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Original Study

Longitudinal Changes in Muscle Mass, Muscle Strength, and Physical Performance in Acutely Hospitalized Older Adults



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A B S T R A C T

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Objectives: Acute hospitalization may lead to a decrease in muscle measures, but limited studies are reporting on the changes after discharge. The aim of this study was to determine longitudinal changes in muscle mass, muscle strength, and physical performance in acutely hospitalized older adults from admission up to 3 months post-discharge.

Design: A prospective observational cohort study was conducted.

Setting and Participants: This study included 401 participants aged ≥ 70 years who were acutely hospitalized in 6 hospitals. All variables were assessed at hospital admission, discharge, and 1 and 3 months post-discharge.

Methods: Muscle mass in kilograms was assessed by multifrequency Bio-electrical Impedance Analysis (MF-BIA) (Bodystat; QuadsScan 4000) and muscle strength by handgrip strength (JAMAR). Chair stand and gait speed test were assessed as part of the Short Physical Performance Battery (SPPB). Norm values were based on the consensus statement of the European Working Group on Sarcopenia in Older People.

Results: A total of 343 acute hospitalized older adults were included in the analyses with a mean (SD) age of 79.3 (6.6) years, 49.3% were women. From admission up to 3 months post-discharge, muscle mass (-0.1 kg/m^2 ; $P = .03$) decreased significantly and muscle strength (-0.5 kg ; $P = .08$) decreased nonsignificantly. The chair stand ($+0.7$ points; $P < .001$) and gait speed test ($+0.9$ points; $P < .001$) improved significantly up to 3 months post-discharge. At 3 months post-discharge, 80%, 18%, and 43% of the older adults scored below the cutoff points for muscle mass, muscle strength, and physical performance, respectively.

Conclusions and Implications: Physical performance improved during and after acute hospitalization, although muscle mass decreased, and muscle strength did not change. At 3 months post-discharge,

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muscle mass, muscle strength, and physical performance did not reach normative levels on a population level. Further research is needed to examine the role of exercise interventions for improving muscle measures and physical performance after hospitalization.

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Low muscle mass, muscle strength, and physical performance are diagnostic measures of sarcopenia.^{1,2} The prevalence of sarcopenia in hospitalized older adults is up to 40% depending on the diagnostic criteria.³ Sarcopenia is associated with poor health outcomes such as loss of activities in daily living (ADLs),⁴ falls, fractures,⁵ and mortality.¹ Approximately one-third of acutely hospitalized older adults experience a loss of ADLs during their hospital stay,^{6,7} despite the successful treatment of the primary medical illness.⁸ Physical inactivity and bed rest may lead to a loss of muscle mass and muscle strength.⁹ Bed rest studies in healthy older adults reported more than 10% loss of muscle mass and up to 13% of knee extensor muscle strength over 7 to 10 days of inactivity.^{9,10} Medical illness with acute hospitalization as a result, might affect muscle mass and muscle strength even more in older adults; this could be a facilitator of functional decline and loss of physical performance.^{8,11,12}

Detailed information is lacking on longitudinal changes in muscle mass, muscle strength, and physical performance from admission to post-discharge. A systematic review concluded that muscle mass and muscle strength did not change in acute hospitalized older adults during hospitalization.¹³ Few studies reported on the changes in muscle mass, muscle strength, and physical performance in older adults after acute hospitalization. Studies on the changes in muscle mass and muscle strength post-discharge were inconclusive; muscle strength was unchanged¹⁴ or improved at 1 month post-discharge.¹⁵ Physical performance improved at 1 month post-discharge, but remained below reference levels for independent living.^{14,15} It has been shown that it is important to regain functionality within 3 months after hospitalization to prevent permanent functional decline.¹⁶ Insight in the changes in muscle mass, muscle strength, and physical performance may help to understand the underlying mechanisms of how older adults lose functionality after acute hospitalization. Recent publications from our Hospital Associated Disability and impact on daily Life (Hospital-ADL) study showed that psychosocial factors, such as depressive symptoms, fatigue, and fear of falling are highly prevalent and persistent after hospitalization and are associated with functional decline.^{17,18} Information on the changes in muscle mass, muscle strength, and physical performance from admission to post-discharge and which factors could confound these changes, may provide specific starting points for tailored interventions to counteract sarcopenia and to prevent functional decline after acute hospitalization.

This study aimed to determine the longitudinal changes in muscle mass, handgrip strength, and physical performance from hospital admission up to 3 months post-discharge, adjusted for depressive symptoms, cognition, fatigue, fear of falling, risk of malnutrition, and comorbidity, in acutely hospitalized older adults.

Methods

Study Design and Setting

This multicenter observational prospective cohort study was conducted by a multidisciplinary team.¹⁹ Participants were recruited among those admitted to the internal medicine, cardiology, or geriatric wards at 6 participating hospitals between October 1, 2015, and June 1, 2017. The study was approved by the institutional review board

and performed according to the Medical Research Involving Human Subjects Act and the ethical standards laid down in the Declaration of Helsinki (1964) and its later amendments.

Study Population

Older adults aged ≥ 70 years who were acutely admitted for at least 48 hours to the hospitals were approached for participation. In addition, further inclusion criteria were applied: (1) approval of the treating medical doctor; (2) Mini-Mental State Examination (MMSE) score ≥ 15 points; (3) sufficient Dutch language proficiency to complete questionnaires. Older adults were excluded if (1) they had a life expectancy of fewer than 3 months, as assessed by the treating medical doctor; or (2) were disabled in all 6 basic ADLs as determined with the Katz-6 ADL index.

Data Collection

A geriatric team, consisting of a psychologist and physical therapist, visited the participating wards and contacted all eligible older adults within 48 hours after hospital admission. Participants were enrolled in the study after written informed consent was obtained. The psychologist completed the questionnaires and the physical therapist carried out performance tests at baseline (within 48 hours after admission) and on discharge. Highly trained students visited the participant's home or residence to perform the assessments at 1 and 3 months post-discharge. All assessors were trained to administer the study protocol in a standardized way to prevent variability. All measurements were taken at the same time points.

