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REVIEW

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A discursive review of the effectiveness and utility of exercise therapy in the subacute stage of recovery from critical illness

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Abstract

Background The coronavirus pandemic precipitated an increase in admissions to intensive care units (ICU). The related medium to long-term sequelae of critical illness posed a significant challenge to function and quality of life after discharge from the acute hospital, often requiring continued therapeutic input. Current evidence suggests that exercise therapy is effective in rehabilitating multiple systemic conditions. However, its role in post-ICU recovery remains unclear.

The objective of this article was to discuss the merits and demerits of the exercise in subacute post-ICU settings based on available evidence. Effective, evidence-based rehabilitation from critical illness is crucial due to the increased number of patients and the significant burden on care and participation of those individuals.

Methods The materials for this discursive review were selected after several database searches and analysis of available articles. As a result, six papers were found, four of which provided evidence for the beneficial effect of exercise in subacute rehabilitation of post-ICU patients, and two reported no differences between interventions and control groups.

Results Most of the studies found cardiovascular exercise to be safe and somewhat beneficial. However, adherence and attrition were problematic in this patient group, and the studies suffered methodological and measurement problems regarding group selection, exercise prescription and outcome measures applied.

Conclusion The existing evidence base did not allow an informed consensus regarding the value of exercise in the subacute post-ICU recovery or lack thereof. Therefore, further investigation into patient retention strategies, exercise prescription and the choice of appropriate outcome measures is necessary.

Keywords Rehabilitation, Exercise therapy, Critical illness, Post-ICU, Subacute rehabilitation, Cardiovascular, Strength, Exercise

Introduction

Subacute rehabilitation of patients recovering from critical illness is an important field of inquiry due to the recent and ongoing coronavirus (COVID-19) pandemic. A significant proportion of critically ill and those most severely affected by COVID-19 require intensive medical care and ventilatory support, leaving them to face long-term functional challenges [1], increased morbidity and mortality and mental health disruptions. The functional impact and therapeutic management of patients

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post-critical illness are rarely considered. The picture is further complicated by the recently identified sequelae of COVID-19, which present as depressed lung function Torres-Castro et al. [3] and other non-specific debilitating symptoms [2]. Existing publications on the topic contain a variety of research designs and therapeutic approaches to post-hospital recovery from critical illness. Still, the evidence base remains insufficient to inform the rehabilitation approach. The existing systematic reviews on the topic have not found sufficient evidence [4–6] to formulate practice recommendations for this patient group. The multitude of factors influencing the outcomes of this patient population is an important topic for investigation. This review endeavours to debate the possible factors affecting the discrepancy in the findings by analysing the merits and shortcomings of the currently proposed subacute rehabilitation approaches for patients recovering from critical illness and considering their implications for the current practice.

Methods

The present publication analysed the available evidence regarding the impact of therapeutic exercise, delivered in subacute settings, on the functional and physiological outcomes of adults recovering from critical illness. The scoping review admitted all experimental designs apart from case–control studies. Comparisons were made between exercise modalities, exercise and standard care and outcomes relative to baseline results. The review was not prospectively registered.

The articles describing the positive effects of subacute rehabilitation are referred to as 'PRO' (Table 1), and those with opposite outcomes as 'CONTRA' (Table 2).

The term subacute is understood as the stage of recovery immediately after discharge from acute care. The subacute phase entails interventions carried out as an inpatient in an intermediate rehabilitation centre or as an outpatient in an ambulatory clinic or community setting. The intermediate care settings refer to specialist rehabilitation units/hospitals where the patients reside during the interventions.

The literature searches conducted via PubMed and Ovid used Boolean phrases, MeSH terms and keywords (Appendix). The terms used included: outpatients, subacute, rehabilitation, exercise, intensive care, critical care, critical illness, critically ill, intensive care-acquired weakness (ICUAW). After removing the duplications, searches yielded 410 results for title analysis (Fig. 1). The title review revealed 52 abstracts for further analysis. Further, 12 articles were chosen for a full-text review. The six remaining publications described the subacute phase of recovery and included therapeutic interventions following discharge from the hospital as well as subjective functional or physiological outcome measures. The six which fulfilled the criteria are listed below in Tables 1 and 2.

The design of the analysed studies

Both groups of analysed studies (PRO and CONTRA) predominantly contain randomised control trials (RCT) except for the cohort study by Merholtz et al. [5] in the PRO (Table 1). All discussed articles used exercise to improve patients' function after leaving the intensive care unit (ICU). The PRO literature included studies in community and outpatient settings, patients travelling to a clinic or following exercise prescription at home [7, 11] compared to inpatient/residential specialist rehabilitation [5, 9]. The outpatient interventions involved patients requiring a minimum of 3-day [7] and 4-day ventilatory support [8] and participating in three moderate-intensity exercise sessions per week for 8 and 6 weeks, respectively. The inpatient protocol proposed by Merholtz et al. [5] was a cohort study of undetermined length that included patients with at least 21 days in ICU with a component of mechanical ventilation and 14 additional days of critical illness requiring treatment in the ICU. Veldema et al. [9] conducted a 4-week RCT where patients were enrolled in the study and transferred to the specialist unit after ICU (1 to 4.5 months after the diagnosis). Still, the exact length of required ICU admission or ventilatory support was unavailable. In the CONTRA literature, Denehy et al. [10] required an ICU admission of over 5 days, while McWilliams, Benington and Atkinson [11] specified a minimum of 5 days of ventilatory support.

