



EFFECT OF PHYSIOTHERAPY ON REGAINING INDEPENDENT WALKING IN PATIENTS WITH INTENSIVE-CARE-UNIT-ACQUIRED MUSCLE WEAKNESS: A COHORT STUDY

Simone THOMAS, PT, PhD^{1#}, Jan MEHRHOLZ, PT, PhD^{1#}, Ulf BODECHTEL, MD² and Bernhard ELSNER, PT, PhD³
 From the ¹Wissenschaftliches Institut, Private Europäische Medizinische Akademie der Klinik Bavaria in Kreischa, ²Comprehensive Sepsis Center Dresden/Kreischa, Klinik Bavaria in Kreischa, Kreischa and ³Department of Public Health, Medical Faculty, TU Dresden, Germany
 #These authors contributed equally to this publication.

Objectives: To describe physiotherapeutic interventions used in the post-acute inpatient rehabilitation of chronic critically ill patients with intensive-care-unit-acquired muscle weakness, and to determine the influence of such interventions on patients' ability to walk.

Methods: Chronic critically ill patients with intensive-care-unit-acquired muscle weakness who were in post-acute and rehabilitation units were included in a cohort study. During post-acute rehabilitation, the patients' functional status at baseline, all daily physiotherapeutic interventions, and ability to walk were documented.

Results: A total of 150 patients were investigated. In patients who regained walking ability, the most frequent interventions in the first 2 weeks of post-acute rehabilitation were practicing walking, sit-to-stand training, and balance training while sitting (total time per week: 48.03 (standard deviation (SD) 41.10), 20.13 (SD 21.12), and 12.37 (SD 26.95) min, respectively). The most frequent interventions in those who did not regain walking ability were passive-assistive movements, sit-to-stand training, and balance training while sitting (total time per week: 15.29 (SD 22.93), 15.15 (SD 22.75), and 14.85 (SD 16.99) min, respectively). The time spent walking increased the chance of regaining walking ability (adjusted hazard ratio=1.017 per min walking, $p < 0.0001$).

Conclusion: These results suggest that physiotherapy interventions in the rehabilitation of chronic critically ill patients with intensive-care-unit-acquired muscle weakness may stimulate walking function.

Key words: critical care; rehabilitation; walking; physical therapy modalities.

Accepted Sep 6, 2019; Epub ahead of print Sep 23, 2019

J Rehabil Med 2019; 51: 797–804

Correspondence address: Jan Mehrholz, Wissenschaftliches Institut, Private Europäische Medizinische Akademie der Klinik Bavaria in Kreischa GmbH, An der Wolfsschlucht 1-2, 01731 Kreischa, Germany. E-mail: jan.mehrholz@klinik-bavaria.de

Stay in an intensive care unit (ICU) may be associated with long-term impairments, such as ICU-acquired muscle weakness (ICUAW) and participation in life situations (1). Consequently the Society of Cri-

LAY ABSTRACT

The aim of this study was to describe physiotherapeutic interventions during post-acute inpatient rehabilitation of chronic critically ill patients with intensive-care-unit-acquired muscle weakness, and to determine the relationship of such interventions with patients' recovery of walking ability. The study included 150 patients with chronic critical illness and acquired muscle weakness, and documented what interventions physiotherapists applied during rehabilitation and how well patients regained walking function. The most frequent interventions in the first 2 weeks of rehabilitation in patients who regained walking ability were: practicing walking, sit-to-stand training, and balance training while sitting. In those who did not regain walking ability the most frequent interventions were: passive-assistive movements, sit-to-stand training, and balance training while sitting. The time spent walking in physiotherapy was correlated with walking function. Physiotherapy in the rehabilitation of chronically critically ill patients with intensive-care-unit-acquired muscle weakness may be correlated with achieving independent walking.

tical Care Medicine (SCCM) recommends improving the continuity of care for ICU survivors, involving comprehensive treatment, such as physiotherapy, occupational and cognitive therapies during all phases of recovery (2). People with severe ICUAW may take months to improve their physical and mental function (1, 3), and recent studies have shown that ICUAW may have longer-term consequences, beyond the acute phase (7–14 days) (2, 4). For example, ICUAW may be part of post-intensive care syndrome, including physical, mental, and cognitive dysfunction, which extends beyond the acute hospitalization phase and has a major impact on quality of life in ICU survivors (4).

Some researchers have found that ICUAW is independently associated with post-ICU mortality and with clinically relevant lower physical functioning at 6 months after discharge from the ICU (5). Other studies have shown that the presence of ICUAW at discharge from the ICU is associated with poor long-term outcome, e.g. health-related quality of life (6–8). Longitudinal studies have described the recovery of critically ill people with relatively short stays in the ICU (1, 5, 9–11). However,

there are fewer studies of chronic critically ill patients (12), defined as >21 days ICU-treatment including more than 6 h of mechanical ventilation daily (13, 14).