Muscle Mass

Muscle mass was assessed with multifrequency Bio-electrical Impedance Analysis (MF-BIA; Bodystat; Quadscan 4000). The participant had to lie in a supine position with legs and arms not touching the body with 2 surface electrodes placed on the right foot and hand, with a distance of 5 cm between both electrodes. This test was not conducted in case of a pacemaker or Implantable Cardioverter Defibrillator because the risk of dysregulation of the device. The MF-BIA Quadscan 4000 was reported reliable and interchangeable at the population level with the dual-energy X-ray absorptiometry methods.²⁰ Skeletal muscle mass in kilograms was calculated with the formula as used by Janssen et al.²¹ and divided by the squared height (m^2) to calculate the skeletal muscle mass index (SMI). The cutoff points for the SMI for low muscle mass were ≤ 10.70 kg/ m^2 for men and ≤ 6.75 kg/ m^2 for women as a diagnostic measure for sarcopenia.^{2,22}

Muscle Strength

Handgrip strength was used as a measure of general upper body strength^{2,23} and assessed using a JAMAR handgrip strength dynamometer (Lafayette Instrument Company, Lafayette, IN), expressed in kilograms. Participants were assessed, encouraged, and performed the task 3 times alternating bilaterally.²³ The highest score of either hand was used for the analysis. Handgrip strength showed good to excellent

reliability and validity among hospitalized older adults.²⁴ The cutoff points for low handgrip strength are <16 kg for women and <27 kg for men.¹

Physical Performance

Physical performance was assessed by the Short Physical Performance Battery (SPPB) was used.²⁵ The SPPB is a reliable and valid measurement tool and consists of the balance test, gait speed test, and chair stand test. Balance was assessed by side-side, semi-tandem, and tandem stands. Participants received a score of 0 points if they were unable to complete the task and 4 points when all tests were held for 10 seconds.²⁵ Gait speed was assessed with the 4-m walking test at usual walking speed.^{1,25} Participants received a score of 0 points if they were unable to complete the task, 1 point when the time over 4 m was more than 8.70 seconds, 2 points between 6.2 and 8.7 seconds, 3 points between 4.8 and 6.2 seconds, and 4 points under 4.8 seconds.²⁵ A cutoff value of lower than 1.2 m per second (1, 2, or 3 points) is considered as low.^{26,27} For the chair stand test,^{1,25} participants were asked to rise 5 times as fast as possible with the arms crossed on the chest. Participants received a score of 0 if they were unable to complete the task, 1 point when the time for 5 rises was between 16.7 and 60.0 seconds, 2 points when the time was between 13.7 and 16.7 seconds, 3 points when the time was between 11.2 and 13.7 seconds, and 4 points when the time was less than 11.2 seconds. A cutoff value of higher than 13.7 seconds (0, 1, or 2 points) was considered as low physical performance.²⁷ For chair stand and gait speed test sub-scores were analyzed. For the complete SPPB test, a cutoff score of ≤ 8 points was considered as low physical performance.^{1,25–28}

Other Variables

Potential confounding variables on the longitudinal changes in muscle mass, handgrip strength, chair stand, and gait speed were assessed at admission, discharge, and 1 and 3 months post-discharge. Depressive symptoms were assessed with the geriatric depression scale-15 item (GDS-15),²⁹ cognitive impairment with the MMSE,³⁰ fatigue and fear of falling on a numeric rating scale, and the Short Nutritional Assessment Questionnaire (SNAQ) was used to identify the risk of malnutrition.³¹ The Charlson Comorbidity Index (CCI) was used to assess the number and severity of comorbidities at baseline.³² Additional data were collected at baseline for age, sex, marital status, living arrangement, length of stay (LOS) in hospital, and body mass index (BMI). Sarcopenia was defined as reported by the revised consensus statement of the European Working Group on Sarcopenia in Older People (EWGSOP2) using the cutoff points as outlined previously.² Functional decline was defined as experienced loss of 1 point on the Katz-6 ADL index (bathing, dressing, toileting, transferring, continence, and feeding) between 2 weeks before hospitalization and 3 months post-discharge.³³

Statistical Analysis

Baseline characteristics were presented with mean and SD or median and interquartile range using descriptive statistics and stratified by sex. Linear mixed models (LMM)³⁴ were performed to analyze the longitudinal changes in muscle mass, handgrip strength, chair stand, and gait speed. First, interaction effects of time, sex, and age were analyzed to decide if stratification was needed for these variables was needed. Second, for every potential confounder, such as age, sex, LOS, BMI, cognition, comorbidity, depressive symptoms, fatigue, nutrition, and fear of falling, it was determined if the beta of muscle mass, handgrip strength, chair stand, and gait speed changed >10%.³⁵ Third, confounding factors were then included in the adjusted model. Variables had to be present minimally at one time point to be included

in the final analysis. To analyze the effect of missing data, a sensitivity analysis was performed with data at all time points. To compare the variables, standardization was performed using Z-scores and tested on differences over time by multivariate analysis, with a baseline score of zero for all variables. All parameter estimates were expressed with 95% confidence interval and were considered statistically significant if $P < .05$. A trend was defined as P value $\geq .05$ and $< .10$. Analyses were conducted with the Statistical Package for the Social Sciences for Mac (version 24; SPSS Inc., Chicago, IL).

Results

Participant Characteristics

Of the 1024 acute hospitalized older adults admitted for ≥ 48 hours between October 2015 and February 2017, 519 (50.7%) did meet the inclusion criteria (Figure 1) and of these 118 (22.7%) were not interested in participating. Of the 401 older adults who agreed to participate, 40 participants (10%) were deceased and 87 participants (21.7%) were lost to follow-up at 3 months post-discharge. In the analysis, 58 participants were excluded because no data were available at any time-point due to no permission or not able to perform the tests at all. Therefore, 343 of 401 older adults with a mean age (SD) of 79.3 (6.6), 49.3% women, were included. Table 1 shows the baseline characteristics of all participants stratified by sex. In Supplementary Table 1 the proportions of older adults below the norm values are presented.