The lack of uniformity of requirement for ventilatory support could have had a potentially significant effect on the baseline characteristics of the cohorts and, therefore, the final study outcomes due to the impact of the length of ICU stay and ventilatory support on the severity of disability [12].

A notable difference in the design of studies was the time point for enrolment. In the PRO literature, McDowell et al. [8] assumed 2 weeks between hospital discharge and the start of the trial. For Batterham et al. [7], the estimated interval was eight to 16 weeks. The extensive time interval was justified by the attempted maximisation of recruitment. However, the elapsed period, as well as the exclusion of all people unable to climb stairs (Table 1), was likely to affect participants' stage of recovery and functional level, presenting the possibility that the cohort studied by [7] was less severely affected at the outset and further in their recovery compared to the individuals in the other PRO trials. The participants in the inpatient trials had differing lengths of ICU and acute admission and therefore had varying rehabilitation potential. The time

Table 1 PRO articles and their characteristics

Authors	Design	Sample (sex)	Inclusion/exclusion	Intervention	Outcome measures
Batterham et al.,2014 [7]	Single-centre, parallel-group minimised controlled trial	*N* = 59 (F:21, M:38)	Inclusion: -Age: 18–65 years old, -Ventilator support > 3 days Exclusion: -Inability to climb a flight of stairs -enrolment in another rehabilitation programme -contraindications to cardiopulmonary exercise testing	2 × /week for 8 weeks supervised ergometry for 40 min at 12–14 Borg RPE and 1 × 40 min unsupervised home exercise-encouraged/week at 12–14 Borg RPE Control: standard care	AT (ml O_2 min^{-1}·kg^{-1}) SF-36
Merholz et al., 2015a [5]	Cohort study	*N* = 150 (F:50, M:100)	Inclusion: -Age > 18 years old, -Critical illness -MRC result of < 48, -Electrophysiological diagnosis of ICUAW, -RASS score of − 1 to 2, -written informed consent of the patient or legal guardian Exclusion: -Palliative status, -Injury/comorbidity of -Limbs restricting upright -Posture and/or walking, -Previous neuromuscular diagnosis, -Severe physical condition prior to critical illness (e.g., frailty due to neurological conditions)	Individualised, multimodal physiotherapy Details of intervention N/A Control: N/A	Primary: FAC Secondary: Barthel index ERBI MRC HGD FSS-ICU PFIT-s NPRS Reach forward test MoCA 6MWT
McDowell et al., 2016 [8]	Multicentre, prospective, randomised controlled trial, with blinded outcome assessment	*N* = 60 (F:28, M:34)	Inclusion: -Age ≥ 18 years -Mechanical ventilation for > 96 h, P -To be discharged home -Medically fit to participate Exclusion: Participation in another rehabilitation programme	2 × /week for 6 weeks supervised, multimodal exercise for < 60 min and 1 × /week unsupervised bout based on the supervised exercise Control: standard care	Primary: SF-36 Secondary: RMI HGD 9-hole peg test ISWT MRCDS HADS Readiness to change questionnaire Chronic disease self-efficacy scale
Veldema et al., 2019 [9]	Single centre, parallel-group, randomised control trial	*N* = 39 (F:16, M:23)	Inclusion: -Clinical and electrophysiological ICUAW diagnosis, -Severely limited walking ability (FAC 0–3), - Preserved active movement of the lower limbs Exclusion: -Pre-existing diagnosis of a neurological condition	5 × /week for 4 weeks Ergometry: > 20 min cycling at 13 Borg RPE Resistance: Total of 9 Different exercises (3/session) at 16 Borg RPE, performed over a total of 20 min, with set duration of 45–60 s Control: standard care	Primary and secondary outcomes not specified FAC TUG 10-MWT 6-MWT PWCFT SF-36

Term Glossary: *F* Females, *M* Males, *AT* Anaerobic threshold, *ERBI* Early Rehabilitation Barthel Index, *FAC* Functional Ambulation Category, *HADS* Hospital anxiety and depression scale, *FSS-ICU* Functional Status Score for the Intensive Care Unit, *HGD* Handgrip dynamometry, *ISWT* Incremental shuttle walk, *MRC* Medical Research Council Muscle Scale, *MRCDS* Medical Research Council dyspnoea score, *MoCA* Montreal Cognitive Assessment, *NPRS* Numeric Pain Rating Scale, *RASS* Richmond Agitation-Sedation Scale, *RMI* Rivermead Mobility Index, *PFIT-s* Physical Function in ICU Test–Scored, *PWCFT* Physical working capacity of the fatigue threshold test, *RPE* Rate of perceived exertion, *SF-36* Short-form Health Survey, *TUG* Timed up-and-go, *10-MWT* 10 Metre Walk Test, *6-MWT* Six-minute walk test