The amount, intensity and frequency of physical rehabilitation is regarded as an important part of motoric recovery, such as regaining walking, e.g. after stroke (15, 16). Overall, it is suggested that increasing the intensity of, and time spent in, rehabilitation may have favourable outcomes (17). Some studies have described the content and amount of physical rehabilitation and applied therapies for people with ICUAW. For example, in 2012 Berney et al. described the goals and detailed interventions, such as manual hyperinflation, positioning and manual techniques of respiratory physiotherapy management in the acute phase in the ICU in Australia (18). In a recently published cohort study out-of-bed rehabilitation in 4 metropolitan hospitals was described (19). The authors concluded that out-of-bed rehabilitation was not commonly provided in patients who presented with ICUAW (19).

Another example is the approach of early mobilization in critically ill adults (20). In a survey in academic ICUs in Canada (20) both physicians and physiotherapists underestimated the incidence of ICUAW and felt inadequately trained to mobilize patients receiving mechanical ventilation.

All of these studies, however, described current practice in the acute and subacute hospitals or subacute weaning centres. However, little is known about the interventions that physiotherapists apply during post-acute inpatient rehabilitation in chronic critically ill patients with ICUAW.

In 2019, Schreiber et al. found that patients who achieved more demanding programme steps in physiotherapy showed higher weaning success, and that physiotherapy interventions were an important predictor of successful weaning (21). However, there is a lack of studies that describe the specific contents and type of physical rehabilitation and applied therapies in people with ICUAW who are chronically critically ill and there is no evidence-based standard for what type of therapy interventions should be mandatory.

To date, there is no published research on the influence of time, intensity, frequency, type and amount of rehabilitation interventions in chronic critically ill people with ICUAW.

The aim of this study was therefore to describe all physiotherapeutic interventions during post-acute inpatient rehabilitation for chronic critically ill patients with ICUAW.

The hypothesis for this study was that specific types of physiotherapy in the rehabilitation of chronic critically ill patients with ICUAW might be related to the achievement of independent walking.

Furthermore, from the clinical point of view, mobilizing seriously ill persons may be stressful for physiotherapists and therefore the type of interventions chosen may be limited to less-demanding modalities. To our knowledge there has been no research into people with ICUAW who are chronic critically ill. A secondary aim of the current study was therefore to evaluate the perceived stress levels among physiotherapists during therapy of patients with ICUAW.

METHODS

Study design

Data were collected as part of a single-centre cohort study that aimed to describe the time course of recovery of patients with ICUAW.

The study was conducted according to the Declaration of Helsinki and approval was obtained from the local ethics commission (Sächsische Landesärztekammer, EK-BR-32/13-1/106755). The study was registered prior to publication (German Register of Clinical Trials, DRKS00006528). The STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines were followed in performing this study and writing this paper.

Patients and setting

All patients admitted to the post-acute ICU, weaning and early rehabilitation departments, Klinik Bavaria Kreischa, Germany, between January 2013 and March 2015 were screened (14). The post-acute department integrates specialized weaning and mobilization and rehabilitation approaches for patients immediately after discharge from the acute stage and ICU hospitals. Patients in this cohort were admitted to this setting after an acute ICU treatment of more than 3 weeks, e.g. carried over transferred from University Hospital Dresden.

Based on the inclusion and exclusion criteria listed below, patients were recruited to the post-acute rehabilitation department, as described previously (14).

Inclusion criteria

- Patient is in the post-acute phase and is *chronically* critically ill, defined as >21 days ICU-treatment including mechanical ventilation and at least 14 additional days of ICU treatment (13, 14).
- ICUAW, defined as a Medical Research Council (MRC) total score (upper and lower limb) <48 points (22).
- Muscle weakness pathology, e.g. a clinical diagnosis of critical illness myopathy (CIM) and/or critical illness polyneuropathy (CIP).
- Aged 18 years or older.
- Richmond Agitation Sedation Scale (RASS) score of -1 to 2 (23).
- Written informed consent of the patient or his/her legal guardian.

Exclusion criteria

- Patients receiving palliative care.
- Co-morbidities of the trunk or lower limbs interfering with upright posture and walking (e.g. amputation or fracture of lower limb).

- Other neuromuscular or neurological disease and/or syndromes causing weakness, e.g. Guillain-Barré syndrome, myasthenia gravis, porphyria, Lambert-Eaton syndrome, amyotrophic lateral sclerosis, vasculitic neuropathy, cervical myelopathy and botulism.
- Severe physical co-morbidity before becoming critically ill (e.g. frailty due to neurological conditions, and not able to sit-to-stand or walk).

Interventions

All patients received individual rehabilitation from the first day of admission to the post-acute ICU and rehabilitation units. Rehabilitation included physiotherapy and occupational therapy every weekday, for approximately 60 min for each type of therapy, in addition other appropriate therapies. All patients received individual treatment plans according to their individual goals, such as regaining walking function and activities of daily living (ADL). The content and intensity of therapies and approaches were, however, dependent on the severity of critical illness and individual goals. It was not possible to measure the content and amount of treatments in the early acute stage in the ICU before discharge to our setting, although this information would have been very important.

