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ORIGINAL ARTICLE

Functional training and timed nutrition intervention in infectious medical patients

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BACKGROUND/OBJECTIVES: Bed rest and decreased nutrition intake in hospitalized patients have been shown to impair the clinical course negatively, including reduced function after hospital stay. Recent reviews have shown that early physical rehabilitation for acute hospitalized old adults leads to functional benefits. The aim of our study was to assess whether it was possible to influence nutrition intake, loss of muscle function and quality of life, with an evidence-based intervention in acutely ill hospitalized infectious medical patients.

SUBJECTS/METHODS: For potentially frail patients, functional training three times weekly, and an individually adjusted self-training program for use 1–2 times daily, was given by a physiotherapist. Oral nutritional supplement with 5–10 g whey protein was timed straight after training 2 times daily, and dietetic advice was provided. A historical control group was used to compare nutrition intake. Functional measures and health-related quality of life (HRQoL) were done on admission and discharge.

RESULTS: The study included 59 patients in the intervention group. Historic control included 145. Energy and protein intake increased by 3053 kJ ($P < 0.001$) and 28 g of protein ($P < 0.001$), compared with historic controls. Functional parameters (De Mortons Mobility Index (DEMMI), Timed Up and Go and the 30-s chair test) and HRQoL improved significantly for the overall group, most remarkably in patients >70 years of age, from hospitalization to discharge.

CONCLUSION: The intervention with dietician and timed oral supplement to functional training by physiotherapist in hospitalized infectious medical patients improved function as well as nutrition intake and HRQoL.

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INTRODUCTION

Both nutritional risk and bed rest in hospitalized patients have been profoundly shown to impair clinical outcome negatively. Functional decline in patients during hospitalization is associated with potential long-lasting undesirable outcomes and complications including nosocomial infections, falls and pressure ulcers. Medical patients are particularly at risk of developing complications during and after hospitalization, due to physical inactivity and prolonged immobilization.[1–5] Functional decline has been strongly related to patients' age and preadmission activities of daily living status.[4,6–8] This is furthermore important for the high number of readmissions in this patient group.[4,6] Patients with longer hospital stays have been shown to be more physically inactive during hospital stay, compared with patients with shorter lengths of stay.[7] Although bed rest and consequent inactivity associated with illness and hospitalization have significant implications for medical patients, both in hospital and after discharge and rehabilitation, recent reviews showed that early physical rehabilitation care for acute hospitalized old adults leads to functional benefits.[3,9] In general, physical activity, mobilization and resistance training seem most frequently investigated in frail old patients. Thus, many studies focus primarily on frailty related to age, rather than on frailty related to acute disease.[4,6–8,10–19] Studies have overall shown that age and preexisting conditions including physical and cognitive function, comorbidity and body composition characterize older patients at high risk of functional decline during and after hospitalization. Studies related to metabolic activity and bed rest related to medical disease in any age group seem to have a lower priority.[1,3] Former studies have shown that impaired nutrition intake below 50–75% of requirements in hospitalized patients has a negative impact on clinical outcome.[20,21] Despite initiatives to fight nutritional risk in hospitals, the big breakthrough remains to be seen, especially regarding protein intake, as well as with regard to nutrition process indicators, such as nutritional screening and estimation of nutritional requirements.[20,22–26]

Although physical activity is known to gain appetite in healthy individuals, especially protein intake within a short time frame after exercise and specifically after resistance training has been shown to be beneficial in increasing muscle mass in adverse groups.[3,13,16,26,27] In hospitals, the ambulation and training of medical patients, however, seem to have an even lower priority in practice than patient nutrition intake.[7,28,29] Many barriers seem to be present regarding training and ambulation, as well as to providing nutrition for patients, even though nurses are present, and may be the relevant partner, closest to the patient.[28,30,31] The aim of our study was to assess whether it was possible to improve muscle function in acutely ill patients by an active approach based on evidence-based nutritional support and early physiotherapy, in an intervention closely integrated in the daily activities of the ward. The secondary aims were to improve health-related quality of life (HRQoL) measured by EQ5D-3L and EQ visual analog scale (VAS) and to improve process indicators for clinical nutrition.

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SUBJECTS AND METHODS

Study design

A prospective intervention study including physiotherapy and dietetic intervention was performed for a 10-month period from September 2013 to May 2014. For the nutrition intervention analysis, a retrospective control group of patient records in patients discharged from the same department for the past 3 months before intervention was included. Unfortunately, no retrospective data were given for physical activity, as physical activity in patients had a low priority in the ward before the intervention, and physiotherapy was formerly only given at specific prescription.

Description of the setting

The setting was a medical specialty ward for Infectious Diseases at Aalborg University Hospital in Denmark. This department cares for life-threatening bacterial infections, serious and rare infections, immunodeficiency diseases, HIV/AIDS and tropical diseases, among others. The ward also receives patients with specific infectious diseases requiring isolation. Furthermore, the ward takes a fraction of internal medical patients. The bed ward where the study took place includes 21 beds and 2 isolation rooms.