Table 2 CONTRA articles and their characteristics

Authors	Design	Sample (sex)	Inclusion/exclusion	Intervention	Outcome measures
Denehy et al., 2013 [10]	Single-centre, assessor-blinded, randomised controlled trial	*N* = 150 (F:55, M:95)	Inclusion: -Residence within a 50-km radius of the hospital -ICU admission > 5 days -RASS − 1 to + 1 Exclusion - Neurological, spinal or musculoskeletal dysfunction preventing participation	Standard care: Not specified Intervention: 8-week outpatient rehabilitation 2 × /week for 60 min protocol-based cardiovascular, PRT and functional exercise	Primary: 6MWT Secondary: -TUG, -AQoL -SF-36
McWilliams, Benington and Atkinson, 2016 [11]	Single centre, randomised controlled trial	*N* = 73 (F:25, M:48)	Inclusion: -Age > 18 years -Ventilator support > 5 days Exclusion: -Inability to perform CPET or to participate rehabilitation classes due to physical condition - Inability to give informed consent or comply with rehabilitation -Participation in another rehabilitation programme -Terminal illness -Poorly controlled cardiorespiratory disease	Control: No further specific input or education post-discharge Intervention: 7-week outpatient rehabilitation: -20 min 3 × /week. (1 supervised, 2 self-directed) -6 × 1 h education sessions	Primary: -AT (ml O_2 $min^{-1} \cdot kg^{-1}$) Secondary: -SF36v2

Term glossary: *F* Females, *M* Males, *AQoL* Assessment of Quality-of-Life instrument, *AT* Anaerobic threshold, *CPET* Cardiopulmonary exercise testing, *RASS* Richmond Agitation-Sedation Scale, *SF-36v2* Short-form Health Survey version two, *TUG* Timed up-and-go, *6-MWT* Six-minute walk test

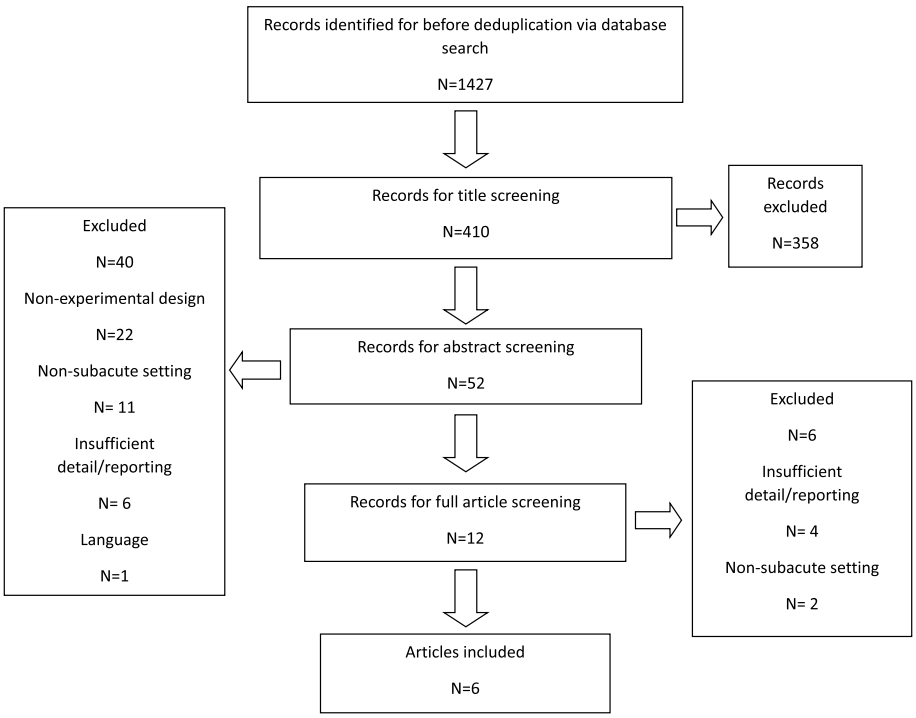

Fig. 1 PRISMA flow-chart describing article selection process

point of the interventions in the CONTRA RCTs are contained in Table 2. Denehy et al. [10] did not specify the enrolment timepoint, and McWilliams, Benington and Atkinson [11] undertook their baseline tests in the 6 weeks following the discharge from the ICU (mean 24 days, ± 13).

The discrepancies between the commencement time points appeared to be a feature of the studies in the subacute rehabilitation of patients recovering from critical illness, leading to challenges in identifying any agreement on the appropriate length of time between hospital discharge and entry into an intervention. Moreover, there was no rationale or evidence regarding the reasonable timeframe translating to the outcomes. The impact of prolonged absence of therapy between discharge and further rehabilitation would need future exploration. Still, appropriate continuity between acute and subacute rehabilitation may help address the potential functional decline in the intervening period and help address some of the barriers to participation.

The cohorts described across PRO and CONTRA research were rarely stratified in terms of functional level. The differences in disability and participation limitations of the participants are poorly understood but may be an important consideration in appropriate therapeutic exercise prescription. The researchers on both sides of the argument have discussed the challenges of stratification and the likely difference in the level of morbidity as factors that may have led to difficulties in participation. Denehy et al. [10] and McDowell et al. [8] considered the length of ICU stay, age, co-morbidities, level of functional impairments, etc., as potential covariates for future investigation into appropriateness for rehabilitation. Among the PRO studies, Batterham et al. [7] only included highly mobile individuals, which may have resolved the stratification question but likely created the risk of selection bias and detracted from the generalisability of the findings.