All therapists were trained and experienced in inpatient rehabilitation. In order to collect all data about the content and duration of physiotherapy and/or physical rehabilitation applied at all stages of illness the content of physiotherapy was documented daily in 5-min segments according to the physiotherapy intervention categories shown in Table I (14). This information was used to obtain a relatively precise picture of the therapy provided in the daily physiotherapy sessions. It was hypothesized that specific types of physiotherapy intervention (measured as total time per week) might be related to achieving independent walking.

Table I. Checklist for therapists to record the amount, intensity and content of physical rehabilitation, such as type of physiotherapy interventions, every working day

Physical rehabilitation	Time per therapy session (min)
<i>Predominately active therapies</i>	
Assistive/active stance	5 10 15 20 25 30
Treadmill training	5 10 15 20 25 30
Electromechanical-assisted walking	5 10 15 20 25 30
Active breathing therapy	5 10 15 20 25 30
Strengthening exercises	5 10 15 20 25 30
Sit-to-stand exercises	5 10 15 20 25 30
Position shift exercises	5 10 15 20 25 30
Balance exercises in the sitting position	5 10 15 20 25 30
Balance exercises in a standing position	5 10 15 20 25 30
Conventional walking training	5 10 15 20 25 30
Stair training	5 10 15 20 25 30
Transfer training	5 10 15 20 25 30
Wheelchair training	5 10 15 20 25 30
<i>Predominately passive therapies</i>	
Passive mobilization into the stand	5 10 15 20 25 30
Patient positioning	5 10 15 20 25 30
Secretion mobilization	5 10 15 20 25 30
Passive/assistive movement	5 10 15 20 25 30
Stretching	5 10 15 20 25 30
Preparation and post-processing time in therapy	5 10 15 20 25 30
Physical thermal applications	5 10 15 20 25 30
Electrotherapeutic applications	5 10 15 20 25 30
Massage techniques and manual lymphatic drainage	5 10 15 20 25 30

Measures and outcomes

The study protocol defined walking ability as the primary outcome (14), with Functional Ambulation Categories (FAC) ≥ 3 . FAC ranges from 0 to 5, and was first described by Holden et al. in 1984 (24). It provides a rapid visual assessment of walking, is simple to use, easy to interpret, and distinguishes 6 levels of walking ability on the basis of the amount of physical support required (25), where 0 indicates a patient who is not able to walk at all or needs the help of 2 therapists (non-functional ambulator) and 5 indicates a patient who can walk everywhere independently, including stairs (independent ambulator) (25).

All patients were followed up for 1 year or until FAC ≥ 3 was reached, whichever was sooner. Time to achieve walking ability was defined as the first time-point when walking was performed successfully (time to event) (14). If a patient was discharged, died or lost to follow-up this information was recorded. Subjects were categorized as reaching FAC ≥ 3 or not reaching FAC ≥ 3 .

The following secondary outcomes were used:

- ADL measured with the Barthel Index (BI; 10 items; 0–100 points). The BI scale was chosen because it is the gold standard measure in Germany to assess the progress of rehabilitation.
- Clinical severity (e.g. mechanical ventilation, dysphagia, tracheostomy) measured with the Early Rehabilitation Barthel Index (ERBI) (26). The ERBI was used because this scale is used in Germany to assess the severity of patients in early rehabilitation.
- Muscle strength of the upper limb (shoulder, elbow and wrist) and lower limb (hip, knee and ankle) using the Medical Research Council (MRC) total score (22).
- Summed grip strength of both hands (measured with a dynamometer). Grip strength was used as a potential marker of recovery from ICUAW (22, 27).
- Functional Status Score for the Intensive Care Unit (FSS-ICU) (28). This scale was used because it was an important prognostic factor in former analysis of patients with ICUAW (29).
- Pain using a numerical pain rating scale. Pain was measured because it is a major impairment after ICUAW.
- “Functional reach” forward as a measure of sitting and standing balance (distance in cm). This scale was used because it was an important prognostic factor in former analysis of patients with ICUAW (29).
- Walking speed (m/s) and distance walked in 6 min (6-min walk test; 6-MWT). These assessments were used to provide important basic assessment for recovery of walking function after ICUAW.

All assessments were administered by trained and experienced therapists. The primary outcome was measured daily and secondary outcomes were measured from baseline (T0) every 2 weeks up to 8 weeks (T1, T2, T3, T4). Baseline (T0) was defined as first admission to the post-acute hospital or inpatient rehabilitation centre, respectively.

In addition, physiotherapists were asked after every single treatment session to rate their subjective perception of physical stress during the session on a visual analogue scale (VAS; 0–10), with 10 being the highest possible perceived physical stress during treatment of patients. That question was included because it was considered that performing physiotherapy for patients with ICUAW might be exhausting for therapists. It may be physically stressful because patients with ICUAW in the post-acute phase may still be severely disabled and dependent on devices, such as respirators and other medical equipment.

Statistical analyses

Descriptive and inference statistics were used depending on the type of test and data distribution. The global alpha level was set at 0.05. Predefined categories of walking ability (FAC ≥ 3) were used to statistically compare all predefined physiotherapy categories of interventions.