Longitudinal Changes of Muscle Mass, Handgrip Strength, Chair Stand, and Gait Speed

Table 2 shows an overview of the data based on the unadjusted LMM analysis. Muscle mass significantly decreased from admission up to 3 months post-discharge (-0.1 kg/m²; $P = .03$) with the lowest value at 1 month post-discharge. Both women and men decreased nonsignificant in muscle mass (resp. -0.2 kg/m²; $P = .08$ and -0.1 kg/m²; $P = .13$). Handgrip strength did not decrease significantly from acute hospitalization up to 3 months post-discharge (-0.5 kg; $P = .08$) with also the lowest value at 1 month post-discharge. For women, handgrip strength decreased significantly (resp. -0.7 kg; $P = .03$) and not significantly for men (-0.2 kg; $P = .55$) at 3 months post-discharge. Chair stand increased significantly ($+0.7$ points; $P < .001$) either for all participants as for women and men separately (resp. $+0.8$ points; $P < .001$ and $+0.5$ points; $P < .001$), from admission up to 3 months post-discharge. Gait speed increased significantly ($+0.9$ points; $P = .00$) for all participants and women and men separately (resp. $+0.7$ points; $P < .001$ and $+1.0$ points; $P < .001$), from admission up to 3 months post-discharge.

Confounders On the Longitudinal Changes of Muscle Mass, Handgrip Strength, Chair Stand, and Gait Speed

Table 3 presents the confounders on the longitudinal changes of muscle mass, handgrip strength, chair stand, and gait speed. Fatigue was identified as a confounder for the longitudinal changes in muscle mass. Fatigue, BMI, and nutrition were identified as confounders and depressive symptoms as an effect modifier in the longitudinal changes of handgrip strength. Fatigue, depressive symptoms, and cognitive impairment were identified as confounders in the longitudinal changes of chair stand and depressive symptoms, BMI, cognitive impairment and fear of falling were identified as confounders in the longitudinal changes of gait speed. Depressive symptoms were identified as an effect modifier in the longitudinal changes in muscle mass.

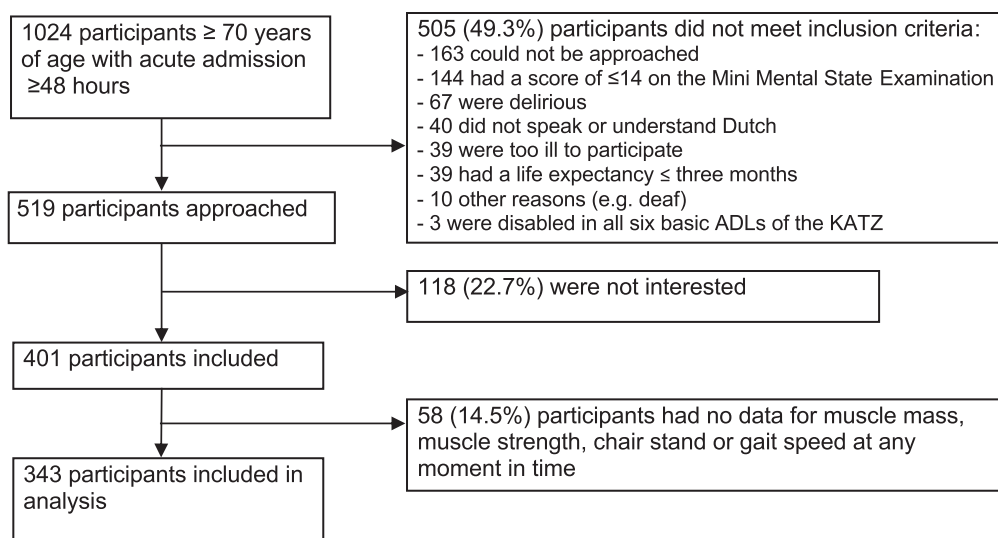


Fig. 1. Flowchart of the acute hospitalized older adults included in the analysis of this study.

Table 1
Baseline Characteristics of Acute Hospitalized Older Adults at Admission

	All (N = 343)	Women (n = 169)	Men (n = 174)
Demographics			
Age, y, mean (SD)	79.3 (6.6)	79.8 (6.8)	78.9 (6.4)
Living arrangements before admission n (%)			
Independent	291 (84.8)	135 (79.9)	156 (89.7)
Nursing home	7 (2.0)	5 (3.0)	2 (1.1)
Senior residence/assisted living	45 (13.1)	29 (17.1)	16 (9.2)
Marital status, n (%) [*]			
Married or living together	182 (53.1)	60 (35.5)	122 (70.1)
Single or divorced	54 (15.7)	35 (20.7)	96 (10.9)
Widow/widower	107 (31.2)	74 (43.8)	33 (19.0)
Primary admission diagnosis, n (%)			
Cardiovascular disease	100 (29.2)	48 (28.4)	52 (29.9)
Gastrointestinal disease	42 (12.2)	21 (12.4)	21 (12.1)
Pulmonary disease	66 (19.2)	33 (19.5)	32 (18.4)
Infection	51 (14.9)	23 (13.6)	28 (16.1)
Other	84 (24.5)	44 (26.0)	41 (23.6)
BMI, mean (SD)	25.5 (4.9)	25.7 (5.2)	25.3 (4.6)
Length of stay, median (IQR)	5.7 (3.9–8.7)	5.6 (3.9–8.9)	5.5 (3.9–8.2)
Charlson comorbidity index (CCI), median (IQR)	2 (1–3)	2 (1–3)	2 (1–3)
Diagnostic measures of sarcopenia			
Muscle mass SMI (BIA), mean (SD) [*]	8.0 (1.8)	6.7 (1.1)	9.2 (1.5)
Handgrip strength (JAMAR), mean (SD) [*]	27.4 (10.2)	20.5 (5.8)	34.0 (9.1)
Chair stand test (SPPB), median score (IQR) [*]	1 (0–2)	0 (0–2)	1 (0–3)
Gait speed test (SPPB), median score (IQR)	2 (0–3)	2 (0–3)	2 (1–3)
Other variables			
Cognitive level (MMSE), median (IQR)	26 (25–28)	27 (24–28)	27 (25–27)
Depressive symptoms (GDS), median (IQR) [*]	3 (2–5)	4 (2–6)	3 (2–5)
Fatigue (NRS), mean ± (SD) [*]	5.4 (2.9)	6.0 (2.8)	4.9 (3.0)
Fear of Falling (NRS), mean ± (SD) [*]	2.8 (3.3)	3.6 (3.4)	2.0 (3.0)
Severe risk of malnutrition (SNAQ), n (%)	132 (32.9)	69 (33.5)	63 (32.3)
ADL score (KATZ 6), median (IQR) [*]	1 (0–3)	1 (1–3)	0 (0–2)
Sarcopenia, n (%)	45/283 (14.1)	17/156 (10.1)	28/163 (17.2)
Functional decline, n (%)	35/239 (10.2)	18/115 (10.7)	17/124 (9.8)