On the other hand, the inpatient rehabilitation interventions (PRO) were explicit regarding the participants' limited function as expressed by walking ability measured via Functional Ambulation Categories (FAC) [5, 6, 9] and low functional level (battery of functional outcome measures) [5, 6] further complicating the comparison to potentially more heterogenous outpatient cohorts. On the CONTRA side, McWilliams, Benington and Atkinson [11] split the population according to the 6-min walk test (6MWT) results and prescribed a lower exercise intensity to patients who could not reach 200 m. The correlation of patients' functional ability and psychological burden with their ability to complete the interventions or comparisons of patients who successfully participated to those who absconded or experienced difficulties adhering to the protocol was not undertaken. The model of stratification of patients recovering from critical illness proposed by Herridge et al. [12], separated the patients into four disability risk groups based on their age, Functional Independence Measure (FIM) and length of ventilatory support. Applying such a framework may be a starting point to structure future research to provide a rehabilitation prescription corresponding to patients' functional levels and improve adherence.

The statistical analysis was characterised by inconsistencies in both PRO and CONTRA studies. Several studies lack power calculation and confidence intervals. In several cases, participant attrition and small sample sizes limited the ability to draw inferences from the results. Among the PRO investigations, half of the publications disclosed their power calculations. Batterham and colleagues [7] did not include a power calculation for significance prediction. They reported that over half of follow-up data was lost due to 'indeterminate measures' of their primary outcomes, stemming from the difficulties in performing the test (hyperventilation and mouthpiece accommodation) and attrition. Veldema et al. [9] did not produce a power calculation, and the study's sample size ($N=39$) was recognised as a limiting factor. On the other hand, McDowell et al. [8] reached their predetermined sample size at the post-test but not at the 6-month follow-up.

The influence of attrition was not analysed, but its deleterious impact on the internal and external validity of results at 6 months needed to be considered. Merholtz et al. [5] calculated power using the 'ten events per variable rule (EPV)' and recruited the targeted number of participants ($N=150$). The CONTRA literature research comprised two RCTs (Table 2), neither of which achieved a sufficient sample to meet the power assumptions (80%, $\alpha=0.05$). Denehy et al. [10] reported difficulties in result interpretation due to insufficient recruitment and retention, suffering from substantial attrition, as only 41% of its cohort completed the intervention. Conversely, 75% of the cohort in McWilliams, Benington and Atkinson's [11] study completed all supervised sessions, but only 50% of the participants completed all the prescribed unsupervised exercise sessions. The adherence to the independently executed programme has not been described in detail. Still, insufficient adherence could affect the results because the unsupervised exercise was meant to constitute two-thirds of the total prescribed volume.

Additionally, nearly 14% of participants were lost before follow-up, further decreasing the power of the study. The cohorts in the randomised studies had small samples, which, along with the difficulties in recruitment and retention of ICU patients, risked measurement errors and limited the generalisability of the findings. The methodological limitations of the research increased the risk of bias and made it difficult to

compare and reliably ascertain the quality of research to guide clinical practice [4].

The exercise prescription and training variables

The articles on both sides used exercise as the treatment intervention. Considering the absence of discrete guidelines for the rehabilitation of patients recovering from critical illness, the rationale for exercise prescription is either absent [5–7, 9] , sourced from general guidelines [11] or interventions used in other conditions [10, 13]. The publications by Berney et al. [13] and Denehy et al. [10] were a part of the same study, but the former described the exercise protocol in detail. It was therefore referred to in the present paper interchangeably, where appropriate. Four articles [5, 8–10] combined cardiovascular, resistance and functional exercises, while two [7, 11] focused solely on cardiovascular exercise. The duration of the protocols varied between the studies from 4 to 8 weeks (Tables 1 and 2). However, McDowell et al. [8] decided to extend the time frame of their intervention to 11 weeks. The cohort study by Merholz et al. [5] was the only trial where the patient's functional ability was decisive for discharge. The frequency of exercise sessions differed between the protocols. The inpatient PRO papers [5, 9] provided exercise 5 days per week, and the remaining interventions espoused two to three sessions weekly.

The outpatient PRO studies [7, 8] contained two supervised and one unsupervised session. On the CONTRA side, the exercise was either fully supervised [10] or two out of three sessions were independent [11].

Four weeks of resistance training was reported sufficient for significant neuromuscular adaptations [14], while cardiovascular adaptations after 21-day bedrest occurred almost immediately after endurance training was commenced [15]. Moreover, the negligible difference between the effects of two versus three exercise sessions per week [16] suggests that the length and frequency of the interventions were likely sufficient to achieve systemic and functional effects. However, the discrepancy in exercise frequency between the outpatient and inpatient programmes was important and likely to impact rehabilitation outcomes because the inpatient cohorts have received significantly more therapy (5 days per week), adherence notwithstanding. Furthermore, half of the studies (Tables 1 and 2) contained an element of self-reported exercise which may promote individual self-reliance and responsibility for rehabilitation but, on the other hand, presented the risk of reduced compliance and therefore risked reliability of the results. The comparison of impact of the exercise frequency on rehabilitation outcomes is further complicated by the ad hoc extension in McDowell et al. [8] study to meet the required number of sessions and the low rate of completion of home exercise (circa 50% of participants) in McWilliams, Benington and Atkinson [11]. The inconsistent adherence and participation may have been a product of the challenges faced by the post-ICU population, underscoring the importance of investigating and eliminating barriers to rehabilitation. Considering the apparent differences in participant populations' functional abilities, the overall 24-h level of activity or sedentary behaviour outside of therapy, which was a salient variable for other clinical cohorts [17], may have impacted on patient outcomes. However, the daily pattern of activity was not measured or analysed by any of the authors. The effect of fatigue, low exercise tolerance and long-term functional limitations play an essential role in both research and clinical practice of rehabilitation of the post-ICU cohorts. The interventions' frequency and mode of delivery require careful planning and monitoring to allow full participation leading to optimisation of adherence and, therefore, physiological adaptations to stimuli.

