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Effect of Exercise Intervention on Functional Decline in Very Elderly Patients During Acute Hospitalization
A Randomized Clinical Trial

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Invited Commentary

Author Audio Interview

Video and Supplemental content

IMPORTANCE Functional decline is prevalent among acutely hospitalized older patients. Exercise and early rehabilitation protocols applied during acute hospitalization can prevent functional and cognitive decline in older patients.

OBJECTIVE To assess the effects of an innovative multicomponent exercise intervention on the functional status of this patient population.

DESIGN, SETTING, AND PARTICIPANTS A single-center, single-blind randomized clinical trial was conducted from February 1, 2015, to August 30, 2017, in an acute care unit in a tertiary public hospital in Navarra, Spain. A total of 370 very elderly patients undergoing acute-care hospitalization were randomly assigned to an exercise or control (usual-care) intervention. Intention-to-treat analysis was conducted.

INTERVENTIONS The control group received usual-care hospital care, which included physical rehabilitation when needed. The in-hospital intervention included individualized moderate-intensity resistance, balance, and walking exercises (2 daily sessions).

MAIN OUTCOMES AND MEASURES The primary end point was change in functional capacity from baseline to hospital discharge, assessed with the Barthel Index of independence and the Short Physical Performance Battery (SPPB). Secondary end points were changes in cognitive and mood status, quality of life, handgrip strength, incident delirium, length of stay, falls, transfer after discharge, and readmission rate and mortality at 3 months after discharge.

RESULTS Of the 370 patients included in the analyses, 209 were women (56.5%); mean (SD) age was 87.3 (4.9) years. The median length of hospital stay was 8 days in both groups (interquartile range, 4 and 4 days, respectively). Median duration of the intervention was 5 days (interquartile range, 0); there was a mean (SD) of 5 (1) morning and 4 (1) evening sessions per patient. No adverse effects were observed with the intervention. The exercise intervention program provided significant benefits over usual care. At discharge, the exercise group showed a mean increase of 2.2 points (95% CI, 1.7-2.6 points) on the SPPB scale and 6.9 points (95% CI, 4.4-9.5 points) on the Barthel Index over the usual-care group. Hospitalization led to an impairment in functional capacity (mean change from baseline to discharge in the Barthel Index of −5.0 points (95% CI, −6.8 to −3.2 points) in the usual-care group, whereas the exercise intervention reversed this trend (1.9 points; 95% CI, 0.2-3.7 points). The intervention also improved the SPPB score (2.4 points; 95% CI, 2.1-2.7 points) vs 0.2 points; 95% CI, −0.1 to 0.5 points in controls). Significant intervention benefits were also found at the cognitive level of 1.8 points (95% CI, 1.3-2.3 points) over the usual-care group.

CONCLUSIONS AND RELEVANCE The exercise intervention proved to be safe and effective to reverse the functional decline associated with acute hospitalization in very elderly patients.

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The provision of inpatient acute care for frail older adults who are at risk of adverse outcomes is becoming a major clinical issue in our aging societies.[1-4] In this regard, acute hospital admissions are a major contributor to disability in the elderly.[5] Despite resolution of the reason for hospitalization, patients, especially those who are frail, are often discharged with a new major disability.[6] More than half of all older adults do not recover to their preadmission functional levels 1 year after discharge, with high rates of nursing home placement and death.[7-9] This is a problem that health care professionals and policy makers should prioritize given the expectations of further growth of the population segment composed of elderly people.

Acute hospitalized older patients, including those who are able to walk independently, spend most of their hospital time in bed.[9,10] In addition to deteriorating their functional status, bed rest increases the risk for cognitive decline and dementia in the elderly.[11] The epidemic of low mobility during hospitalization is caused by several factors, including a failure to apply efficient models for management of older patients,[12,13] the notion that reducing mobility will prevent falls, the culture of bed rest, or hospital design.[14]

Exercise and early rehabilitation protocols applied during acute hospitalization can prevent functional and cognitive decline in older patients and are associated with a reduced length of stay and lower costs.[15] Yet, patients with cognitive impairment or multimorbidity at baseline are commonly excluded from exercise intervention trials, and only conservative or traditional programs (ie, focusing on light walking while avoiding resistance training) have been typically applied to elders who are acutely hospitalized.[14,16] The benefits of a multicomponent exercise intervention consisting of resistance (power), balance, and gait-retraining exercises to attenuate functional decline in frail nonagenarians in long-term care have been shown.[17] To the best of our knowledge, this type of intervention has not been implemented in acutely hospitalized patients of advanced age (including octogenarians and nonagenarians).