BIA, Bioelectrical Impedance Analysis; BMI, body mass index, square of the body height in kg/m²; CCI, Charlson comorbidity index range 0–31; Fatigue and Fear of Falling NRS, Numeric Rating Scale range 0–10; GDS, Geriatric Depression Scale range 0–15; IQR, interquartile range; KATZ 6 ADL, Activities of Daily Living range 0–6; MMSE, Mini Mental State Examination range 0–30; SD, standard deviation; SMI, Skeletal Muscle Index in kilograms/meter²; SNAQ, Short Nutritional Assessment Questionnaire; SPPB, Short Physical Performance Battery in points.

^{*}Significant difference between women and men ($P < .05$).

Table 2
Unstandardized Linear Mixed Model Analysis for the Longitudinal Changes in Muscle Mass, Handgrip Strength, the Chair Stand Test, and the Gait Speed Test at Admission, Discharge, and 1 and 3 Months Post-discharge in Acute Hospitalized Older Adults

Diagnostic Measure*	Admission	Discharge	One Month	Three Months	P Value
Muscle mass SMI (kg/m ²)	7.9 (7.8–8.2)	7.9 (7.7–8.1)	7.7 (7.5–7.9)	7.8 (7.6–8.0)	.03 [†]
♀ Muscle mass SMI (kg/m ²)	6.7 (6.5–6.9)	6.7 (6.5–6.9)	6.5 (6.3–6.7)	6.5 (6.3–6.7)	.08
♂ Muscle mass SMI (kg/m ²)	9.1 (8.9–9.4)	9.1 (8.9–9.3)	8.8 (8.6–9.0)	9.0 (8.7–9.2)	.13
Handgrip strength (kg)	27.1 (26.1–28.1)	27.2 (26.1–28.2)	26.1 (25.1–27.2)	26.6 (25.6–27.7)	.08
♀ Handgrip strength (kg)	20.2 (19.4–21.1)	20.3 (19.4–21.1)	19.4 (18.5–20.3)	19.5 (18.6–20.5)	.03 [†]
♂ Handgrip strength (kg)	33.6 (32.3–34.9)	33.7 (32.4–35.5)	32.6 (31.3–33.9)	33.4 (32.1–34.7)	.55
Chair stand (pts)	1.1 (1.0–1.3)	1.5 (1.3–1.6)	1.6 (1.4–1.7)	1.8 (1.7–2.0)	<.001 [†]
♀ Chair stand (pts)	0.9 (0.7–1.1)	1.2 (1.0–1.4)	1.4 (1.2–1.6)	1.7 (1.5–2.0)	<.001 [†]
♂ Chair stand (pts)	1.4 (1.2–1.6)	1.7 (1.5–1.9)	1.8 (1.6–2.0)	1.9 (1.7–2.2)	<.001 [†]
Gait speed (pts)	1.9 (1.8–2.1)	2.3 (2.2–2.5)	2.1 (2.0–2.3)	2.8 (2.6–3.0)	<.001 [†]
♀ Gait speed (pts)	1.7 (1.5–1.9)	2.0 (1.8–2.1)	1.8 (1.6–2.1)	2.4 (2.2–2.7)	<.001 [†]
♂ Gait speed (pts)	2.1 (1.9–2.3)	2.6 (2.4–2.8)	2.4 (2.2–2.6)	3.1 (2.9–3.3)	<.001 [†]

♀, women; ♂, men; pts, points; SMI, Skeletal Muscle Mass Index.

*Presented with mean (95% confidence interval).

[†]Significantly different over time ($P < .05$).

Table 3
Longitudinal Changes in Muscle Mass, Handgrip Strength, Chair Stand, and Gait Speed, Adjusted for Confounding Factors

	Model 1: Crude Model			Model 2: Adjusted Model*		
	B	95% CI		B	95% CI	
		Lower Bound	Upper Bound		Lower Bound	Upper Bound
Muscle mass	-0.08	-0.12	-0.03	-0.10 ¹	-0.15	-0.01
Handgrip strength	-0.17	-0.33	-0.00	-0.19 ¹⁻³	-0.39	0.02
Chair stand	0.23	0.18	0.28	0.12 ^{1,4,5}	0.05	0.18
Gait speed	0.24	0.17	0.30	0.27 ²⁻⁶	0.20	0.33

B, unstandardized beta regression coefficient; CI, confidence interval.

Unstandardized beta controlled for: ¹ = fatigue; ² = body mass index; ³ = risk of malnutrition; ⁴ = depressive symptoms; ⁵ = cognitive impairment; ⁶ = fear of falling.

*Age, sex, comorbidity and length were not identified as statistically significant confounders or effect modifiers for muscle mass, handgrip strength, chair stand and gait speed.