The intensity of provided exercise was mainly assessed using the Borg rating of perceived exertion (RPE) [18] or Borg modified dyspnoea scale and heart rate (HR) [11]. The sole exception was the Merholz et al. [5] study which did not specify the intensity parameters. The Borg RPE (6–20 point scale), validated for exercise prescription and diagnostics, was originally designed as a complementary measure to be used in conjunction with objective physiological observations in a clinical application [18]. Furthermore, the RPE score was reported to have a significant inter-individual variability, risking an individual having the perception of exercising hard while failing to reach the threshold for physiological effectiveness [19]. HR or alternative objective measures of exertion were only monitored by McWilliams, Benington and Atkinson [11] due to their use of HR reserve to maintain exercise intensity level. Despite the importance of the patient experience of exertion and a strong correlation with HR and other physiological measures [18], the lack of additional objective data makes it difficult to ascertain the extent to which the pre-set physiological parameters were met during the training. Therefore, the lack of physiological markers indicating overload on the results is a likely limitation in most proposed interventions. Including additional 'minute-by-minute' objective outcome measures of exertion during exercise as a standard would allow greater precision in exercise prescription and adjustment in future studies and clinical practice.

Borg RPE was used to measure the intensity of resistance exercise in half of the studies (Tables 1 and 2). The scale was shown to correlate with one repetition maximum but also overestimated the load associated with the corresponding rating. Additionally, the rating was reported to vary depending on the number of prior sets

and the length of rest periods between them [20]. The relationship between Borg RPE and the objective exercise intensity measures would need further exploration as fatigue and low exercise tolerance likely influenced the perception of exertion in the post-ICU population. The investigation of subjective measures such as 'repetitions in reserve' [21, 22] as an alternative to current intensity monitoring, as well as combining them with objective parameters (repetition maximum and load magnitude) could prove beneficial in improving the reliability of findings and inform clinical practice.

The reporting on the prescription of training variables differed between studies. The only PRO paper to provide the exercise programme was the study by [9]. The remaining publications proposed individualised exercise prescriptions [5, 6, 8] or a general progression based on Borg RPE [7]. The CONTRA publications used the percentages of HR maximum and five-repetition maximum (5RM) [10] or the percentage of HR reserve [11]. The latter trial was the only example of sample stratification, which prescribed exercise at 50–60% HR reserve to the high-risk patients and 60–70% to the low-risk group. Across the available literature, only Denehy et al. [10] and [9] described their exercise prescription. However, the details regarding the progression of time, intensity and load were not disclosed.

The aerobic component proposed by Denehy et al. [10] assumed progression from 20 to 30 min of continuous work at 80% of maximal HR. Still, HR was not measured throughout the exercise but extrapolated from the Borg RPE score. Veldema et al. [9] opted for 20 min of stationary cycling at the intensity level of 13 Borg RPE. The investigators assumed an incremental gain in cardiovascular and motor function; therefore, the objective was to maintain the level of RPE, believing that the constant subjective rating would reflect enhanced cardiovascular capacity. The two papers contrasted on cardiovascular exercise programming, with Denehy et al. [10] proposing an extensive approach, i.e., prolonging the exercise, while Veldema et al. [9] intensified the exercise by increasing pedal resistance but the magnitude of the increase was not specified. Denehy et al. [10] found no difference between intervention and control groups, while the latter reported a positive effect of exercise on function. However, the reported attrition of 59% of patients cast doubt on the validity and reliability of the results.

Only Veldema et al. [9] compared aerobic exercise to another modality, indicating that stationary cycling was more efficacious in improving walking ability in patients with ICUAW than resistance training. However, the results need to be treated with caution due to the small study sample, lack of power calculation and a higher baseline function in the cycling group. Additionally, strength gains have been reported after endurance exercise in the untrained [23], and the patients recovering from critical illness would likely fit into that category. Therefore, it is possible that the results could be attributed to variables other than the exercise modality, especially given the lack of objective reporting of the exercise intensity and the magnitude of physiological response to the effort. The available research was designed with heart rate percentages as a measure of intensity, yet most researchers did not monitor it during the exercise. Adding an objective HR measurement to the Borg RPE in future research and clinical practice would improve the understanding of the patient's capacity and allow adherence to the precepts of the intervention.