The present study is in line with the long trajectory of research that has explored the possibilities of modifying traditional models of hospitalization in Acute Care of Elderly (ACE) units[8,18] but goes a step further by adding the individualized and adapted prescription of multicomponent exercise to each patient. The main purpose of our study was therefore to assess the effects of a multicomponent exercise intervention performed by older adults during acute hospitalization for functional, cognition, and well-being status. Other outcomes, such as length of stay or falls, were also assessed.

Key Points

Question Can the functional and cognitive impairment associated with the acute hospitalization of older adults be reversed?

Findings This randomized clinical trial including 370 hospitalized elderly patients shows that the prescribed exercise intervention provided significant benefits over usual care. At discharge, significant differences between the exercise intervention and the control groups were noted for functional independence as well as cognitive and quality of life level.

Meaning An individualized, multicomponent exercise program proved safe and effective to reverse the functional decline associated with acute hospitalization in very elderly patients.

Methods

Design

The study was a randomized clinical trial (RCT) performed according to the SPIRIT 2013 and the CONSORT statement for transparent reporting.[19,20] The protocol is available in Supplement 1. The RCT was conducted from February 1, 2015, to August 30, 2017, in the ACE unit of the department of geriatrics in a tertiary public hospital (Complejo Hospitalario de Navarra, Pamplona, Spain). This department has 35 beds allocated to the unit and its staff is composed of 8 geriatricians (distributed in the ACE unit, orthogeriatrics, and outpatient consultations). Admissions in the ACE unit are mainly from the accident and emergency department, with heart failure and infectious diseases being the main causes of admissions (eTable in Supplement 2). When the disability generated by the pathologic factors that caused admission in the ACE unit requires long-term care, patients are usually referred to another, medium-stay hospital.

The study followed the principles of the Declaration of Helsinki[21] and was approved by the Complejo Hospitalario de Navarra Clinical Research Ethics Committee. All patients or their legal representatives provided written informed consent. There was no financial compensation.

Acutely hospitalized patients who met inclusion criteria were randomly assigned to the intervention or control (usual-care) group within the first 48 hours of admission. Usual care is offered to the patient by the geriatricians of our department and consists of standard physiotherapy focused on walking exercises for restoring the functionality conditioned by potentially reversible abnormalities. A formal exercise prescription was not provided at study entry and patients were instructed to continue with the current activity practices through the duration of the study.

Participants and Randomization

All of the patients admitted to the ACE unit were evaluated by geriatricians. We focused on a particularly vulnerable population segment, but at the same time with a level of functional reserve and cognitive capacity high enough to allow them to perform the programmed exercise intervention. Thus, a trained research assistant (N.M.-V., A.C.-H., A.G.-B., J.A.-R., B.G.-G., M.G.-L., or I.A.I.) conducted a screening interview to determine whether potentially eligible patients met the following inclusion criteria: age 75 years or older, Barthel Index score of 60 or more (scale, 0 [severe functional dependence] to 100 [functional independence]),[22] being able to ambulate (with/without assistance), and being able to communicate and collaborate with the research team. Exclusion criteria included expected length of stay less than 6 days, very severe cognitive decline (ie, Global Deterioration Scale score, 7),[23] terminal illness, uncontrolled arrhythmias, acute pulmonary embolism, recent myocardial infarction, recent major surgery, or extremity bone fracture in the past 3 months.

After the baseline assessment was performed, participants were randomly assigned following a 1:1 ratio, without restrictions.[24] The assessment staff were blinded to the main study design and group allocation. Participants were explicitly informed and reminded not to discuss their randomization assignment with the assessment staff.