Standardized Longitudinal Changes in Muscle Mass, Handgrip Strength, Chair Stand, and Gait Speed

Figure 2 shows the standardized longitudinal changes in muscle mass, handgrip strength, chair stand test, and gait speed. Muscle mass and handgrip strength were not significantly different from each other. The longitudinal changes in muscle mass and handgrip strength were significantly different as for chair stand and gait speed ($P < .001$).

Sensitivity Analysis

Supplementary Table 2 show the complete cases with data at all timepoints for 108 older adults. The mean age (SD) for the complete cases was 77.8 years (6.0), 43% women. The mean (SD) value for muscle mass (SMI) was 8.1 kg/m² (1.7), for handgrip strength 30.5 kg (10.0) and the median (IQR) value for chair stand was 1 point (0–3), for gait speed 3 points (1–4) and for the complete SPPB was 7 points (3–10). For the complete cases, longitudinal changes in muscle mass and handgrip strength showed a nonsignificant decrease up to 3 months post-discharge.

Discussion

This multicenter prospective cohort study determined the longitudinal changes of the diagnostic measures of sarcopenia: muscle mass, handgrip strength, chair stand, and gait speed after

hospitalization up to 3 months post-discharge. Physical performance improved although muscle mass decreased and handgrip strength did not change from acute hospitalization up to 3 months post-discharge, with differences between women and men. The lowest level of muscle mass was determined at 1-month post-discharge. Chair stand and gait speed improved from admission up to 3 months post-discharge. A considerable part of the older adults stayed below the normative levels of muscle mass, handgrip strength, and physical performance, at 3 months post-discharge.

The decline in muscle mass and absence of improvement in handgrip strength can be explained by the combination of inactivity and inflammation of older adults during and after acute hospitalization.^{9,10,36} During hospitalization, muscle mass and handgrip strength did not change. The relatively short admission period, which is comparable to other studies,⁶ and the ongoing deterioration could explain that a decline in muscle mass and muscle strength were observed only after 1-month post-discharge and not during hospitalization. In addition, low muscle function, recognized as sarcopenia, might already have been developed before hospitalization.^{12,13} However, this cannot be confirmed in this study. The decline in muscle mass and handgrip may have relevance for clinical practice because the first month after discharge is reported as a critical period,¹⁶ after which disabilities have a high chance of becoming permanent among older hospitalized adults. It can be hypothesized that the decline in muscle mass and handgrip strength have an impact on the physical performance. In this study, the improvement of the physical performance can be seen as part of the expected recovery after acute illness with hospitalization, where older adults are at their lowest level of functioning at hospital admission. A similar improvement was seen in a previous study,¹⁵ in which the physical performance improved up to 3 weeks following discharge, but aberrant to another study¹⁴ where no difference was reported 30 days post-discharge. Our study showed additionally that this improvement continued up to 3 months post-discharge with different patterns between gait speed and chair stand. An explanation for the different patterns for gait speed and chair stand might be that chair stand is conditional to the complex task of walking.³⁷ Although physical performance improved, not all older adults reach normative level. This means that older adults are still at risk for being (re)hospitalized with deteriorating health, at 3 months after discharge from hospital.^{1,25,38}

The transition from hospital to the home situation seems to be crucial and older adults need specific guidance during this critical period. Previous studies from the Hospital-ADL study group reported that geriatric syndromes are highly prevalent after discharge from the hospital and are associated with functional decline.^{17,18} The current