The details of the resistance training prescription were absent in four out of six discussed publications. Denehy et al. [10] and Veldema et al. [9] were the only two publications providing information about the exercise parameters on the CONTRA and PRO sides, respectively. Denehy et al. [10] based the resistance training intensity on a 5RM percentage and prescribed one to two sets of 12 to 15 repetitions at 75% of that resistance. It would follow that the patients' 5RM was tested, but no baseline or follow-up 5RM tests were described. As a performance benchmark, 5RM demonstrated reliability in healthy, recreational athletes Künzell, [24] and appeared to be a reasonable intensity measure mitigating injury risk in untrained, compared to one repetition maximum (1RM).

The existing research into training parameters in the older population suggested that length of intervention, total time under tension, intensity and time of the rest periods were the variables producing the largest effect sizes for strength gain, suggesting that intensity of 70–79% of 1RM, repetition duration of 6 s and a rest period of 60 s to be optimal [25]. The intensity prescribed by Denehy et al. [10] approximated 60% of 1RM, therefore was lower than that found most beneficial for the older population. However, given the morbidity and functional limitations of the participants, the use of lower loads and exercise volume could be justified.

Veldema et al. [9] reported the length of sets as a measure of the volume of exercise instead of traditional repetitions, sets and load format. Four sets of 45 to 60 s of activity and 30 to 40-s rests were performed. Neither the tempo nor the load was disclosed, and the intensity of exercise was measured via Borg RPE instead of the percentage of repetition maximum. Considering the strong relationship between movement velocity and the load magnitude [26, 27] a potential variance in the number of repetitions between patients and inconsistency of load used could affect the targeted motor skill and physiological response. Additionally, the choice of exercises by Veldema et al. [9] was questionable due to their potential

lack of carryover to ambulation and, therefore, lack of specificity [28].

On the other hand, the Borg RPE scale was reported to be correlated with one repetition maximum in resistance training but prone to overestimation of the load correlated with the corresponding rating. Additionally, the RPE varied depending on the number of prior sets and the rest periods between them [20]. Between-set recovery has not been investigated in the post-ICU population. The relationship between Borg RPE and the objective exercise intensity measures would need further exploration as the likely lack of previous training, severe fatigue and low exercise tolerance could influence the perception of exertion in the post-ICU population. The variance stemming from a lack of a designated number of repetitions and imprecise load monitoring was compounded by the potential variance of Borg RPE self-reporting, resulting in difficulties establishing goals and achieving training adaptations. Overall, the intensity and volume parameters were poorly monitored and reported, despite their role in shaping strength and hypertrophy [29]. Application of multi-repetition maximum tests along with subjective exertion reporting would improve the understanding of patients' capacity and aid in rehabilitation programme design. Additionally, following established methods of planning and recording exercise volume and intensity (sets, repetitions and load) would allow for more precise progress tracking and goal setting and provide an objective expression of achievement.

Outcome measures

The number of outcome measures employed in the analysed articles was extensive and varied between authors. The description of all of them exceeded the scope of this paper; therefore, only selected examples have been discussed. Nevertheless, it was necessary to mention the use of metrics due to their role in establishing the effects and, therefore, the utility of rehabilitation. The outcome measures used in the publications included objective functional and physiological measures and subjective questionnaires (Tables 1 and 2). [7] in the PRO and McWilliams, Benington and Atkinson [11] in the CONTRA literature opted for objective physiological tests in their studies. Both teams investigated the relative oxygen consumption at the anaerobic threshold (AT), and the latter measured peak oxygen consumption (VO_2 peak). The muscle loss [30] and change in muscle fibre type [31] observed in the critically ill on extended ventilatory support were likely to affect cellular metabolism, which the physiological measures could reflect. However, neither side of the argument considered a broader treatment context involving the medications and their effect on the physiological response to exercise [32]. The primary concern for using physiological tests in one of the studies was the lack of habituation to the testing procedures resulting in the loss of over half of the follow-up data [7]. Additionally, the test result is indeed effort-dependent, which may reduce the test's reliability given the limitations of this patient group.

Half of the analysed publications used an objective functional gait measure. Two of the PRO articles used Functional Ambulation Categories test (FAC) and 6MWT to measure the impact of their corresponding interventions on walking independence and speed [5, 6, 9]. On the CONTRA side of the argument, Denehy et al. [10] used 6MWT as the primary functional outcome. FAC indicates the level of necessary support to accomplish walking. However, the measure has not been validated, nor has its reliability been tested in the investigated patient population. On the other hand, 6MWT describes the distance walked by a participant in 6 min and has been reported as a reliable and valid measure of function in patients with critical illness [33–35]. Merholz et al. [5] found significant improvements in both measures in 76% of patients throughout the study while Veldema et al. [9] reported no differences in either FAC or 6MWT between the groups but significant within-group improvement from baseline to follow-up was found in all experimental conditions. In Denehy et al. [10], the control group outperformed the intervention group in 6MWT in two out of four follow-ups, and no significant difference was found between the groups at 12 months. Despite the improvement of the 6MWT distance in all studies, the results remained below what is considered the norm for a healthy age-matched population, which provokes questions about the minimal clinically important difference for this outcome measure and the role of organic recovery of mobility. The 6MWT was argued to have carry-over to daily activities due to reliance on aerobic metabolism and the test's self-paced nature [36]. However, Alison et al. [33] noted a presence of a floor effect as patients with the most significant impairment could not perform the test, signalling a need for alternative measurement tools to monitor this population segment. Overall, the ambulation outcome measures indicated a level of improvement in patients regardless of therapeutic input. However, further investigation of the validity and reliability of FAC for patients post-ICU, as well as exploration of additional functional metrics for patients with a severe level of disability, is necessary.