Based on an *a priori* sample size calculation, 150 patients were needed to be recruited (14). The probability of regaining walking function was calculated using the method of Kaplan & Meier (30). Univariate and multivariate Cox regression analyses with a selection of possible predictor variables for primary outcome were used as described below (31, 32). The main result of such analysis is a multivariate adjusted hazard ratio (HR), which provides a comparison between the probability of regaining walking function in a subgroup of the cohort and the probability of regaining walking function in another subgroup. The HR was used to describe whether patients receiving a specific physiotherapy intervention progress at a different rate from patients not receiving that type of therapy.

As an example, a HR of 1.5 means that, with a specific treatment, patients progress 1.5 times faster than patients not receiving that type of therapy.

Univariate analysis. Univariate Cox regression analysis of the following variables was performed: total time (in min) of all physiotherapy interventions per week for the first 2 weeks of rehabilitation (total min per week) spent in walking activities, age at baseline, body mass index (BMI), sex, lower limb strength, duration of illness, duration of mechanical ventilation, and number (total) of secondary diagnoses.

Multivariate analysis and model building. All statistically significant variables (alpha level 0.2 for selection) were candidate predictor variables, and those with the highest global χ^2 score were selected first and entered into a multivariate regression analysis (31, 32). To remain in the multivariate model a variable had to be significant at the 0.1 level (32). The multivariate models were then compared with remaining variables on global score χ^2 statistic (best subset selection) and on Akaike's information criterion (AIC) and Schwarz's Bayesian criterion (SBC) for the final multivariate model (31, 32). The effects of the final multivariate model were expressed as HRs with 95% confidence interval (95% CI). A Kaplan–Meier estimate of the final multivariate adjusted Cox proportional hazards model was provided. SAS/STAT 9.3 was used for all statistical procedures (SAS Institute Inc., Cary, NC, USA) and proportional hazards assumptions were tested with the implemented function.

RESULTS

A total of 150 patients with ICUAW between January 2013 and March 2015 were included in this cohort study (Fig. 1). The demographic and clinical characteristics of subjects at study onset in post-acute rehabilitation (T0) are shown in Table II. All therapeutic interventions and the total time (in min) per week per intervention category are shown in Table III, categorized according to walking ability achieved.

At study onset no patients were able to walk. During post-acute rehabilitation walking ability was achieved after a median of 28.5 days (interquartile range (IQR) 45 days) after the start of individual rehabilitation.

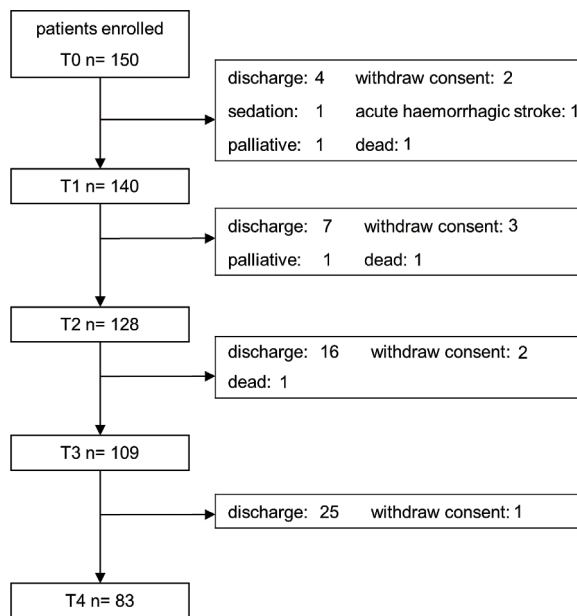


Fig. 1. Study flow chart. T0: baseline; T1 to T4: every 2 weeks up to 8 weeks.

The amount and content of therapy in the first 2 weeks did not differ between subgroups. However, different interventions were applied in patient subgroups. The most frequent interventions in the first 2 weeks of rehabilitation in patients who regained walking ability were: practicing walking, sit-to-stand training, and balance training while sitting (mean total time per week: 48.03 (SD 41.10), 20.13 (SD 21.12) and 12.37 (SD 26.95) min, respectively).

The most frequent interventions in the first 2 weeks of rehabilitation in those patients who did not regain walking ability were: passive-assistive movements, sit-to-stand training, and balance training while sitting (mean total time per week: 15.29 (SD 22.93), 15.15 (SD 22.75) and 14.85 (SD 16.99) min, respectively).

To test the robustness of the relationship between the amount and content of therapy in the first 2 weeks the

Table II. Baseline characteristics of study subjects (at first admission to post-acute hospital or inpatient rehabilitation)

Variable (n = 150)	Median (IQR)	Mean (SD)
Age, years	71 (12)	69.16 (9.02)
BMI, points	27.4 (6.7)	29.11 (8.25)
Duration of illness, days*	41 (30)	49.13 (29.13)
Duration of mechanical ventilation, days	53 (42)	65.22 (45.14)
APACHE II, points	16 (5)	16.45 (4.08)
Barthel Index, points	5 (25)	14.68 (19.20)
MRC total score at baseline, upper limb	9.5 (3.25)	9.45 (2.6)
MRC total score at baseline, lower limb	9 (3.25)	8.45 (2.5)

*Duration of illness was defined as the time between the first day on ICU (first admission to the acute hospital due to the onset of primary illness) until study onset (admission to post-acute hospital or inpatient rehabilitation). ICU: intensive care unit; IQR: interquartile range; SD: standard deviation; BMI: body mass index; MRC: Medical Research Council; APACHE II: Acute Physiology and Chronic Health Evaluation II.