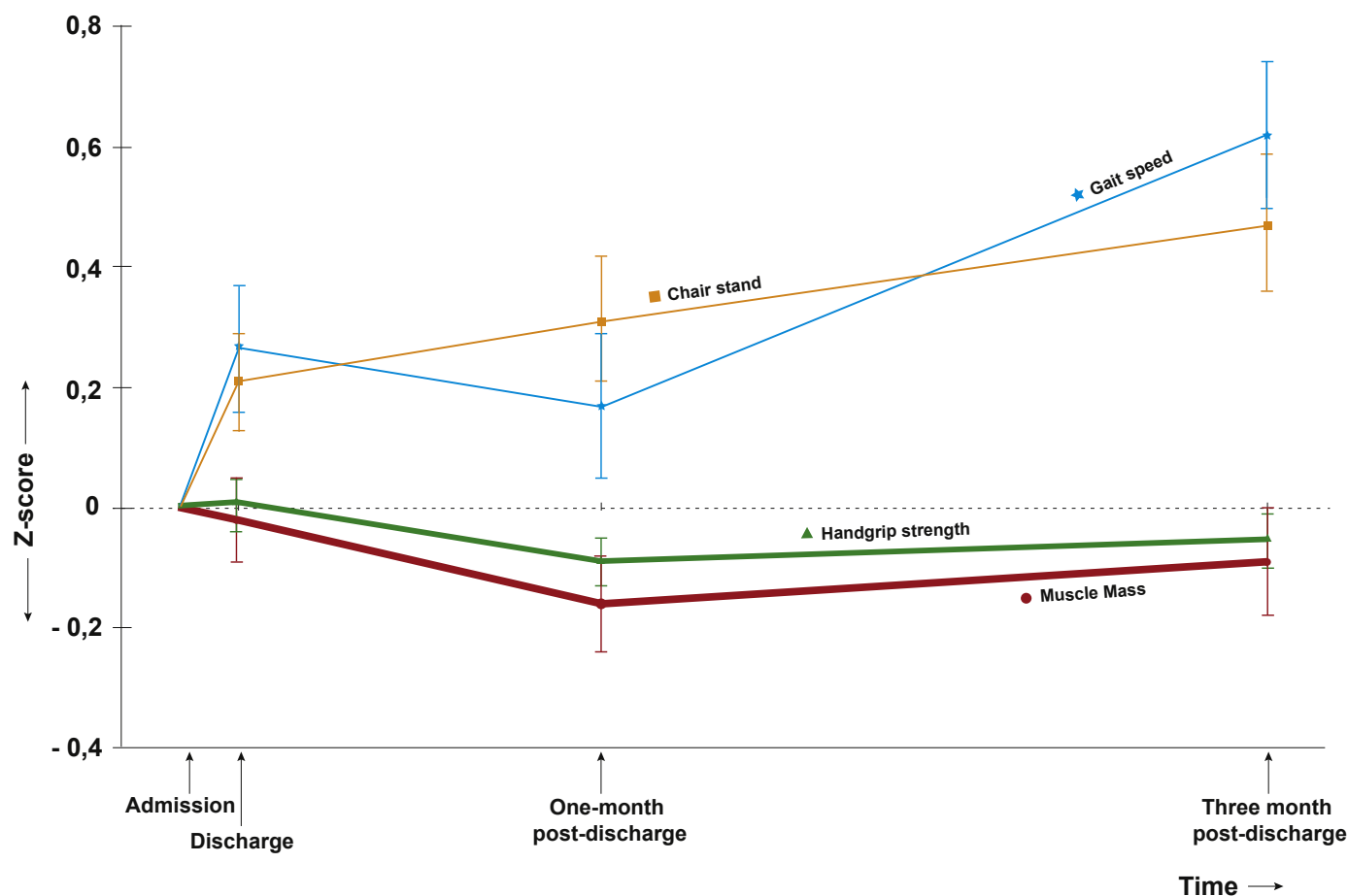


Fig. 2. Standardized (Z-scores) longitudinal changes in muscle mass, handgrip strength, chair stand, and gait speed from hospital admission up to 3 months post-discharge in acute hospitalized older adults.

study confirmed the involvement of psychosocial factors such as depressive symptoms, but also fatigue, nutrition and BMI on the longitudinal changes in muscle mass, muscle strength and physical performance. The finding that depressive symptoms is an effect modifier in the longitudinal change of handgrip strength might indicate the role in the recovery of physical performance but needs further investigation.

The clinical implications of this study can be significant, because a substantial part of the older adults does not return to their level at which they can live independently. Current standard care after discharge from the hospital does not include an exercise program. It could be hypothesized that an exercise intervention is indicated to increase muscle mass and muscle strength in order to improve physical performances. This hypothesis is in accordance with the growing body of knowledge about the effect of exercise interventions for older adults.^{39–42} However, it is unclear if an exercise intervention could have a similar effect on an acutely hospitalized population with geriatric syndromes.^{17,18} These syndromes, may be barriers to regain muscle mass and strength and recover to a higher level of functioning after acute hospitalization. Recent research has demonstrated that an exercise intervention during hospitalization could be an effective therapy for improving muscle strength and reducing functional decline.^{42,43} Future research for this specific population with complex care needs, should focus on the transitional period after hospitalization to improve muscle mass, muscle strength and physical performances in the home situation to prevent functional decline and

achieve normative levels of independent living. The role of geriatric syndromes, such as depressive symptoms, apathy and nutrition, should be considered in the development of this intervention.^{17,18,44–46}

This study has several limitations. First, measurements were taken in a standardized way according to a strict protocol.¹⁹ However, some limitations need to be addressed. Second, data were missing due to several reasons such as inability to perform the test or not available for follow-up which is a known challenge in aging research.⁴⁷ The missing data might have introduced bias. A sensitivity analysis on the complete cases ([Supplementary Table 2](#)) showed nonsignificant differences in muscle mass and handgrip strength and differences in the temporal pattern of gait speed in comparison with the overall LMM analysis including all cases. However, LMM analysis is a sophisticated statistical technique which handles missing values very well.³⁴ Third, measurements were taken both in hospital and in the home situation, where the protocol was sometimes adjusted in some cases due to the organization in the hospital (patients were not always available at the same moment or in fasting condition) or in the home situation (not enough space to perform tests) which might have been influenced the results. Fourth, generalizability of the study might be limited because patients dependent in all 6 basic ADLs were excluded from this study, although this occurred in 3 patients only. Fifth, detailed information on additional treatment and use of medication of the patients is lacking. It remains unknown whether these factors might have influenced the results.

Conclusions and Implications

In conclusion, physical performance improved during and after hospitalization although muscle mass decreased, and handgrip strength did not change. At 3 months post-discharge, muscle mass, handgrip strength, and physical performance did not reach normative levels for the population. Further research is needed to examine the role of exercise as a therapy for improving muscle mass, muscle strength, and physical performance after acute hospitalization in older adults.