Participants

Inclusion criteria were in-patients who were expected to be hospitalized for a minimum of 2 days, no severe cognitive deficits, capable to collaborate and to speak and understand Danish. Exclusion criteria were contraindication assessed by the medical staff, thus, critical metabolic conditions or other severe illnesses, where the medical staff assessed that a strict resistance training program would stress disease. Furthermore, patients with terminal stage illness and patients who were routinely referred to physiotherapy and occupational therapy were excluded. The retrospective control group included all patients discharged from the department during the past 3 months up to the start of intervention. These patients were treated with general nutritional practice due to national recommendations. Thus, when patients are found to be at risk by NRS-2002, a nutritional plan and monitoring should be made. The nutritional plan mostly includes nutritional supplements. No advice or intervention was given regarding nutrition to exercise in hospital.

Interventions

The intervention was a comprehensive program for patients with functional impairment, initiated on the day of admission. It consisted of minimum three individual training sessions per week, each of 45 min, provided by an experienced physiotherapist. Individualized advice and goal setting, training program and training equipment including a pedometer were provided. The focus was on muscle strengthening exercises starting with around the assumed 50–60% rising to 70–80% of the assumed one Repetition Maximum during the sessions.[32] The patients were emphasized to self-training all other days and to use the exercise bikes and other aerobic activities.[33,34] The primary focuses of training were the large muscle groups. Two exercise bikes were installed at the ward, and pamphlets and other nudging interventions toward physical activity and improved dietary intake were provided as well.

Dietary advice was initiated at the day of inclusion, especially advice in relation to training and illness. The dietician had a dialog with each patient about barriers for adequate nutritional intake. Five to ten grams of whey protein support, providing around 100 kcal/420 kJ, was offered within 30 min after the daily training with physiotherapist to optimize the effect of training. Furthermore, the patients were offered the same amount of whey protein support supplement in the evening, preferably right after self-training, and on 'non physiotherapist' days, that is, weekends. The supplement chosen was offered with regard to individual patient preferences, in order to assure the likelihood of patients to comply with the intervention. Thus, supplementation could be provided as milk or juice-based oral nutritional supplements, milk and cocoa or fruit juice with 5 g of protein powder added. Food intake was monitored for 1–2 days. This routine has proven very difficult to implement in clinical practice.[20,22] The clinical dietician gave advice to all included patients and reported this to the staff as well on a daily basis. The patients were furthermore provided an individualized diet plan if they scored more than three points by nutrition screening with NRS-2002, as it is the practice in the hospital.[35] Recommendations for protein intake were set to 1.3 g/kg/day and energy recommendations 25 kcal/kg/day.

Inclusion

Every morning on weekdays the project physiotherapist screened the patient list at the ward, to identify newly admitted patients eligible for inclusion. Patients admitted at weekends were included in the list at the first coming weekday. Patients were hereafter discussed with the medical and nursing staff, before contacting the patient. Eligible patients were then informed about the study by the project physiotherapist and invited to participate. Immediately after consent, the clinical dietician and the staff were informed about the inclusion. The physiotherapist had her daily time on the site during weekdays and made sure that the nursing and physician staffs were continuously informed, to promote coherence.

Data from the historic control group were extracted from the electronic patient medical records.

Outcome measures

For physical condition, the primary outcome was the number of repetitions in a Sit-To-Stand 30-s test on inclusion vs discharge. The results were analyzed overall and into two groups of below and above 70 years of age.

For nutrition, the primary outcomes were energy and protein intake during intervention, compared with the historic cohort.

For physical condition, secondary outcome measures were sought at inclusion and discharge. Nutrition process indicators were compared with a historic cohort of patients discharged from the ward 3 months retrospectively from the data of intervention start.

Dietary intake monitoring method

Food intake registration was carried out by the unit nursing staff, on the diet record paper sheet, which was implemented 10 years ago, for use in daily practice. The method was furthermore used for nutrition intervention studies, including the present unit.[20,22] It has been adjusted for new food items on a regular basis. In the food registration system, food items and drinks were pre-measured for energy (calories and kilojoules) and protein (grams) and registered in a computer program. Registrations were divided into registration of three main meals, three in-between meals, other meals and drinks. Calculations for the main servings, drinks and supplements were registered by the patients or nursing staff on the paper registration schedule that was placed on the bed side table. Each food item and drink was written down on the schedule when served to, or taken by the patient. Food was registered in pieces or approximate quartile portion sizes as pre-given on the schedule, and drinks were registered in approximate milliliters, as also noted in glass and cup size on the schedule. When the patient's tray or dish was taken out, it was noted how much of the portion was taken, measured by what was left of the served portion. During the night shift, the nursing staff replaced the schedules and calculated the intake in the computer program. Results were registered on the schedule and in the patient files.