The costs derived from the intervention were basically those generated by hiring 1 physiotherapist (M.L.S.deA.) ad hoc for the project and the collaboration of a researcher (with a PhD background in exercise physiology) (F.Z.-F.) who shared the work during 7 days a week for the duration of the study. An initial investment of €4000 (US $4645) was made to buy the weight-training equipment (ie, €3500 [US $4064] for the sum of 1 leg press, 1 bilateral knee extension, and 1 seated bench [chest] press machine) (**Video 1**) and approximately €500 (US $580) for dumbbells, ankle weights, and handgrip balls (**Video 2**).

Intervention

The usual-care group received habitual hospital care, which included physical rehabilitation when needed. The intervention was programmed in 2 daily sessions (morning and evening) of 20 minutes' duration during 5 to 7 consecutive days (including weekends). An experienced fitness specialist with in-depth training on safe patient handling techniques (F.Z.-F.) supervised each patient's session and provided instructions and encouragement. Adherence to the exercise intervention program was documented in a daily register. A session was considered completed when 90% or more of the programmed exercises were successfully performed.[25] Participants and their family members were familiarized with the training procedures before the start of the intervention.

Each session was performed in a room equipped ad hoc in the geriatric ACE unit. Exercises were adapted from the multicomponent physical exercise program Vivifrail to prevent weakness and falls.[26] The morning sessions included individualized supervised progressive resistance, balance, and walking training exercises. The resistance exercises were tailored to the individual's functional capacity using variable resistance training machines (Matrix; Johnson Health Tech and Exercycle S.L., BH Group) aiming at 2 to 3 sets of 8 to 10 repetitions with a load equivalent to 30% to 60% of the 1-repetition maximum.[25] Participants performed 3 exercises involving mainly lower-limb muscles (squats rising from a chair, leg press, and bilateral knee extension) and 1 involving the upper-body musculature (seated bench [chest] press) (Video 1). They were instructed to perform the exercises at a high speed to optimize muscle power output, and care was taken to ensure proper exercise execution.

Balance and gait retraining exercises gradually progressed in difficulty and included the following: semi-tandem foot standing, line walking, stepping practice, walking with small obstacles, proprioceptive exercises on unstable surfaces (foam pads sequence), altering the base of support, and weight transfer from 1 leg to the other (**Video 3**). The evening session consisted of functional unsupervised exercises using light loads (ie, 0.5- to 1-kg anklets and handgrip ball), such as knee extension and flexion, hip abduction, and daily walking in the corridor of the acute care unit with a duration based on the clinical physical exercise guide Vivifrail[26] (Video 2).[18] Participants in the videos were filmed at discharge.

As soon as the clinician in charge of the patient considered that their hemodynamic situation was acceptable and the patient could collaborate, the following end points were assessed and the intervention was started. End points were also assessed on the day of discharge.

End Points

The primary end point was change in functional capacity from baseline (beginning of the intervention) to hospital discharge, as assessed with the Short Physical Performance Battery (SPPB), which combines balance, gait velocity, and leg strength as a single score on a 0 (worst) to 12 (best scale),[27] and the Barthel Index of independence during activities of daily living (ADLs) from 2 weeks prior to admission to hospital discharge. The magnitude of meaningful change (ie, clinically significant) was 1 point for the SPPB[28] and 5 points for the Barthel Index.[29,30]

