First Post-fracture Year.

	Men				**Women**			
	No fracture n=125	**Fractured**			**No fracture** n=181	**Fractured**		
		Survived first year n=22	**Died during first year** n=10			**Survived first year** n=111	**Died during first year** n=33	
	Mean (SD)	Mean (SD)	Mean (SD)	P^b	Mean (SD)	Mean (SD)	Mean (SD)	P^b
Gait Speed, m/s	1.7 (0.5)	1.6 (0.5)	1.4 (0.4)	0.125	1.4 (0.4)	1.5 (0.3)	1.2 (0.3)	**<0.001**
Knee extension strength, N	356.3 (104.1)	320.5 (67.4)	267.4 (118.1)	**0.014**	217.6 (81.7)	226.4 (68.0)	189.6 (69.6)	0.053
Grip Strength, N	351.8 (100.9)	329.0 (57.1)	295.2 (169.4)	0.177^c	204.0 (68.3)	210.8 (58.2)	167.4 (68.1)	**0.004**
Body Height, cm	169.2 (6.2)	168.5 (6.3)	173.1 (5.7)	0.128	155.2 (5.6)	156.5 (5.4)	155.2 (5.0)	0.125
Body Weight, kg	74.2 (11.0)	71.2 (9.3)	84.1 (17.5)	**0.011**^{c}	66.6 (11.6)	65.6 (10.1)	65.4 (11.3)	0.670
Body Mass Index, kg/m2	25.9 (3.5)	25.1 (3.1)	28.2 (6.2)	0.092^c	27.7 (4.7)	26.8 (3.9)	27.1 (4.2)	0.228
Education, years	6.3 (4.0)	5.8 (3.0)	6.0 (2.8)	0.869	5.9 (3.2)	6.0 (3.5)	5.8 (2.0)	0.900
Chronic conditions, number	1.7 (1.3)	1.4 (1.0)	1.7 (0.7)	0.535^c	2.1 (1.5)	1.8 (1.4)	2.0 (1.4)	0.228
Time to fracture, years^a	--	5.6 (4.3)	5.9 (2.9)	0.803^d	--	6.8 (4.3)	7.7 (3.9)	0.270^d

Note. [a] = time after baseline measures to fracture, [b] = One-way analysis of variance, [c] = Welch test for variables with unequal variances between groups, [d] =t-test. Bold typeface indicates statistically significant at the significance level of 0.05.

Table 2. Univariate Cox Regression Analysis of Risk Factors for Mortality Risk Stratified by Sex.

Variable	**Men** n=157 HR (95% CI)	**Women** n=325 HR (95% CI)
Age at baseline (80 vs.75 years)	**1.58 (1.11-2.24)**	**1.96 (1.52-2.52)**
Physical Activity (low vs. high)	**2.00 (1.39-2.89)**	1.19 (0.91-1.55)
Smoker ever (yes vs. no)	1.41 (0.95-2.07)	1.24 (0.85-1.82)
Maximal gait speed (per -1m/s)	**3.16 (2.17-4.60)**	**3.48 (2.45-4.95)**
Grip strength (per -100N)	**1.37 (1.14-1.63)**	**1.62 (1.36-1.93)**
Knee extension strength (per -100N)	**1.31 (1.11-1.55)**	**1.44 (1.23-1.68)**
Number of chronic conditions	**1.34 (1.16-1.56)**	**1.23 (1.13-1.35)**
Height (per 1cm)	0.99 (0.97-1.02)	0.98 (0.95-1.00)
Weight (per 1kg)	1.00 (0.98-1.01)	0.99 (0.97-1.00)
BMI (per 1kg/m^2)	0.99 (0.94-1.04)	0.98 (0.95-1.01)
Length of education (per 1 year)	0.99 (0.94-1.04)	0.96 (0.93-1.00)

Note. HR= Hazard Ratio; CI= Confidence interval; Bold typeface indicates statistically significant hazard ratios at the significance level of 0.05.

Table 3. Relative Risks (RR) of Death After a Fracture during Fracture State Compared to Non-Fracture State Stratified by Sex.

	Men **n=157** RR (95% CI)	**Women** **n=325** RR (95% CI)
Non-fracture state	1.00	1.00
Fracture state the first post-fracture year	**3.86 (1.98-7.51)**	**3.92 (2.66-5.77)**
Fracture state after the first post-fracture year	**1.77 (1.07-2.92)**	**1.79 (1.31-2.44)**

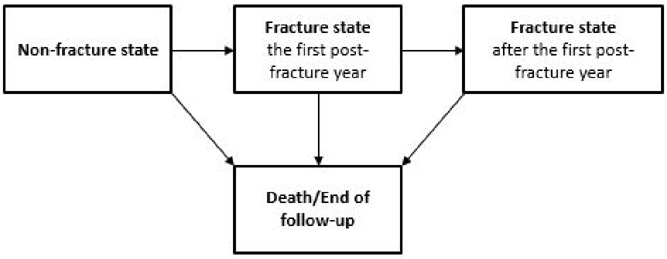
Note. CI= Confidence interval; RR= relative risks. Reference group: Non-fracture state (no fracture during the follow-up and time before fracture occurrence of the participants sustaining a fracture). Adjusted for age, number of chronic conditions and physical activity.

Table 4. The Associations of Gait Speed and Muscle Strength on Mortality Risk during Non-fracture State and Fracture State (the First Post-Fracture Year and after the First Post-Fracture Year).

	Men (n=157)	**Women (n=325)**
	RR (95% CI)	RR (95% CI)
Fracture and gait speed, per decrease of 0.1m/s		
Gait speed $_{\text{non-fracture state}}$	**1.09 (1.04-1.14)**	**1.10 (1.05-1.16)**
Gait speed $_{\text{the first post-fracture year}}$	**3.61 (1.75-7.46)**	**4.21 (2.82-6.28)**
Gait speed $_{\text{after the first post-fracture year}}$	**1.75 (1.03-2.99)**	**1.76 (1.26-2.46)**
Fracture and grip strength, per decrease of 100N		
Grip strength $_{\text{non-fracture state}}$	1.02 (1.00-1.04)	1.03 (1.00-1.06)
Grip strength $_{\text{the first post-fracture year}}$	**3.51 (1.72-7.14)**	**3.62 (2.39-5.49)**
Grip strength $_{\text{after the first post-fracture year}}$	**1.76 (1.07-2.91)**	**1.75 (1.28-2.40)**
Fracture and knee extension strength, per decrease of 100N		
Knee extension strength $_{\text{non-fracture state}}$	1.01 (0.99-1.03)	**1.03 (1.01-1.06)**
Knee extension strength $_{\text{the first post-fracture year}}$	**2.85 (1.28-6.31)**	**3.80 (2.54-5.67)**
Knee extension strength $_{\text{after the first post-fracture year}}$	**1.75 (1.06-2.91)**	**1.74 (1.27-2.38)**

Note. RR= Relative risk; CI= Confidence Interval; non-fracture state = no fracture during the follow-up and time before fracture occurrence of the participants sustaining a fracture. All models were adjusted for number of chronic conditions, age and physical activity.

Figure 1


Non-fracture state
Fracture state the first post-fracture year
Fracture state after the first post-fracture year
Death/End of follow-up