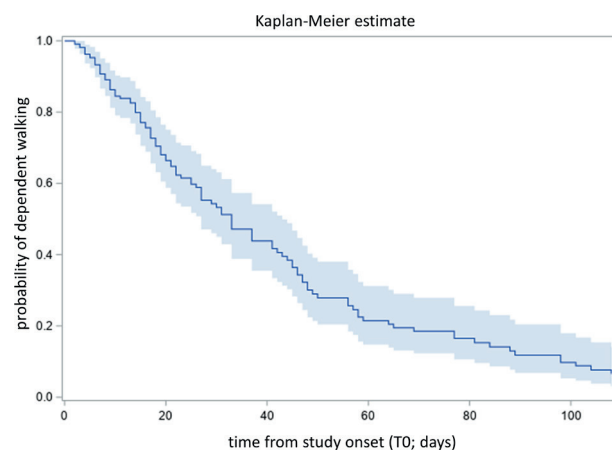


Fig. 2. Kaplan–Meier estimate of final multivariate adjusted Cox proportional hazards model for regaining walking ability.

(confounding) effects of the following variables were analysed: total time (in min) of all physiotherapy interventions per week in the first 2 weeks of rehabilitation, total time (in min) per week spent with walking activities, age at baseline, body mass index (BMI), sex, lower limb strength, duration of illness, duration of mechanical ventilation, and the number (total) of secondary diagnosis in adjusted Cox proportional hazard models. After adjusting for these variables it was found that patients who practised walking post-acute ICU and rehabilitation units had a higher chance of regaining walking ability.

The final multivariate adjusted Cox proportional hazards model included: total time (in min) per week spent in walking activities (adjusted HR = 1.017; 95%

CI 1.013–1.021; per min walking, $p < 0.0001$). An adjusted HR of 1.017 means that the specific treatment results in the patient progressing 1.017 times faster than patients not receiving that type of therapy. In other words, every minute of physiotherapy in walking activities per week increases the chance of regaining walking ability by 1.7% (95% CI 1.3–2.1). Adjusted HR means that the effect of time spent in walking activities is controlled for other components of physiotherapy in rehabilitation. A Kaplan–Meier estimate of the final multivariate adjusted Cox proportional hazards model (Fig. 2) was made. This estimate shows the adjusted time course of regaining walking function.

The subjectively perceived physical stress of physiotherapists during therapies was lower than expected and did not differ significantly between patients who regained or did not regain walking ability during post-acute rehabilitation (mean 4.03 (SD 1.57) vs 3.61 (SD 1.31), respectively, $p = 0.19$).

A summary of all secondary outcome measures at all time-points has been described elsewhere (33, 34).

DISCUSSION

This cohort study of severely ill persons of considerable age with ICUAW found that persons regaining walking ability received task-oriented practice in terms of walking, sit-to-stand, and balance exercises in the first 2 weeks of post-acute rehabilitation. This was in contrast to those not regaining walking ability in an ICU setting. Overall, relatively good recovery

Table III. Results of independent walking categorized by physiotherapeutic intervention

Physiotherapeutic intervention	People who did not achieve FAC ≥ 3		People who achieved FAC ≥ 3		
	Total time (min per week) $n = 36$	Mean (SD)	Total time (min per week) $n = 114$	Mean (SD)	
Assistive/active stance	8.24	(15.8)	4.61	(10.1)	0.15
Treadmill training	0.0	(0.0)	0.97	(6.06)	0.27
Electromechanical-assisted walking	0.0	(0.0)	0.0	(0.0)	1.00
Active breathing therapy	4.27	(8.36)	3.07	(7.48)	0.46
Strengthening exercises	10.74	(16.43)	8.60	(12.89)	0.61
Sit-to-stand training	15.15	(22.75)	20.13	(21.12)	0.06
Position shift training	6.32	(7.82)	4.56	(6.99)	0.19
Balance exercises in the sitting position	14.85	(16.99)	12.37	(26.95)	0.12
Balance exercises in a standing position	1.62	(5.03)	4.78	(11.40)	0.04
Conventional walking training	6.62	(21.52)	48.03	(41.09)	<0.001
Stair training	0.29	(1.72)	5.00	(12.14)	0.01
Transfer training	6.62	(11.85)	10.35	(10.93)	0.01
Wheelchair training	2.21	(6.98)	3.07	(8.71)	0.48
Passive mobilization into the stand	2.94	(9.62)	1.05	(5.04)	0.18
Patient positioning	14.41	(16.60)	4.30	(10.52)	<0.001
Secretion mobilization	9.27	(14.98)	1.71	(5.40)	<0.001
Passive/assistive movement	15.29	(22.93)	3.07	(10.30)	<0.001
Stretching	1.18	(3.27)	0.44	(3.09)	0.03
Pre- and post-processing time	36.62	(21.45)	39.17	(22.56)	0.50
Physical heat applications	3.03	(8.10)	0.26	(2.09)	<0.001
Electrotherapeutic applications	0.00	(0.00)	0.00	(0.00)	1.00
Massage techniques and manual lymphatic drainage	0.91	(3.18)	0.09	(0.94)	0.01