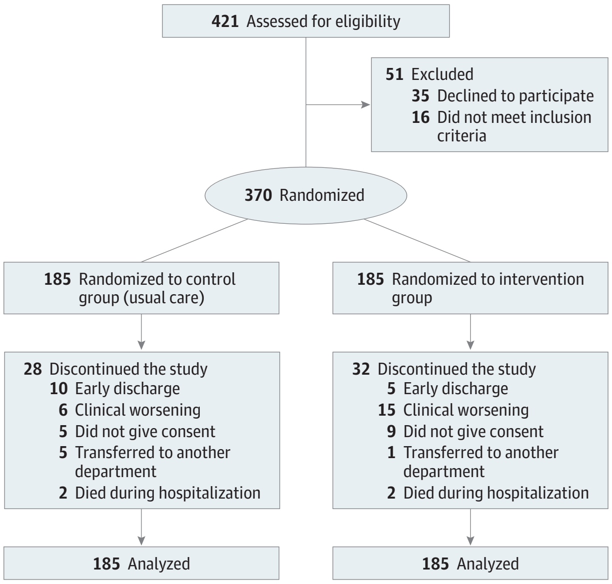
Secondary end points included changes in cognitive capacity as assessed with the Mini-Mental State Examination (30-point questionnaire; scale of 0 [worst] to 30 [best]),[31] mood status (15-item Yesavage Geriatric Depression Scale; Spanish version; scale of 0 [best] to 15 [worst]),[23] visual analog scale of the EuroQol-5 Dimension (EQ-5D) questionnaire for quality of life (QoL) assessment (Spanish version of the EQ-5D[32]; scale of 0 [worst health state imaginable] to 100 [best health state imaginable]), and handgrip strength (dominant hand).[33] Other secondary end points included development of delirium (as assessed with the Confusion Assessment Method; feature 1, acute onset and fluctuating course; feature 2, inattention; feature 3, disorganized thinking; and feature 4, altered level of consciousness, with diagnosis of delirium requiring the presence of features 1 and 2 and either 3 or 4),[34] length of hospital stay, falls during hospitalization, transfer after discharge, and readmission rate and mortality at 3 months after discharge.

Statistical Analysis

We used the intention-to-treat approach. Between-group comparisons of continuous variables were conducted using linear mixed models. Time was treated as a categorical variable. The models included group, time, and group by time interaction as fixed effects, and participants as random effect. For each group, data are expressed as change from baseline (admission) to discharge, determined by the time coefficients (95% CI) of the model. The primary conclusions about effectiveness of exercise intervention were based on between-group comparisons of change in functional capacity from baseline (beginning of the intervention) to hospital discharge, as assessed with the SPPB and the Barthel Index of independence during ADLs and determined by the time by group interaction coefficients of the model.

Comparisons of secondary end points indicative of adverse events or hospitalization were performed with the Mann-Whitney test for nonnormally distributed quantitative data, mid-*P* value exact test for rates, and χ^2 or Fisher tests for categorical data. Using the χ^2 test for linear trend, we also compared the proportion of patients in each group showing an

Figure 1. Study Flow Diagram



Progress through the phases of the parallel randomized trial of the groups.

improvement, no change, or worsening at discharge compared with baseline on the SPPB scale and Barthel Index.

All comparisons were 2-sided, with a significance level of .05, except for the analysis of the primary outcome (change in functional capacity as assessed with the SPPB scale and Barthel Index), where the Bonferroni-Holm multiple test adjustment was applied. All statistical analyses were made with SPSS, version 20 (IBM Corp) and R, version 3.2.2 (R Foundation) software.

Results

The study flow diagram is shown in **Figure 1**. No significant differences were found between groups at baseline for demographic and medical characteristics or for study end points (**Table 1**). Of the 370 patients included in the analyses, 209 were women (56.5%); mean age was 87.3 (4.9) years (range, 75-101 years, with 130 patients [35.1%] being nonagenarians). The median length of hospital stay was 8 days in both groups (interquartile range [IQR], 4 and 4 days, respectively). The mean (SD) number of intervention days for each patient was 5.3 (0.5) days (IQR, 0 days), with most training days (97%) being consecutive. The mean number of completed morning and evening sessions per patient was 5 (1) and 4 (1), respectively. Adherence to the intervention was 95.8% for the morning sessions (ie, 806 successfully completed sessions of 841 total possible sessions) and 83.4% in the evening sessions (574 of 688 successfully completed sessions). No adverse effects associated with the prescribed exercises were recorded and no patient had to interrupt the intervention or had their hospital stay modified because of it.