Physical condition methods and HRQoL

To measure physical condition, the patients performed the 30-s chair test, Timed Up and Go, the De Mortons Mobility Index (DEMMI) and Grip Strength, all validated and reliable measures for this population of older hospitalized patients. These measures were obtained at baseline and at discharge. DEMMI is a 15-item instrument validated to measure status and changes in mobility of older acutely hospitalized medical patients. The patients get a DEMMI score between 0 and 100, 100 being the highest mobility score.[32,36–40] Hand grip strength was measured using hand grip dynamometry, a measure that is correlated with nutritional status, mortality and disability using a SAEHAN Hand Dynamometer (North Coast Medical Hydraulic Hand Dynamometer, Canada).[41,42] HRQoL was measured at baseline by EQ5D-3L.[43,44] EQ5D-3L descriptive system comprises the following five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression.

Statistics

Descriptive statistics included number and percentage of patients for categorical variables and mean and standard deviation for continuous variables.

To evaluate the dietary intervention, the intervention group was compared with the historic control group. Differences in categorical variables between the two groups were evaluated by Fisher's exact test, and differences in continuous variables were evaluated by the unpaired *t*-test. To evaluate the exercise intervention, the test results before the

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intervention were compared with the test results after the intervention both for the whole group and for the two subgroups—above and below age 70. Differences in the test results before and after the intervention were evaluated by the paired *t*-test. The normality assumption for the paired *t*-test was assessed by Q-Q plots, and, when the Gaussian distribution of a variable could be questioned, the Wilcoxon signed rank test was applied. It was decided to only report the results of the paired *t*-tests, as the Wilcoxon signed rank test did not alter the conclusions of the *t*-tests.

The answers to the five EQ5D questions have been converted into a single score of quality of life according to Danish standards.[45,46]

Throughout 95% confidence intervals (CI) were reported and *P*-values less than 0.05 were considered as statistically significant. Statistical analyses were performed with Stata Version 13 (Stata Corporation, College Station, TX, USA).

Diagnoses

The patient diseases were stratified into diagnoses inspired by the MRDx (most responsible diagnosis).[47]

Ethical considerations

Before inclusion, the patients were given written and oral information about the study. The participants were informed that they could withdraw from participation at any time during the study. The study was conducted according to the rules of the Helsinki Declaration of 2002. The study was put forward to the local ethic committee of Region North Denmark. The study was approved by The Danish Data Protection Agency (number 2008-58-0028).

RESULTS

Demographic information

The intervention study included 59 patients, 28 female and 31 male. Mean age was 66.2 (s.d. 15.7). Only 14 of the patients were below 60 years of age. Body mass index was 25.6 (s.d. 5.4). The included participants were hospitalized for an average of 8.7 days (s.d. 5.6).

The retrospective cohort included 145 patients. Compared with the intervention group, these patients were younger, aged 57.4 years (s.d. 22.6) ($P < 0.007$). All other demographic parameters were not statistically different from the intervention group, even though length of stay was only 7.4 days ($P < 0.92$). The most common causes for hospitalization were 'Injury, poisoning and other consequences of external causes', which included tropical infections, tuberculosis and HIV/AIDS. The groups were otherwise comparable with regard to demographic information, as shown in Table 1.

Nutritional parameters

The intervention study found a statistically significant improvement in energy and protein intake, compared with the retrospective controls. In the overall group of patients, there was a statistically significant improvement in the fulfilling of 75% of energy and protein requirements. For the group of patients at nutritional risk, the fulfillment of requirements by the cutoff value of 75% improved remarkably, especially for protein; however, the numbers were overall too low to make meaningful statistics for this stratification. There was no significant increase for nutritional process indicators, as screening and measuring requirements. Table 2 shows the results for nutritional parameters.

Functional parameters

Overall, the 30-s chair stand test improved significantly in the group between baseline and discharge with approximately three more repetitions at discharge, and most importantly the number of repetitions was above eight.[48] Patients above 70 years of age had an average difference of 2.4 (95% CI 1.4–3.4) more repetitions at discharge. The Timed up and go did also improve in the group overall. In the subgroup below 70, the mean difference was decreased with 4.6 s, whereas the decrease in the subgroup above 70 was 2.7s (95% CI −4.6 to −0.9) , both statistically significant. DEMMI scores improved statistically significantly for the overall group, as for both below and above 70 years of age. The hand grip

Table 1. Demographic information of patients in intervention study and historic cohort

	Intervention group, n	*Historic cohort for nutritional parameters, n*	P-*value*
Total number of participants (Female %)	59 (47)	145 (48)	
Age, mean (s.d.)	66.2 (15.7)	57.4 (22.6)	0.007
Height in cm, mean (s.d.)	171.5 (8.7)	170.3 (9.7)	0.417
Weight in kg, mean (s.d.)	75.6 (17.9)	74.8 (24.6)	0.831
BMI, mean (s.d.)	25.6 (5.4)	25.7 (7.9)	0.939
BMI groups			
< 18.5	1	6	7
18.5–20.4	8	14	22
20.5–24.9	17	41	58
25.0–29.9	22	28	50
30.0–34.9	3	11	14
> 35	3	11	14
Missing data	5	34	39
Diagnoses (MRDx): N (%)			
Certain infections and parasitic diseases (A00-B99)	3 (5)	25 (17)	
Neoplasms (C00-D48)	3 (5)	8 (6)	
Diseases in the respiratory system (J00-J99)	18 (31)	26(18)	
Diseases in the circulatory system (I00-I99)	5 (8)	16 (11)	
Injury, poisoning and other consequences of causes (tropical infections, TB, HIV/AIDS) (S00-T98)	23 (39)	43 (30)	
Others: Muscle pain, Immunodeficiency's, Arthritis	7 (12)	27 (18)	
LOS, mean (s.d.)	8.7 (5.6)	7.4 (5.8)	0.9169

Abbreviations: BMI, body mass index; LOS, length of stay; MRDx, most responsible diagnosis.