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References

- Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: Revised European consensus on definition and diagnosis. *Age Ageing* 2019;48:16–31.
- Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis Report of the European Working Group on Sarcopenia in Older People. *Age Ageing* 2010;39:412–423.
- Reijnierse EM, Buljan A, Tuttle CSL, et al. Prevalence of sarcopenia in inpatients 70 years and older using different diagnostic criteria. *Nurs Open* 2018;6:377–383.
- Wang DXM, Yao J, Zirek Y, et al. Muscle mass, strength and physical performance predicting activities of daily living: a meta-analysis. *J Cachexia Sarcopenia Muscle* 2020;11:3–25.
- Yeung SSY, Reijnierse EM, Pham VK, et al. Sarcopenia and its association with falls and fractures in older adults: A systematic review and meta-analysis. *J Cachexia Sarcopenia Muscle* 2019;10:485–500.
- Meskens CGM, Reijnierse EM, Numans ST, et al. Association of handgrip strength and muscle mass with dependency in (instrumental) activities of daily living in hospitalized older adults - The Empower Study. *J Nutr Heal Aging* 2019;23:232–238.
- Pérez-Zepeda MU, Sgaravatti A, Dent E. Sarcopenia and post-hospital outcomes in older adults: A longitudinal study. *Arch Gerontol Geriatr* 2017;69:105–109.
- Buurman BM, Hoogerduijn JG, de Haan RJ, et al. Geriatric conditions in acutely hospitalized older patients: Prevalence and one-year survival and functional decline. *PLoS One* 2011;6:e26951.
- Kortebein P, Symons TB, Ferrando A, et al. Functional impact of 10 days of bed rest in healthy older adults. *J Gerontol A Biol Sci Med Sci* 2008;63:1076–1081.
- Coker RH, Hays NP, Williams RH, et al. Bed rest promotes reductions in walking speed, functional parameters, and aerobic fitness in older, healthy adults. *J Gerontol A Biol Sci Med Sci* 2015;70:91–96.
- Covinsky KE, Pierluissi E, Story THEPS. Hospitalization-associated disability: "She was probably able to ambulate, but I'm not sure." *JAMA* 2011;306:1782–1794.
- Welch C, Hassan-Smith ZK, Greig CA, et al. Acute sarcopenia secondary to hospitalisation - an emerging condition affecting older adults. *Aging Dis* 2018;9:151–164.
- Van Ancum JM, Scheerman K, Jonkman NH, et al. Change in muscle strength and muscle mass in older hospitalized patients: A systematic review and meta-analysis. *Exp Gerontol* 2017;92:34–41.
- Bodilsen AC, Pedersen MM, Petersen J, et al. Acute hospitalization of the older patient: Changes in muscle strength and functional performance during hospitalization and 30 days after discharge. *Am J Phys Med Rehabil* 2013;92:789–796.
- Moen K, Ormstad H, Wang-Hansen MS, Brovold T. Physical function of elderly patients with multimorbidity upon acute hospital admission versus 3 weeks post-discharge. *Disabil Rehabil* 2017;8288:1–8.
- Boyd CM, Landefeld CS, Counsell SR, et al. Recovery of activities of daily living in older adults after hospitalization for acute medical illness. *J Am Geriatr Soc* 2008;56:2171–2179.
- van Seben R, Reichardt LA, Aarden JJ, et al. The course of geriatric syndromes in acutely hospitalized older adults: The Hospital-ADL Study. *J Am Med Dir Assoc* 2019;200:152–158.e2.
- Reichardt LA, van Seben R, Aarden JJ, et al. Trajectories of cognitive-affective depressive symptoms in acutely hospitalized older adults: The hospital-ADL study. *J Psychosom Res* 2019;120:66–73.
- Reichardt LA, Aarden JJ, van Seben R, et al. Unravelling the potential mechanisms behind hospitalization-associated disability in older patients; the Hospital-Associated Disability and impact on daily life (Hospital-ADL) cohort study protocol. *BMC Geriatr* 2016;16:59.
- Achamrah N, Colange G, Delay J, et al. Comparison of body composition assessment by DXA and BIA according to the body mass index: A retrospective study on 3655 measures. *PLoS One* 2018;13:1–13.
- Janssen I, Heymsfield SB, Baumgartner RN, Ross R. Estimation of skeletal muscle mass by bioelectrical impedance analysis. *J Appl Physiol* 2017;89:465–471.
- Janssen I, Baumgartner RN, Ross R, et al. Skeletal muscle cutpoints associated with elevated physical disability risk in older men and women. *Am J Epidemiol* 2004;159:413–421.
- Reijnierse EM, de Jong N, Trappenburg MC, et al. Assessment of maximal handgrip strength: How many attempts are needed? *J Cachexia Sarcopenia Muscle* 2017;8:466–474.
- Bohannon RW. Hand-grip dynamometry provides a valid indication of upper extremity strength impairment in home care patients. *J Hand Ther* 1998;11:258–260.
- Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: Association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol* 1994;49:85–94.
- Studenski S, Perera S, Wallace D, et al. Physical performance measures in the clinical setting. *J Am Geriatr Soc* 2003;51:314–322.
- Bohannon RW. Reference values for the five-repetition sit-to-stand test: A descriptive meta-analysis of data from elders. *Percept Mot Skills* 2006;103:215–222.
- Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. *JAMA* 2011;305:50–58.
- Friedman B, Heisel MJ, Delavan RL. Psychometric properties of the 15-item Geriatric Depression Scale in functionally impaired, cognitively intact, community-dwelling elderly primary care patients. *J Am Geriatr Soc* 2005;53:1570–1576.
- Folstein MF, Folstein SE, McHugh PR. A practical state method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189–198.
- Kruizenga HM, Seidell JC, de Vet HCW, et al. Development and validation of a hospital screening tool for malnutrition: The short nutritional assessment questionnaire (SNAQ). *Clin Nutr* 2005;24:75–82.
- Frenkel WJ, Jongerius EJ, Mandjes-van Uiterter MJ, et al. Validation of the Charlson comorbidity index in acutely hospitalized elderly adults: A prospective cohort study. *J Am Geriatr Soc* 2014;62:342–346.
- Buurman BM, Han L, Murphy TE, et al. Trajectories of disability among older persons before and after a hospitalization leading to a skilled nursing facility admission. *J Am Med Dir Assoc* 2016;17:225–231.
- Twisk J, De Boer M, De Vente W, Heymans M. Multiple imputation of missing values was not necessary before performing a longitudinal mixed-model analysis. *J Clin Epidemiol* 2013;66:1022–1028.
- Van Der Esch M, Holla JF, Van Der Leeden M, et al. Decrease of muscle strength is associated with increase of activity limitations in early knee osteoarthritis: 3-year results from the cohort hip and cohort knee study. *Arch Phys Med Rehabil* 2014;95:1962–1968.
- Liu JYJ, Reijnierse EM, van Ancum JM, et al. Acute inflammation is associated with lower muscle strength, muscle mass and functional dependency in male hospitalised older patients. *PLoS One* 2019;14:e0215097.
- Brach JS, VanSwearingen JM. Interventions to improve walking in older adults. *Curr Transl Geriatr Exp Gerontol Rep* 2013;2:10–1007.
- Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: Consistency across studies, predictive models, and value of gait speed alone compared with the Short Physical Performance Battery. *J Gerontol A Biol Sci Med Sci* 2000;55:221–231.
- Suetta C, Magnusson SP, Beyer N, Kjaer M. Effect of strength training on muscle function in elderly hospitalized patients: Review. *Scand J Med Sci Sport* 2007;17:464–472.
- Liu C-J, Shiroy DM, Jones LY, Clark DO. Systematic review of functional training on muscle strength, physical functioning, and activities of daily living in older adults. *Eur Rev Aging Phys Act* 2014;11:95–106.
- Aarden JJ, Van Der Schaaf M, Van Der Esch M, et al. Muscle strength is longitudinally associated with mobility among older adults after acute hospitalization: The Hospital-ADL study. *PLoS One* 2019;14:1–11.
- Sáez de Asteasu ML, Martínez-Velilla N, Zambom-Ferraresi F, et al. Changes in muscle power after usual care or early structured exercise intervention in acutely hospitalized older adults. *J Cachexia Sarcopenia Muscle* 2020;11:997–1006.
- Martínez-Velilla N, Casas-Herrero A, Zambom-Ferraresi F, et al. Effect of exercise intervention on functional decline in very elderly patients during acute hospitalization: A randomized clinical trial. *JAMA Intern Med* 2019;179:28–36.
- van Dronkelaar C, Tieland M, Aarden JJ, et al. Decreased appetite is associated with sarcopenia-related outcomes in acute hospitalized older adults. *Nutrients* 2019;11:932.
- Scheerman K, Raaijmakers K, Otten RHJ, et al. Effect of physical interventions on physical performance and physical activity in older patients during hospitalization. A systematic review 2018;18:288.
- Sáez de Asteasu ML, Martínez-Velilla N, Zambom-Ferraresi F, et al. Assessing the impact of physical exercise on cognitive function in older medical patients during acute hospitalization: Secondary analysis of a randomized trial. *PLoS Med* 2019;16:e1002852.
- Hardy SE, Allore H, Studenski SA. Missing data: A special challenge in aging research. *J Am Geriatr Soc* 2009;57:722–729.