All studies except Merholz et al. [5] employed measures of quality of life (QOL) and self-reported physical function. The Short-Form (SF-36) Health Survey was the most popular tool but was mainly used as a secondary measure. The SF-36 has shown acceptable reliability and validity in the critically ill population [37]. However, some

researchers only used its constituent parts. McDowell et al. [8] used the physical domain of the instrument as the primary outcome and reported no significant differences between the intervention and control ($p=0.26$). The difference was deemed clinically important, but the lack of instrument sensitivity and condition specificity were cited as limitations. The two CONTRA trials have shown contrasting results. Denehy et al. [10] saw no differences in scores between the groups and attributed it to poor adherence and barriers to participation. McWilliams Benington and Atkinson [11], on the other hand, reported significant positive effects of exercise on the QOL in both physical ($p=0.048$) and mental ($p=0.017$) components of the questionnaire, with a nearly two-fold (28.8 to 56.8) improvement in self-reported physical function. The patients who expressed their views in prior qualitative studies have mentioned engagement in mobility practice and physiotherapy as a means to attain more meaningful goals and placed it as one of the priorities in the subacute phase of their journey [38]. Ågård et al. [39] described 'recovering physical strength' and 'regaining physical capacity' as two of the main objectives for individuals regaining independence. Therefore, the patients themselves saw rehabilitation as essential, but a greater understanding of the patient views specific to subacute rehabilitation is needed.

Analysis

Four of the articles (PRO) indicated a positive impact of rehabilitation on quality of life and self-reported function [8], anaerobic threshold [7] and objective measures of ambulation and function [5, 9]. Two of the analysed papers (CONTRA) found no significant impact of subacute therapy on patients recovering from critical illness. The PRO research papers used varying approaches to trial design, treatment prescription, and outcome measures. Two of the PRO studies addressed rehabilitation of patients with ICUAW [5, 9]. Most studies were limited by small sample sizes and a lack of power analysis. The inferences were frequently drawn from populations significantly affected by attrition or questionable adherence to the designed protocol. The limitations resulted in confounded outcomes, highlighting the design and execution challenges rather than the role of subacute rehabilitation in recovery from critical illness. The effects of the investigations indicated a lack of unanimity, which led to an inability to infer guidance for clinical practice.

The investigators faced design challenges due to the nature of the post-ICU population. The attrition and lack of adherence were the most threatening to the integrity of the studies. However, two principal controllable variables stand out. The heterogeneity of patients' functional ability was apparent in all but one paper. The groups either lacked stratification according to patients' functional levels or when the physical ability was considered, it was not factored into the analysis of the results [11]. Conversely, in one study, only patients with relatively high physical ability were admitted, risking selection bias [7]. The outpatient trials appeared appropriate for highly functional participants, while the inpatient programmes focused on patients with more significant care needs. That said, a part of the population participating in the outpatient studies experienced difficulties leading to attrition and indicating this population may have needed an alternative approach to rehabilitation. The alterations by McDowell et al. [8] showed that those patients might require one-to-one attention in their environment to promote adherence. The second problem was the variability of the time point of entry into the studies, both between and within the studies. This issue is somewhat related to the first study design challenge, as the period in question could impact the functional level of the recruited population through differences in the stage of recovery post-ICU on entry into the study. Both limitations appear controllable as stratification frameworks exist [12], and the study entry time points are, in principle, dependent on the investigators. Research into the relationship between functional status and appropriate therapy prescription and the optimal time between discharge from the acute setting and rehabilitation would be crucial for establishing the contour for clinical practice with this patient population.

The therapeutic exercise prescription and its parameters appeared to exist in separation from the physiological and strength and conditioning evidence base. Accurate identification of the targeted physiological systems and motor skills has not been undertaken in the analysed papers. The anaerobic threshold was the target of two investigations [7, 11]. The self-reported measures of exertion are a valuable intensity indicator, but reliance on them without objective outcomes is a limitation of current research. Separate research has shown the potential lack of reliability of those tools, which may be exacerbated by the level of strength and cardiovascular fitness of the patients recovering from critical illness. Therefore, objective exercise measurements are needed to establish patient tolerance and the intervention's carry-over to daily function.

Similarly, the intensity and volume of resistance training frequently lacked a description of repetitions, sets and load. The baseline and follow-up strength assessment through repetition maximum testing was only described by Veldema et al. [9]. However, its results were not used to set the intensity of strength exercise, and self-reported measures were employed instead. Additionally, the researchers have not specified the targeted adaptation to

the resistance training (muscular hypertrophy, strength, power etc.), therefore avoiding the discussion about the target of the intervention and different approaches to address it. The research did not indicate a tolerated or adequate level of volume or intensity of the exercise for patients recovering from critical illness. The current insufficiency of evidence regarding rehabilitation parameters could prompt an investigation monitoring the basic exercise intensity metrics, both tolerated and beneficial to patients post-ICU. Additionally, a focus on the physiological effects of critical illness and corresponding exercise approaches, adaptable to clinical settings, could help guide future clinical practice.