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Table 2. Nutritional parameters before and after intervention

	Intervention	*Retrospective controls*	*Difference (95% CI) intervention - control*	P-*value*
Participants included, *N*	59	145		NA
Screening for nutritional risk by NRS-2002, *N* (%)	47 (80)	108 (74)		0.586
Nutritional risk by NRS-2002 screening, *N* (%)	14 (29)	33 (30.5)		0.337
Energy intake, kJ (± s.d.)	8470 (±2274)	5417 (±2476)	3053 (1657; 4449)	< 0.001
Protein intake, g (± s.d.)	72 (±20)	43 (±21)	28 (16; 41)	< 0.001
Energy requirements kJ, mean (± s.d.)	8498 (±1648)	8061 (±1478)	437 (−519; 1395)	0.364
Protein requirements, g (± s.d.)	93 (±18)	86 (±15)	7 (−4; 17)	0.197
Energy requirements fulfilled (% fulfillment)	103 (±32)	71 (±41)	32 (11; 53)	0.004
Protein requirements fulfilled (% fulfillment)	80 (±24)	53 (±31)	27 (11; 42)	0.001
Energy requirements > 75% fulfilled, % (*N*)	84 (32)	44 (7)		0.006
Protein requirements > 75% fulfilled, % (*N*)	63 (24)	13 (2)		0.001

Abbreviations: CI, confidence interval; NA, not applicable.

Table 3. Comparison of functional parameters at discharge vs baseline

Test	*N*	*Baseline*		*Discharge*		*Difference (95% CI)*	*T-test*
		Mean	s.d.	*Mean*	s.d.		P-*value*
Sit-to-Stand 30 s	48	7.0	4.8	9.8	5.2	2.9 (2.0–3.7)	< 0.001
⩽70 years	28	7.6	4.8	10.8	5.0	3.2 (1.9-4.5)	< 0.001
>70 years	20	6.1	4.9	8.5	5.4	2.4 (1.4–3.4)	< 0.001
Timed Up and Go	45	15.2	12.1	11.6	8.5	−3.6 (−6.4 to −0.8)	0.012
⩽70 years	26	12.9	11.8	8.6	3.0	−4.2 (−9.0–0.5)	0.080
>70 years	19	18.3	12.2	15.6	11.6	−2.7 (−4.6 to −0.9)	0.005
DEMMI	50	64.4	20.5	73.1	18.6	8.7 (5.3–12)	< 0.001
⩽70 years	29	70.5	20.3	79.2	17.2	8.7 (3.9–13.5)	0.001
>70 years	21	56.0	18.1	64.5	17.4	8.6 (3.6–13.5)	0.002
Grip strength	49	27.7	12.7	27.7	13.0	0.1 (−1.4–1.7)	0.929
⩽70 years	28	31.4	12.4	30.8	13.4	−0.6 (−3.2–2.0)	0.632
>70 years	21	22.8	11.4	23.8	11.6	1.0 (−1.0–2.9)	0.304

Abbreviations: CI, confidence interval; DEMMI, De Mortons Mobility Index.

strength maintained the same levels from admission to discharge (Table 3).

HRQoL measured by EQ5D-3L

HRQoL by EQ5D increased statistically significantly for both index and VAS scores, regardless of age groups after intervention on nutrition and physical activity. The mean health state EQ5D index score was 0.10 (s.d. 0.18) higher at discharge ($P < 0.001$). Mean VAS raised as well significantly ($P < 0.001$).

The following dimensions mobility, self-care and usual activities showed improvement at discharge in both age groups. Best improvements were seen in the dimension of mobility, and for the age group above 70 years there were remarkable improvements in Self-care and Usual activity. Table 4 shows HRQOL by EQ5D-3L at baseline and discharge, also illustrated in Figure 1.

No adverse effects were observed during the study period. Only one patient was assessed by physicians as not eligible for inclusion.

DISCUSSION

This study aimed to improve energy and protein intake and improve function in patients admitted to a medical hospital ward for infectious diseases, in a Danish University Hospital. The intervention furthermore aimed at integration in the everyday life of the ward, involving physicians and nurses in the decision-making of the ability of patients to be included and hence improving the spillover effect to benefit further strategies after the project period.