The primary analyses showed that the exercise intervention program provided a significant benefit over usual care. At discharge (ie, at the primary time point), the exercise group showed a mean increase of 2.2 points (95% CI, 1.7 to 2.6 points) on the SPPB scale and 6.9 points (95% CI, 4.4 to 9.5 points) on the Barthel Index over the usual-care group (**Table 2**). Patients

Table 1. Main Demographic, Clinical, Functional, and End Point Data at Baseline by Group[a]

Variable	Mean (SD) Control Group (n = 185)	Mean (SD) Intervention Group (n = 185)
Demographic data		
Age, y	87.1 (5.2)	87.6 (4.6)
Women, No. (%)	109 (58.9)	100 (54.1)
BMI	26.9 (4.9)	27.1 (4.4)
Clinical data		
No. of diseases[b]	9 (6)	9 (6)
CIRS, median (IQR), score[c]	12 (5)	13 (5)
Zarit Caregiver Burden Interview, median (IQR), score[d]	41 (14)	44 (13)
MNA, median (IQR), score[e]	24 (4)	24 (4)
6-m Gait velocity test, s	16.1 (8.8)	16.2 (13.1)
1RM leg press, kg	62 (31)	57 (25)
1RM chest press, kg	25 (12)	24 (11)
1RM knee extension, kg	41 (14)	39 (13)
Primary end point measures		
SPPB scale[f]	4.7 (2.7)	4.4 (2.5)
Barthel Index[g]	83 (17)	84 (17)
Secondary end point measures		
Mini-Mental State Examination[h]	23 (4)	22 (5)
Yesavage Geriatric Depression Scale[i]	3.6 (2.9)	4.0 (2.4)
Quality of life[j]	60 (21)	58 (22)
Delirium, %[k]	12	17
Handgrip, kg	17 (8)	17 (6)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CIRS, Cumulative Illness Rating Scale; IQR, interquartile range; MNA, Mini-Nutritional Assessment; 1RM, 1 repetition maximum; SPPB, Short Physical Performance Battery.

[a] No statistically significant differences were found between groups (all $P > .10$).

[b] The most prevalent diseases were hypertension, heart failure, dyslipidemia, osteoarthritis, cardiac arrhythmias, chronic obstructive pulmonary disease, chronic gastritis/gastroesophageal reflux, chronic kidney disease, and urinary incontinence.

[c] The CIRS scale evaluates individual body systems, ranging from 0 (best) to 56 (worst).

[d] The Zarit Caregiver Burden Interview ranges from little or no burden (0-21 points), mild to moderate burden (21-40 points), moderate to severe burden (41-60 points), to severe burden (61-88 points).

[e] The Mini-Nutritional Assessment ranges from normal nutritional status (24-30 points), risk of malnutrition (17-23.5 points), or malnourished (<17 points).

[f] The SPPB scale ranges from 0 (worst) to 12 (best).

[g] The Barthel Index ranges from 0 (severe functional dependence) to 100 (functional independence).

[h] The Mini-Mental State Examination ranges from 0 (worst) to 30 (best).

[i] The Yesavage Geriatric Depression Scale ranges from 0 (best) to 15 (worst).

[j] Measured using the visual analog scale of the EuroQol Questionnaire–5 Dimensions, with the score ranging from 0 (worst health state imaginable) to 100 (best health state imaginable).

[k] Measured using the Confusion Assessment Method, with feature 1 indicating acute onset and fluctuating course; feature 2, inattention; feature 3, disorganized thinking; and feature 4, altered level of consciousness, with diagnosis of delirium requiring the presence of features 1 and 2 and either 3 or 4).

Table 2. Results of Primary and Secondary End Points by Group[a]

Variable[b]	Control Group	Intervention Group	Between-Group Difference (95% CI)	*P* Value Between Groups
Primary End Point: Change in Functional Capacity				
SPPB scale (balance, gait ability, leg strength)	0.2 (−0.1 to 0.5)	2.4 (2.1 to 2.7)	2.2 (1.7 to 2.6)	<.001
Barthel Index (ADLs)	−5.0 (−6.8 to −3.2)	1.9 (0.2 to 3.7)	6.9 (4.4 to 9.5)	<.001
Secondary End Points				
Cognitive status				
MMSE	0.3 (−0.1 to 0.6)	2.1 (1.7 to 2.5)	1.8 (1.3 to 2.3)	<.001
Depression (GDS)	0.7 (0.4 to 0.9)	−1.3 (−1.7 to −1.1)	−2.0 (−2.5 to −1.6)	<.001
QoL (EuroQol-5D)	−2.2 (−5.8 to 1.3)	11.0 (7.5 to 14.5)	13.2 (8.2 to 18.2)	<.001
Incident delirium (CAM), %	8.3	14.6	OR, 1.9 (0.9 to 4.0)	.12
Handgrip strength, kg	−0.8 (−1.2 to −0.5)	1.5 (1.1 to 1.8)	2.3 (1.8 to 2.8)	<.001