p -values: based on Wilcoxon rank-sum tests (also known as Wilcoxon 2-sample test, a statistical test of the null hypothesis that there is no difference between the effects of the 2 categories). FAC: Functional Ambulation Categories; SD: standard deviation.

of walking function was found and, in these patients with ICUAW, physiotherapy interventions were identified that might be correlated with achieving this important activity. If, in the first 2 weeks, walking activities overground or assisted walking was used in physiotherapy then it was more likely that patients would achieve independent walking. Patients who did not regain walking ability received predominately passive interventions from physiotherapists in the first weeks of rehabilitation. Walking and sit-to-stand exercises and balance manoeuvres in sitting were the most often used interventions in the rehabilitation of patients with ICUAW.

The results of this study can be summarized as follows: chronic critically ill persons in the post-acute phase benefit from early mobilization, task-oriented walking, muscle training of the lower extremities (e.g. sit-to-stand training) and balance activities in standing. Patients receiving passive treatment are less likely to regain walking ability. In addition, it has been shown that severely affected patients tolerate the frequency, time and intensity of the same exercises (35).

Overall, there has been little research on specific aspects of rehabilitation interventions with respect to time, intensity, frequency and amount in chronic critically ill people with ICUAW. This study could therefore be regarded as a first step in describing physiotherapeutic interventions in patients with ICUAW during inpatient rehabilitation.

The subjectively perceived physical stress among physiotherapists during therapies was 4 out of 10 marks in the mean load on a scale of 1 to 10 and in stress levels between physiotherapists who treated patients who regained or did not regain walking ability. These results may indicate that the therapists were experienced and used their tacit knowledge, since there is little research into stress levels, especially in patients with ICUAW.

Johnson et al. recently described a retrospective pre-/post-subgroup analysis in 114 acute critically ill cardiovascular patients with a mean daily treatment time at baseline of 51.7 min and a mean frequency of treatment in the ICU of 0.59 per day (36). Their analysis showed that an increased amount of therapies resulted in shorter length of stay.

The chronic critically ill patients in the current study, however, received physiotherapy every working day at a relatively high level, given that the patients were very severely affected and, in some cases, still not weaned from the respirator. This could, however, be due to the fact that the patients had a lower APACHE II score (which provides information about severity) at baseline with a median of 16 out of 34 points compared with Johnson et al. with a mean of 20 out of 34 points. However, comparable with our study, Johnson et al.

described highly active therapies, such as sit-to-stand transfers and marching on the spot (36), and used a clinical decision-making flowsheet for progression.

As discussed by Tyson et al. in 2018, it appears to be important that physiotherapists (re)organize treatment sessions in order to maximize the intensity of practice of functional tasks (37).

Study limitations

This study has a number of limitations. The cohort study design means that no conclusion can be drawn regarding a causal relationship between walking time in therapy and walking ability achieved. Although the study found that more therapy time was spent with walking in those patients who regained good walking function, this is only an correlation. In addition, some patients in this study may have been too severely affected to be able to participate in any gait training. Future studies should therefore use randomized controlled study designs to explore causal relationships between the content and dose of interventions and the likelihood of regaining walking ability (12, 38). However, the current study indicates that walking training, in particular, is correlated with regaining walking ability, which is in line with current knowledge (35).

A recent Cochrane Review, however, described the lack of randomized trials of people with ICUAW with a defined diagnosis of CIP or CIM (39), indicating that little is known about which therapies are effective. Randomized trials with a detailed description of intensity and frequency of physiotherapy interventions are therefore warranted in people with ICUAW with a defined diagnosis of CIP and/or CIM. The content and amount of treatments in the very early acute stage before the rehabilitation stay were not measured in the current study. It is unclear how this might have influenced the outcome. Future cohorts should measure the start, content and amount of treatments at all stages of recovery.

It can be argued that the primary diagnosis, the cause of acute ICU treatment, might affect the outcome of walking training. However, in a previous analysis we showed that the severity after the ICU stay, rather than the cause of the illness, might be the more important prognostic factor (33). Only those patients who were able to perform our *a priori* defined assessments were included in the current cohort study. The study might be therefore limited by excluding some sedated or very agitated patients, and therefore may limit generalizability of the results to the entire chronic critically ill population. In addition, the diagnosis of CIP and CIM as a major cause of acquired muscle weakness is argued to need clinical *and* electrophysiological investigations (40). A possible limitation is therefore that we did not always perform

an electrophysiological examination. Furthermore, future studies should investigate different rehabilitation strategies (e.g. electrostimulation) to improve function.