The study method was an intervention study, including baseline and follow-up measurements for functional parameters, and a historical group for comparison of nutritional data. The historical control group was chosen, as patients were most often not hospitalized long enough to make it possible to see a difference in nutrition intake before and after intervention. As functional training was not formerly done, these parameters were not found in the patient records. Thus, historic comparison for these data was not possible. In practice, we prioritized functional training to patients by giving more hours to functional training and physiotherapy, than to dietician support, because there was already awareness to patients' nutritional status and intake, and because the training program was found to be more time-consuming if need to be efficient. Furthermore, patients were monitored for nutrition intake for full days, and knowing the difficulties in monitoring nutrition intake, consequently, we found it safest with regard to data to include whole calendar days, although most patients would actually monitor nutrition intake from the time of dietetic guidance.[20]

The patients in our studied intervention group were hospitalized for an average of 8.7 days, which was statistically comparable to the retrospective control group, who were hospitalized for 7.4 days. The abbreviated MRDx diagnosis system in this study was chosen, as we found it difficult to find a diagnosis system that did not have too many diagnosis codes and yet was able to capture the tropical and other infectious diseases in this specialty.

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Table 4. Health-related quality of life measured by EQ5D-3L and EQ VAS at baseline and discharge

Test	*Baseline*	*Discharge*	*Difference*	*T-test*
EQ5D-3L index score (0–1), mean (s.d.)	0.63 (±0.21)	0.73 (±0.15)	0.10	< 0.001
EQ VAS (s.d.)	51.55 (±19.88)	62.06 (±19.55)	10.51	< 0.001

EQ5D-3L profile	*Mobility*		*Self-care*		*Usual activities*		*Pain/Discomfort*		*Anxiety/Depression*	
	Baseline	*Discharge*	*Baseline*	*Discharge*	*Baseline*	*Discharge*	*Baseline*	*Discharge*	*Baseline*	*Discharge*
No problems, *N* (%)	12 (20)	25 (42)	34 (58)	37 (63)	7 (12)	15 (25)	11 (19)	11 (19)	44 (75)	40 (68)
Some problems, *N* (%)	42 (71)	25 (42)	19 (32)	13 (22)	34 (58)	33 (56)	37 (63)	37 (63)	10 (17)	9 (15)
Extreme problems, *N* (%)	1 (2)	0 (0)	2 (3)	0 (0)	14 (24)	2 (3)	7 (12)	2 (3)	1 (2)	1 (2)
Missing	4 (7)	9 (15)	4 (7)	9 (15)	4 (7)	9 (15)	4 (7)	9 (15)	4 (7)	9 (15)
Total, *N*	59	59	59	59	59	59	59	59	59	59

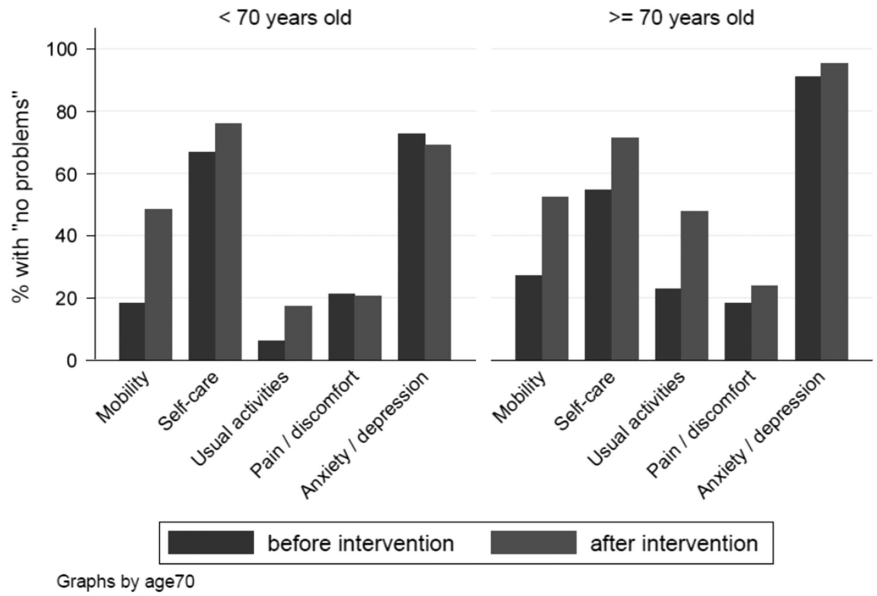

Figure 1. The distribution of problems related to the five dimensions of HRQoL measured with the EQ5D-3L, before and after the intervention, in two groups, below and above the age of 70.

We found the system easy to use and also very relevant for the population.[47]

Compared with historical data, the intervention significantly improved energy and protein intake. The individualized energy and protein supplement recommended to both groups in relation to training, and individual dietetic guidance for patients, thereby proved to be efficient. Unfortunately, in the nutrition monitoring, we did not separate energy and protein by nutritional supplements from those from consumption of normal food. In hindsight, this division would have been beneficial, as it might have given a better idea of the relation between functional improvements and timed nutritional supplementation.[13,19,24]