Supplementary Table 1

Percentage of Older Adults Below the Norm Values for Muscle Mass, Handgrip Strength, and the Short Physical Performance Battery From Admission up to 3 Months Post-discharge

Diagnostic Measure	n	Admission	n	Discharge	n	One month	n	Three months
Muscle mass SMI (kg/m ²)	303	223 (73.4)	253	184 (77.0)	228	184 (80.1)	176	142 (80.1)
♀ Muscle mass SMI (kg/m ²)	147	84 (57.1)	125	110 (88.0)	109	70 (64.2)	80	54 (67.5)
♂ Muscle mass SMI (kg/m ²)	156	139 (89.1)	128	74 (57.8)	119	114 (95.8)	96	88 (91.7)
Handgrip strength (kg)	324	69 (21.3)	292	56 (19.2)	255	55 (21.6)	205	37 (18.0)
♀ Handgrip strength (kg)	158	33 (20.1)	149	27 (18.1)	120	29 (24.2)	93	15 (16.1)
♂ Handgrip strength (kg)	166	36 (21.7)	143	29 (20.3)	135	26 (19.3)	112	22 (19.7)
SPPB (pts)	313	236 (75.4)	282	186 (66.0)	310	198 (63.8)	198	87 (43.4)
♀ SPPB (pts)	153	124 (81.0)	142	106 (76.6)	156	108 (69.2)	87	40 (46.0)
♂ SPPB (pts)	160	112 (70.0)	140	80 (57.1)	154	90 (58.4)	111	54 (42.2)

♀, female; ♂, male; pts, points; SMI, Skeletal Muscle Mass Index; SPPB, Short Physical Performance Battery.

Supplementary Table 2

Complete Cases With the Longitudinal Changes in Muscle Mass, Handgrip Strength, the Chair Stand Test, and the Gait Speed Test at Admission, Discharge, One Month, and Three Months Post-discharge

Diagnostic Measure*	Admission	Discharge	One Month	Three Months	P Value
Muscle mass SMI (kg/m ²)	8.1 (7.8–8.5)	8.1 (7.8–8.4)	7.9 (97.6–8.2)	8.0 (7.7–8.4)	.33
♀ Muscle mass SMI (kg/m ²)	6.7 (6.4–7.0)	6.7 (6.4–7.0)	6.7 (6.3–6.8)	6.6 (6.3–6.8)	.62
♂ Muscle mass SMI (kg/m ²)	9.2 (8.8–9.5)	9.1 (8.7–9.4)	8.9 (8.8–9.2)	9.1 (8.8–9.4)	.30
Handgrip strength (kg)	30.5 (28.5–32.4)	30.8 (28.9–32.8)	30.1 (28.2–32.1)	30.9 (28.9–32.8)	.30
♀ Handgrip strength (kg)	22.5 (20.8–24.1)	23.2 (21.5–24.8)	22.0 (20.3–23.6)	22.5 (20.9–24.1)	.98
♂ Handgrip strength (kg)	36.4 (34.2–38.6)	36.5 (34.2–38.7)	36.2 (34.0–38.4)	37.1 (34.9–39.4)	.21
Chair stand (pts)	1.6 (1.3–1.9)	2.1 (1.8–2.3)	2.2 (1.9–2.4)	2.4 (2.1–2.7)	<.001 [†]
♀ Chair stand (pts)	1.2 (0.8–1.6)	1.7 (1.3–2.1)	1.8 (1.4–2.2)	2.2 (1.8–2.6)	<.001 [†]
♂ Chair stand (pts)	1.9 (1.5–2.3)	2.3 (1.9–2.7)	2.4 (2.0–2.8)	2.5 (2.1–2.9)	.02 [†]
Gait speed (pts)	2.2 (2.0–2.5)	2.7 (2.5–3.0)	3.0 (2.8–3.3)	3.2 (2.9–3.4)	<.001 [†]
♀ Gait speed (pts)	2.1 (1.6–2.4)	2.6 (2.1–3.0)	2.9 (2.4–3.2)	3.0 (2.6–3.4)	<.001 [†]
♂ Gait speed (pts)	2.4 (2.1–2.7)	2.9 (2.5–3.2)	3.1 (2.8–3.5)	3.4 (3.0–3.7)	<.001 [†]

♀, female; ♂, male; pts, points; SMI, Skeletal Muscle Index.

*Presented with mean (95% confidence interval).

[†]Significant difference between hospital admission and 3 months post-discharge ($P < .05$).