Conclusion

This is one of the first studies of physiotherapy interventions in the rehabilitation of chronic critically ill patients with ICUAW. This study therefore provides a more detailed understanding of the rehabilitation and might provide implications for the rehabilitation of people with chronic ICUAW. Future RCTs should investigate the effects of early mobilization combined with early walking training on the recovery of people with ICUAW.

This study indicates that chronic critically ill patients with ICUAW in the post-acute phase receiving passive treatment are less likely to regain walking ability than patients who receive early mobilization, task-oriented walking, muscle training of lower extremity (such as sit-to-stand training), and balance activities in standing.

ACKNOWLEDGEMENTS

This work was supported by Klinik Bavaria Kreischa.

The authors have no conflicts of interests to declare.

REFERENCES

- Kress J, Hall J. ICU-acquired weakness and recovery from critical illness. *N Engl J Med* 2014; 370: 1626–1635.
- Elliott D, Davidson JE, Harvey MA, Bemis-Dougherty A, Hopkins RO, Iwashyna TJ, et al. Exploring the scope of post-intensive care syndrome therapy and care: engagement of non-critical care providers and survivors in a second stakeholders meeting. *Crit Care Med* 2014; 42: 2518–2526.
- Hermans G, De Jonghe B, Bruyninckx F, Van den Berghe G. Clinical review: critical illness polyneuropathy and myopathy. *Crit Care* 2008; 12: 238.
- Needham DM, Davidson J, Cohen H, Hopkins RO, Weinert C, Wunsch H, et al. Improving long-term outcomes after discharge from intensive care unit: report from a stakeholders' conference. *Crit Care Med* 2012; 40: 502–509.
- Wieske L, Dettling-Ihnenfeldt DS, Verhamme C, Nollet F, van Schaik IN, Schultz MJ, et al. Impact of ICU-acquired weakness on post-ICU physical functioning: a follow-up study. *Crit Care* 2015; 19: 196.
- Herridge MS, Cheung AM, Tansey CM, Matte-Martyn A, Diaz-Granados N, Al-Saidi F, et al. One-year outcomes in survivors of the acute respiratory distress syndrome. *N Engl J Med* 2003; 348: 683–693.
- Hermans G, Van Mechelen H, Clerckx B, Vanhullebusch T, Mesotten D, Wilmer Aea. Acute outcomes and 1-year mortality of intensive care unit-acquired weakness. A cohort study and propensity-matched analysis. *Am J Respir Crit Care Med* 2014; 190: 410–420.
- Hermans G, Van Mechelen H, Bruyninckx F, Vanhullebusch T, Clerckx B, Meersseman P, et al. Predictive value for weakness and 1-year mortality of screening electrophysiology tests in the ICU. *Intensive Care Med* 2015; 41: 2138–2148.
- Fan E, Dowdy DW, Colantuoni E, Mendez-Tellez PA, Sevransky JE, Shanholtz C, et al. Physical complications in acute lung injury survivors: a two-year longitudinal prospective study. *Crit Care Med* 2014; 42: 849–859.
- Needham DM, Wozniak AW, Hough CL, Morris PE, Dinglas VD, Jackson JC, et al. Risk factors for physical impairment after acute lung injury in a national, multicenter study. *Am J Respir Crit Care Med* 2014; 189: 1214–1224.
- Semmler A, Okulla T, Kaiser M, Seifert B, Heneka MT. Long-term neuromuscular sequelae of critical illness. *J Neurol* 2013; 260: 151–157.
- Mehrholz J, Thomas S, Burridge JH, Schmidt A, Scheffler B, Schellin R, et al. Fitness and mobility training in patients with intensive care unit-acquired muscle weakness (FITonICU): study protocol for a randomised controlled trial. *Trials* 2016; 17: 559.
- Nelson JE, Cox CE, Hope AA, Carson SS. Chronic critical illness. *Am J Respir Crit Care Med* 2010; 182: 446–454.
- Mehrholz J, Mückel S, Oehmichen F, Pohl M. The General Weakness Syndrome Therapy (GymNAST) study: protocol for a cohort study on recovery on walking function. *BMJ Open* 2014; 4: e0006168.
- Outermans JC, van Peppen RP, Wittink H, Takken T, Kwakkel G. Effects of a high-intensity task-oriented training on gait performance early after stroke: a pilot study. *Clin Rehabil* 2010; 24: 979–987.
- Scrivener K, Sherrington C, Schurr K. Amount of exercise in the first week after stroke predicts walking speed and unassisted walking. *Neurorehabil Neural Repair* 2012; 26: 932–938.
- Clark B, Whitall J, Kwakkel G, Mehrholz J, Ewings S, Burridge J. Time spent in rehabilitation and effect on measures of activity after stroke [protocol]. *Cochrane Database of Systematic Reviews* 2017; Art. No.: CD012596. DOI: 012510.011002/14651858.CD14012596.
- Berney S, Haines K, Denehy L. Physiotherapy in critical care in Australia. *Cardiopulm Phys Ther J* 2012; 23: 19–25.
- Berney SC, Rose JW, Denehy L, Granger CL, Ntoumenopoulos G, Crothers E, et al. Commencing out-of-bed rehabilitation in critical care-what influences clinical decision-making? *Arch Phys Med Rehabil* 2019; 100: 261–269 e262.
- Koo KK, Choong K, Cook DJ, Herridge M, Newman A, Lo V, et al. Early mobilization of critically ill adults: a survey of knowledge, perceptions and practices of Canadian physicians and physiotherapists. *CMAJ Open* 2016; 4: E448–E454.
- Schreiber AF, Ceriana P, Ambrosino N, Malovini A, Nava S. Physiotherapy and weaning from prolonged mechanical ventilation. *Respir Care* 2019; 64: 17–25.
- Nordon-Craft A, Moss M, Quan D, Schenkman M. Intensive care unit-acquired weakness: implications for physical therapist management. *Phys Ther* 2012; 92: 1494–1506.
- Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal PV, Keane KA, et al. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. *Am J Respir Crit Care Med* 2002; 166: 1338–1344.
- Holden MK, Gill KM, Magliozzi MR, Nathan J, Piehl-Baker L. Clinical gait assessment in the neurologically impaired. Reliability and meaningfulness. *Phys Ther* 1984; 64: 35–40.
- Mehrholz J, Wagner K, Rutte K, Meissner D, Pohl M. Predictive validity and responsiveness of the Functional Ambulation Category in hemiparetic patients after stroke. *Arch Phys Med Rehabil* 2007; 88: 1314–1319.
- Pohl M, Bertram M, Hoffmann B, Jöbges M, Ketter G, Krusch C, et al. Der Frühreha-Index: Ein Manual zur Operationalisierung. *Rehabilitation* 2010; 49: 22–29.
- Hermans G, Van den Berghe G. Clinical review: intensive care unit acquired weakness. *Crit Care* 2015; 19: 274.
- Zanni JM, Korupolu R, Fan E, Pradhan P, Janjua K, Palmer JB, et al. Rehabilitation therapy and outcomes in acute respiratory failure: an observational pilot project. *J Crit Care* 2010; 25: 254–262.
- Thomas S, Burridge JH, Pohl M, Oehmichen F, Mehrholz J. Recovery of sit-to-stand function in patients with intensive-