Functional parameters

In the present study, hospitalized patients suffering from acute infectious disease had functional training, targeting muscle strength and functional mobility. As most of the former evidence has taken interest in patients at old age, we decided to differentiate the results into ± 70 years of age, besides the total group. The primary outcome '30 s chair stand test' improved significantly overall and in both age subgroups. The test has formerly shown to be well correlated to muscle strength in quadriceps and functional ability and a feasible way of measuring these important aspects. In a large study, it was shown that the threshold value for the Sit-to-Stand 30-s test in relation to loss of functional mobility was 8 repetitions.[49] The mean number of repetitions for this study population was 9.8 at discharge from a starting point of 7.0 at admission and therefore a very important clinical relevant finding. We did not experience problems in the patients rising from chair, as seen in the recent study by Bodilsen *et al*.[48]

The timed-up-and-go test showed overall statistically significant improvements, and this was also the case in both age subgroups; however, none of the values decreased to the reference values for the respective age groups.[37] As this population was in-patients admitted because of illness, this may not be a surprising finding, and the improvements are highly relevant and show that the interventions surely may have contributed strongly to the quite large improvement.

The DEMMI score was validated in older acute medical patients and is thus a reliable tool for estimating the outcome of physical training in this group.[38,50] In our study, we found a clear and important positive improvement in DEMMI functional scores, and

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the improvement is close to the defined minimal clinical important difference.[39] The improvement in this study is in contrasts to the lacking effect of exercise on functional outcome found in the review by de Morton *et al*.[50] However, the review included only randomized controlled trials, whereas we chose a practice similar to the intervention study, giving the possibility more likely to implement strategies afterwards. Maybe even more important, we offered nutritional supplementation in the sensitive period just after training, as found in other studies, where it was indicated that aerobic exercise increases the anabolic effect of nutrient intake in older adults, by an exercise-induced improvement in nutrient-stimulated vasodilatation and nutrient delivery to muscle, formerly improving muscle strength.[13,19]

Hand grip strength and 30 s chair stand were recently tested in acutely admitted older Danish medical patients.[48] Functionally, a wide range was shown in our participants. The heterogeneity was even more pronounced at discharge. Only grip strength, which was included as it has shown to be a significant predictor for evaluation of loss of function, did not show improvements. In the study by Munk *et al*.,[25] the authors found that underpower may be one of the reasons why they did not detect differences between groups regarding hand grip strength and a 6-month nutrition intervention. This might also influence our results; however, only the >70-year olds show a trend to improvement. Meanwhile, the focus of the training intervention was primarily the larger muscle groups and a certain delay might be to grip strength. The nutrition intervention only lasted for a period of days, and the effect to hand grip strength has furthermore been questioned.[25]

Health-related quality of life

This study showed that HRQoL measured with the EQ5D-3L improved for both age groups below and above 70 years after intervention on nutrition and physical activity. Although EQ5D was not validated in infectious medical patients, it has been greatly supported in many other disease groups and is an amended tool in background population studies in Denmark.[46] The high response rates achieved 93% at baseline and 85% at follow-up suggest that the EQ5D instrument may be acceptable to this clinical population. In our study, the mean EQ5D index score raised from 0.63 to 0.73 during intervention. Compared with a random sample from the general Danish population, which found the mean EQ5D index score ranging 0.83 for 70–79 year olds, this is relatively low, which could be expected in the hospitalized patients suffering from acute disease.[46] Furthermore, the minimum clinically important difference for EQ5D mean is 0.074, which indicates a clinically relevant difference of the chances of HRQoL in this population after intervention.[45]

As this is a longitudinal study with no randomization and control group confounders similar to medical illness, other interventions at the ward, for example, might have influenced the improvements seen. Therefore, the results of the study should be interpreted with caution, especially in relation to external validity. Future studies with a randomized controlled design would confirm results and may give a more detailed explanation on causal factors. However, the results of the study underline that an active strategic approach targeting food intake and physical activity in admitted medical patients lead to clinically important improvements.