Abbreviations: ADLs, activities of daily living; CAM, Confusion Assessment Method; EurolQol-5D, EuroQol Questionnaire–5 Dimensions; GDS, Yesavage Geriatric Depression Scale; MMSE, Mini-Mental State Examination; OR, odds ratio; QoL, quality of life; SPPB, Short Physical Performance Battery.

[a] All data, except for CAM, were derived from linear mixed-effects model. For each group, data are expressed as change from baseline (admission) to discharge, determined by the time coefficients (95% CI) of the model. For example, for the SPPB scale, 0.2 corresponds to the coefficient estimated from the model. The between-group difference was determined with time × group interaction coefficient. For CAM, data are the proportion of patients in whom delirium developed.

[b] Explanations of scales used are given in the footnotes to Table 1.

in the intervention group showed improvements at discharge compared with baseline in functional and cognition status indicators, depression, QoL, and handgrip, whereas no such trend was found in the control group (Table 2). Acute hospitalization per se led to significant impairment in patients' functional ability during ADLs (ie, mean change from baseline to discharge on the Barthel Index of −5.0 points (95% CI, −6.8 to −3.2 points) in the control group, whereas the exercise intervention reversed this trend (1.9 points; 95% CI, 0.2 to 3.7 points). Furthermore, the percentage distribution of patients with improvements, no changes, or worsening on the SPPB scale or Barthel Index from admission to discharge significantly differed between the 2 groups, indicating a beneficial intervention effect for both assessments (37.9% vs 85.3% [SPPB] and 9.2% vs 36.3% [Barthel index]; both $P < .001$ for the control and intervention groups, respectively) (**Figure 2**).

We found significant differences between groups in all the secondary end points indicative of cognitive status (Mini-Mental State Examination), depression (Geriatric Depression Scale), and QoL (visual analog scale of the EQ-5D), as well as in handgrip (all $P \le .001$) (Table 2). There were, however, no significant differences between groups in the remainder of secondary outcomes, including incident delirium ($P > .10$) (Table 2), length of hospitalization, proportion of patients having 1 or more falls during hospitalization, 3-month hospital readmission rate/mortality, or patient transfer (all $P > .10$) (**Table 3**).