- care-unit-acquired muscle weakness: results from the General Weakness Syndrome Therapy cohort study. *J Rehabil Med* 2016; 48: 793–798.
30. Kaplan E, Meier P. Nonparametric estimation from incomplete observations. *J Amer Statist Assoc* 1958; 53: 457–481.
 31. Kleinbaum D, Klein M. *Survival analysis. A self-learning text.* New York: Springer; 2012.
 32. Hosmer D, Lemeshow S, May S. *Applied survival analysis: regression modeling of time to event data.* New York: John Wiley & Sons, Inc.; 2008.
 33. Mehrholz J, Mückel S, Oehmichen F, Pohl M. First results about recovery of walking function in patients with intensive-care-unit-acquired muscle weakness from the General Weakness Syndrome Therapy (GymNAST) cohort study. *BMJ Open* 2015; 5: e008828.
 34. Thomas S, Mehrholz J. Health related quality of life, participation and physical and cognitive function of patients with intensive-care-unit-acquired muscle weakness one-year after rehabilitation in Germany, the GYMNAST cohort study *BMJ Open* 2018; 8: e020163.
 35. Kleim JA, Jones TA. Principles of experience-dependent neural plasticity: implications for rehabilitation after brain damage. *J Speech Lang Hearing Res* 2008; 51: S225–S239.
 36. Johnson JK, Lohse B, Bento HA, Noren CS, Marcus RL, Tonna JE. Improving outcomes for critically ill cardiovascular patients through increased physical therapy staffing. *Arch Phys Med Rehabil* 2019; 100: 270–277 e271.
 37. Tyson SF, Woodward-Nutt K, Plant S. How are balance and mobility problems after stroke treated in England? An observational study of the content, dose and context of physiotherapy. *Clin Rehabil* 2018; 32: 1145–1152.
 38. Kho ME, Molloy AJ, Clarke F, Herridge MS, Koo KK, Rudkowski J, et al. CYCLE pilot: a protocol for a pilot randomised study of early cycle ergometry versus routine physiotherapy in mechanically ventilated patients. *BMJ Open* 2015; 6: e011659.
 39. Mehrholz J, Pohl M, Burrridge J, Kugler J, Mückel S, Elsner B. Physical rehabilitation for critical illness myopathy and neuropathy. *Cochrane Database of Systematic Reviews* 2015; Art. No.: CD010942. DOI: 010910.011002/14651858. CD14010942.pub14651852.
 40. Latronico N, Bolton CF. Critical illness polyneuropathy and myopathy: a major cause of muscle weakness and paralysis. *Lancet Neurol* 2011; 10: 931–941.