CONCLUSIONS

An intervention with nutritional support including 5–10 g of whey protein support right after functional training two times daily, dietetic advise and early functional training by physiotherapist in infectious medical patients positively influenced intake of energy and protein, and function measured by the 30-s chair stand test, Timed Up and Go and DEMMI scores. HRQoL improved for all parameters, within the days of training. Caution must of course be taken to interpret these results as being exclusively due to training accompanied by nutrition supplementation, as other factors, including medical therapy, exert considerable influence.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1 Bodilsen AC, Pedersen MM, Petersen J, Beyer N, Andersen O, Smith LL *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.
2 Kiens B, Beyer N, Brage S, Hyldstrup L, Ottesen LS, Overgaard K *et al.* Physical inactivity--consequences and correlations. *Ugeskr Laeger* 2007; **169**: 2442–2445.
3 Pashikanti L, Von Ah D. Impact of early mobilization protocol on the medical-surgical inpatient population: an integrated review of literature. *Clin Nurse Spec* 2012; **26**: 87–94.
4 Volpato S, Onder G, Cavalieri M, Guerra G, Sioulis F, Maraldi C *et al.* Characteristics of nondisabled older patients developing new disability associated with medical illnesses and hospitalization. *J Gen Intern Med* 2007; **22**: 668–674.
5 Covinsky KE, Pierluissi E, Johnston CB. Hospitalization-associated disability: 'She was probably able to ambulate, but I'm not sure'. *JAMA* 2011; **306**: 1782–1793.
6 Callen BL, Mahoney JE, Wells TJ, Enloe M, Hughes S. Admission and discharge mobility of frail hospitalized older adults. *Medsurg Nurs* 2004; **13**: 156–163. quiz 164.
7 Fisher SR, Goodwin JS, Protas EJ, Kuo YF, Graham JE, Ottenbacher KJ *et al.* Ambulatory activity of older adults hospitalized with acute medical illness. *J Am Geriatr Soc* 2011; **59**: 91–95.
8 Fisher SR, Kuo Y, Graham JE, Ottenbacher KJ, Ostir GV. Early ambulation and length of stay in older adults hospitalized for acute illness. *Arch Intern Med* 2010; **170**: 1942.
9 Kosse NM, Dutmer AL, Dasenbrock L, Bauer JM, Lamoth CJ. Effectiveness and feasibility of early physical rehabilitation programs for geriatric hospitalized patients: a systematic review. *BMC Geriatr* 2013; **13**: 107.
10 Pedersen MM, Bodilsen AC, Petersen J, Beyer N, Andersen O, Lawson-Smith L *et al.* Twenty-four-hour mobility during acute hospitalization in older medical patients. *J Gerontol A Biol Sci Med Sci* 2013; **68**: 331–337.
11 Callen BL, Mahoney JE, Grieves CB, Wells TJ, Enloe M. Frequency of hallway ambulation by hospitalized older adults on medical units of an academic hospital. *Geriatr Nurs* 2004; **25**: 212–217.
12 de Morton NA, Keating JL, Berlowitz DJ, Jackson B, Lim WK. Additional exercise does not change hospital or patient outcomes in older medical patients: a controlled clinical trial. *Aust J Physiother* 2007; **53**: 105–111.
13 Esmarck B, Andersen JL, Olsen S, Richter EA, Mizuno M, Kjaer M. Timing of postexercise protein intake is important for muscle hypertrophy with resistance training in elderly humans. *J Physiol* 2001; **535**: 301–311.
14 Guralnik JM, Ferrucci L, Pieper CF, Leveille SG, Markides KS, Ostir GV *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**: M221–M231.
15 Mudge AM, Giebel AJ, Cutler AJ. Exercising body and mind: an integrated approach to functional independence in hospitalized older people. *J Am Geriatr Soc* 2008; **56**: 630–635.
16 Rice KL. Geriatric best practices in nursing: optimizing functional independence. *J Vasc Nurs* 2003; **21**: 151–152.
17 So C, Pierluissi E. Attitudes and expectations regarding exercise in the hospital of hospitalized older adults: a qualitative study. *J Am Geriatr Soc* 2012; **60**: 713–718.