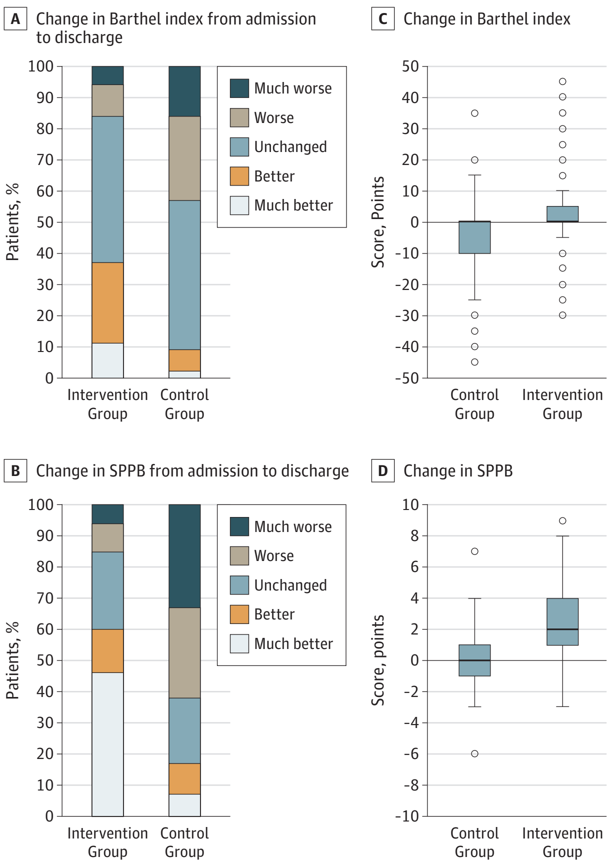
Discussion

Our study shows that an individualized, multicomponent exercise intervention including low-intensity resistance training exercises performed during a short period (mean, 5 days) provides a significant benefit over usual care and can help to reverse the functional decline associated with acute hospitalization in older adults. Acute hospitalization per se led to impairment in patients' functional ability during ADLs, whereas the exercise intervention reversed this trend. We also observed an increase in the SPPB score and handgrip strength after the intervention, with the opposite response found in the control group. We believe that this finding is also important because there is meta-analytic evidence that functional capacity and both muscle strength, as assessed by SPPB and handgrip strength, and muscle mass tend to decrease in the elderly during hospitalization (at least in electively admitted patients),[35] with muscle strength and mass being associated with disability, morbidity, and cardiometabolic disease–related mortality.[36]

Acute hospital admissions play an important role in the disabling process at the elderly years, owing to the deleterious effects of the presenting illness or injury and the hazards of hospital stay.[5] Regarding the latter, nosocomial disability is usually linked to poor mobility, with the most active patients showing lesser functional impairment than their less-active peers.[37] Thus, preservation of functional capacity, mobility, and mental capacities should be the focus of the clinical management of the elderly population with disease,[2,38] including also during acute hospitalization phases. However, a recent RCT showed no significant benefit of a simple in-hospital mobility program consisting of ambulation up to twice daily and a behavioral strategy to encourage mobility in older (mean age, 74 years) patients' ability to perform ADLs after acute hospitalization (median length of stay, 3 days).[16] Thus, our data, together with those of previous research, suggest that interventions beyond walking stimulation are needed to preserve functional capacity in older patients during acute hospitalization.

Few RCTs have evaluated the effects of exercise intervention on functional outcomes in acutely hospitalized older adults. Although in-hospital exercise interventions are virtually free of adverse events and may reduce length of stay or hospital costs, meta-analytic evidence is lacking to support the benefits of such interventions in the functional capacity of acutely ill elderly patients.[15] In this respect, our results indicate that, despite its short duration, a multicomponent exercise approach is effective in improving the functional status (measured by SPPB scale,

Figure 2. Discrete Changes From Baseline to Discharge According to Treatment Group and Within-Group Score Change Distribution for Both Groups



Changes from baseline to discharge (A and B) and within-group punctuation change distribution (C and D). A, Barthel Index changes: *much better* indicates an improvement of more than 10 points, *better* indicates an improvement of 10 or less points, *unchanged* indicates no difference, *worse* indicates a decline of 10 or less points, and *much worse* indicates a decline of more than 10 points. B, Short Physical Performance Battery (SPPB) scale: *much better* indicates an improvement of 3 or more points, *better* indicates an improvement of 2 points, *slightly better* indicates an improvement of 1 point, *unchanged* indicates no difference, and *worse* indicates a decline. Differences between the treatment groups were tested with the χ^2 test for linear trend and revealed a significant intervention effect ($P < .01$) for both the SPPB scale and Barthel Index. The proportion of patients showing overall improvement and worsening in the Barthel Index or SPBB scale was significantly higher and lower, respectively, in the intervention than in the control group (P value <.001 with χ^2 test). In the box plots, the box indicates Q1 to Q3; horizontal line within the box, median; error bars, 1.5 × interquartile range; and solid circles beyond the error bars, outliers.

Table 3. Results of Secondary End Points Indicative of Adverse Events or Hospitalization

End Point	Control (n = 185)	Intervention (n = 185)	*P* Value Between Groups
Length of hospital stay, median (IQR), d	8 (4)	8 (4)	.25[a]
Falls during hospitalization, No./No. (% per group experiencing ≥1 fall)	0/139	4/146 (2.7)	.12[b]
3-mo Hospital readmission rate (10-person/3-mo), median (IQR)	2.5 (1.8-3.3)	2.4 (1.7-3.2)	.82[c]
3-mo Mortality, %	9.7	11.9	.62[d]
Transfer, %			
Home	91.4	92.4	
Institutionalization	1.1	2.2	.55[b]
Other	7.6	5.4	

Abbreviations: ADL, activities of daily living; IQR, interquartile range.