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18 Sullivan DH, Wall PT, Bariola JR, Bopp MM, Frost YM. Progressive resistance muscle strength training of hospitalized frail elderly. *Am J Phys Med Rehabil* 2001; **80**: 503–509.
19 Timmerman KL, Dhanani S, Glynn EL, Fry CS, Drummond MJ, Jennings K *et al.* A moderate acute increase in physical activity enhances nutritive flow and the muscle protein anabolic response to mixed nutrient intake in older adults. *Am J Clin Nutr* 2012; **95**: 1403–1412.
20 Holst M, Mortensen MN, Jacobsen BA, Rasmussen HH. Efficacy of serving bedside in-between meals - An intervention study in three medical departments. *ESPEN J* 2010; **5**: e30–e36.
21 Holst M, Yifter-Lindgren E, Surowiak M, Nielsen K, Mowe M, Carlsson M *et al.* Nutritional screening and risk factors in elderly hospitalized patients: association to clinical outcome? *Scand J Caring Sci* 2013; **27**: 953–961.
22 Holst M, Beermann T, Mortensen MN, Skadhauge LB, Lindorff-Larsen K, Rasmussen HH. Multi-modal intervention improved oral intake in hospitalized patients. A one year follow-up study. *Clin Nutr* 2014; **34**: 315–322.
23 Holst M, Staun M, Kondrup J, Bach-Dahl C, Rasmussen HH. Good Nutritional Practice in Hospitals during an 8-year period: The impact of accreditation. *ESPEN J* 2014; **9**: e155–e160.
24 Cermak NM, Res PT, de Groot LC, Saris WH, van Loon LJ. Protein supplementation augments the adaptive response of skeletal muscle to resistance-type exercise training: a meta-analysis. *Am J Clin Nutr* 2012; **96**: 1454–1464.
25 Munk T, Beck AM, Holst M, Rosenbom E, Rasmussen HH, Nielsen MA *et al.* Positive effect of protein-supplemented hospital food on protein intake in patients at nutritional risk: a randomised controlled trial. *J Hum Nutr Diet* 2014; **27**: 122–132.
26 Clark PG, Blissmer BJ, Greene GW, Lees FD, Riebe DA, Stamm KE. Maintaining exercise and healthful eating in older adults: the SENIOR project II: study design and methodology. *Contemp Clin Trials* 2011; **32**: 129–139.
27 English KL, Paddon-Jones D. Protecting muscle mass and function in older adults during bed rest. *Curr Opin Clin Nutr Metab Care* 2010; **13**: 34–39.
28 Doherty-King B, Yoon JY, Pecanac K, Brown R, Mahoney J. Frequency and duration of nursing care related to older patient mobility. *J Nurs Scholarsh* 2014; **46**: 20–27.
29 Villumsen M, Jorgensen MG, Andreasen J, Rathleff MS, Molgaard CM. Very low levels of physical activity in older patients during hospitalization at an acute geriatric ward - a prospective cohort study. *J Aging Phys Act* 2014; **23**: 542–549.
30 Doherty-King B, Bowers BJ. Attributing the responsibility for ambulating patients: a qualitative study. *Int J Nurs Stud* 2013; **50**: 1240–1246.
31 Padula CA, Hughes C, Baumhover L. Impact of a nurse-driven mobility protocol on functional decline in hospitalized older adults. *J Nurs Care Qual* 2009; **24**: 325–331.
32 Bohannon RW. Test-retest reliability of the five-repetition sit-to-stand test: a systematic review of the literature involving adults. *J Strength Cond Res* 2011; **25**: 3205–3207.
33 American College of Sports Medicine Position Stand. Exercise and physical activity for older adults. *Med Sci Sports Exerc* 1998; **30**: 992–1008.
34 American College of Sports Medicine Position Stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. *Med Sci Sports Exerc* 1998; **30**: 975–991.
35 Kondrup J, Rasmussen HH, Hamberg O, Stanga ZAd Hoc ESPEN Working Group. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. *Clin Nutr* 2003; **22**: 321–336.
36 Braden HJ, Hilgenberg S, Bohannon RW, Ko MS, Hasson S. Gait speed is limited but improves over the course of acute care physical therapy. *J Geriatr Phys Ther* 2012; **35**: 140–144.
37 Bohannon RW. Reference values for the timed up and go test: a descriptive meta-analysis. *J Geriatr Phys Ther* 2006; **29**: 64–68.
38 de Morton NA, Berlowitz DJ, Keating JL. A systematic review of mobility instruments and their measurement properties for older acute medical patients. *Health Qual Life Outcomes* 2008; **6**: 44.
39 de Morton NA, Davidson M, Keating JL. Validity, responsiveness and the minimal clinically important difference for the de Morton Mobility Index (DEMMI) in an older acute medical population. *BMC Geriatr* 2010; **10**: 72.
40 Laan W, Zuithoff NP, Drubbel I, Bleijenberg N, Numans ME, de Wit NJ *et al.* Validity and reliability of the katz-15 scale to measure unfavorable health outcomes in community-dwelling older people. *J Nutr Health Aging* 2014; **18**: 848–854.
41 Bohannon RW. Hand-grip dynamometry predicts future outcomes in aging adults. *J Geriatr Phys Ther* 2008; **31**: 3–10.
42 Massy-Westropp NM, Gill TK, Taylor AW, Bohannon RW, Hill CL. Hand Grip Strength: age and gender stratified normative data in a population-based study. *BMC Res Notes* 2011; **4**: 127.
43 Sorensen J, Sorensen JB, Skovgaard T, Bredahl T, Puggaard L. Exercise on prescription: changes in physical activity and health-related quality of life in five Danish programmes. *Eur J Public Health* 2011; **21**: 56–62.
44 Petrou S, Hockley C. An investigation into the empirical validity of the EQ-5D and SF-6D based on hypothetical preferences in a general population. *Health Econ* 2005; **14**: 1169–1189.
45 Walters SJ, Brazier JE. Comparison of the minimally important difference for two health state utility measures: EQ-5D and SF-6D. *Qual Life Res* 2005; **14**: 1523–1532.
46 Wittrup-Jensen KU, Lauridsen JT, Gudex C, Brooks R, Pedersen KM. Estimating Danish EQ-5D tariffs using the Time Trade-off (TTO) and visual analogue scale (VAS) methods. In: Norinder AL, Pedersen KM, Roos P (eds). EuroQol Plenary Meeting Copenhagen 6-7 September 2001. IHE, Lund 2002, pp 257–292.
47 Lee EJ, Hwang SH, Lee JA, Kim Y. Variations in the hospital standardized mortality ratios in Korea. *J Prev Med Public Health* 2014; **47**: 206–215.
48 Bodilsen AC, Juul-Larsen HG, Petersen J, Beyer N, Andersen O, Bandholm T. Feasibility and inter-rater reliability of physical performance measures in acutely admitted older medical patients. *PLoS One* 2015; **10**: e0118248.
49 Rikli RE, Jones CJ. Development and validation of criterion-referenced clinically relevant fitness standards for maintaining physical independence in later years. *Gerontologist* 2013; **53**: 255–267.
50 de Morton NA, Keating JL, Jeffs K. Exercise for acutely hospitalised older medical patients. *Cochrane Database Syst Rev* 2007; **24**: CD005955.

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