[a] Mann-Whitney test.

[b] Fisher exact test.

[c] Mid–*P* value exact test.

[d] χ^2 Test.

Barthel Index) of very old adults. These benefits have been rarely demonstrated in the literature,[39] especially after such a short period.[37] By contrast, previous trials using early mobilization with no resistance exercises have proven beneficial in improving the functional recovery of critically ill younger adults.[40-42] It therefore seems that a more complete, multicomponent exercise intervention, such as the one described herein, particularly with the addition of resistance training, is needed to counteract the muscle weakness of older hospitalized patients, with muscle tissue deterioration being a main determinant of functional independence in the elderly years. Although beneficial effects were obtained in the ability to perform ADLs and physical performance, the intervention did not change readmission rate and mortality at 3 months. In effect, in a very old population such as ours, with a theoretically short life expectancy after hospitalization, the objective of our intervention should be to increase the quality rather than quantity of life. Future follow-up analyses might allow us to determine if our intervention can benefit patients in terms of other important outcomes, such as readmission rate, hip fracture prevention, or length of future hospitalizations.

Our results also showed significant intervention benefits at the cognitive, affective, and QoL levels. Although there is some disagreement regarding the effects of exercise interventions on the cognitive function of the elderly, it seems that multicomponent exercise training, such as the one applied in this RCT, may have the most beneficial results.[43] The intervention was, however, unable to influence the occurrence of incident delirium, which is in line with previous research.[44] Because delirium is an independent predictor of sustained poor cognitive and functional status during the year after hospitalization in the elderly,[45] future research should explore whether other in-hospital exercise interventions could perhaps have a preventive effect on the incidence of delirium.

Limitations

Our study has some limitations. The poor condition of several patients precluded assessment of change from baseline to discharge on the SPPB scale and Barthel Index in 7 (2.3%) and 19 (6.1%), respectively, of the participants who completed the intervention. This prevalence limits the generalizability of our findings to the most debilitated patients. Also, we did not collect functional and cognitive data prior to the acute illness. However, functional status 2 weeks before admission was indirectly measured with the Barthel Index score at baseline, but the risk of bias is likely to increase when retrospective information is recruited with this subjective self-report scale. In addition, this was a single RCT; thus, replication is needed in other cohorts.

Our study, nevertheless, has several strengths, including its novelty. Most exercise interventions in geriatric patients have been performed in nonacute settings, that is, at the community level, in institutionalized elders, or in those hospitalized for rehabilitation purposes. Furthermore, older patients with multiple comorbidities are routinely excluded from exercise studies owing to acute medical conditions, whereas the patients had a mean (SD) of 9 (6) comorbidities. We did not exclude patients with dementia (except for very severe cases, ie, those with the highest score [7] on the Global Deterioration Scale) or those who were unable to walk independently. Besides the very poor health status of our patients compared with those of previous RCTs evaluating acutely hospitalized elders, our study is unique in several aspects, such as the advanced age of the cohort (overall mean, 87.3 years; range, 75-101 years, with 130 patients (35.1%) being nonagenarians), the large sample size, and the innovative protocol we applied by adding specific resistance-training machines and with daily individualized adjustment of loads. To minimize potential bias, end point assessment was consistently performed following a standardized test protocol and the investigators were unaware of a patient's previous test scores when retesting.

Conclusions

An individualized, multicomponent exercise program proved to be safe and effective to reverse functional decline associated with acute hospitalization in very elderly patients. It also was shown to provide benefit in other end points, such as cognitive status and QoL. These findings open the possibility for a shift from the traditional disease-focused approach in hospital acute care units for elders to one that recognizes functional status as a clinical vital sign that can be impaired by traditional (bed rest-based) hospitalization but effectively reversed with specific in-hospital exercises.

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