The outcome measures used in post-ICU rehabilitation were inconsistent across the publications. The measurement of VO_2 peak and AT resulted in a significant proportion of lost data [7] or failed to show substantial differences between the experimental groups [11]. Using mouthpieces and facemasks for testing in patients with a history of ventilatory support provoked hyperventilation and anxiety, as described by the authors. This could be concerning considering the prevalence of psychological trauma resulting from critical illness [40]. Therefore, the appropriateness of this testing mode in the post-ICU population is questionable. The sensitivity of the tests is also unknown as the research suggested no significant differences in AT and VO_2 peak between those in exercise versus the control group. However, this area would need to be explored further due to the questionable exercise prescription, potentially reducing the overload necessary to impact the physiological adaptations. The 6MWT is among the gold standard measures for the functional assessment of patients recovering from critical illness [35]. However, the test was generally underutilised in the subacute rehabilitation literature. The authors who used the 6MWT as the primary outcome confirmed that patients post-ICU achieved shorter distances than the age-matched, healthy population. The use of FAC has not been validated for use in the investigated population. Therefore, further exploration of the utility of this outcome measure in rehabilitation from critical illness seems warranted.

The SF-36 Health Survey was the most frequently used subjective and self-reported physical function measure. Overall, the instrument has shown improvement in perceived physical function. Still, the researchers pointed to the lack of the instrument's sensitivity and its lack of disease-specific character as limitations. The SF-36 has shown acceptable reliability and validity in the critically ill population [37]. However, additional qualitative studies combining self-reported scales and patient experiences specific to subacute rehabilitation would increase the resolution of patient perspective on the therapeutic process.

Conclusion

Rehabilitative exercise appeared to enhance the recovery of patients post-ICU. However, designing an evidence-based therapeutic prescription based on the described sources would be difficult due to insufficient data on recommendable variables. A mode of intervention delivery which would minimise attrition and encourage participation has not been described thus far. The meaningful outcome measures for this population have significant limitations and were not usually measured simultaneously to explore their interactions. The physiological and functional targets of therapy were not concretely delineated, which led to the exercise prescription being poorly described, making the tracking of progress difficult. Cardiovascular endurance exercise appeared to be the safest and most beneficial exercise mode for post-ICU recovery. However, the exact type (or combination of types), dosage and intensity require further investigation. The sparsity of the evidence prevented authors of this paper from conclusively adjudicating the utility of exercise in rehabilitation following critical illness. Present review is by no means exhaustive which constitutes its main limitation. The subject of subacute post-ICU rehabilitation requires further well-designed and reported RCTs as well as systematic reviews with meta-analysis of data where possible.

Appendix

Search strategy

MeSH terms search:

(("Critical Illness/rehabilitation"[Mesh] AND "Critical Illness/therapy"[Mesh])).

Boolean terms searches:

1. (((((critical illness) OR (intensive care unit-acquired weakness)) OR (ICU-Acquired weakness)) AND (Rehabilitation))
2. (((((critical illness) OR (intensive care unit-acquired weakness)) OR (ICU-Acquired weakness)) AND (Exercise))
3. (((((critical illness) OR (intensive care unit-acquired weakness)) OR (ICU-Acquired weakness)) AND (Training))

Ovid Search:

Database: AMED (Allied and Complementary Medicine) <1985 to December 2021>, Embase Classic+Embase <1947 to 2021 December 15>, Global Health <1973 to

2021 Week 50>, Journals, Ovid MEDLINE(R) ALL <1946 to December 15, 2021>

Search Strategy:

1 "Critical Care".mp. [mp=ab, hw, ti, tn, ot, dm, mf, dv, kf, fx, dq, cw, tx, sh, ct, bt, nm, ox, px, rx, an, ui, sy, ux, mx] (253895)

2 "Critical illness".mp. [mp=ab, hw, ti, tn, ot, dm, mf, dv, kf, fx, dq, cw, tx, sh, ct, bt, nm, ox, px, rx, an, ui, sy, ux, mx] (105669)

3 "Intensive Care Unit Acquired Weakness".mp. [mp=ab, hw, ti, tn, ot, dm, mf, dv, kf, fx, dq, cw, tx, sh, ct, bt, nm, ox, px, rx, an, ui, sy, ux, mx] (864)

4 "ICU-acquired weakness".mp. [mp=ab, hw, ti, tn, ot, dm, mf, dv, kf, fx, dq, cw, tx, sh, ct, bt, nm, ox, px, rx, an, ui, sy, ux, mx] (1445)

5 Rehabilitation.mp. [mp=ab, hw, ti, tn, ot, dm, mf, dv, kf, fx, dq, cw, tx, sh, ct, bt, nm, ox, px, rx, an, ui, sy, ux, mx] (1028734)

6 Exercise.mp. [mp=ab, hw, ti, tn, ot, dm, mf, dv, kf, fx, dq, cw, tx, sh, ct, bt, nm, ox, px, rx, an, ui, sy, ux, mx] (1323785)

7 Training.mp. [mp=ab, hw, ti, tn, ot, dm, mf, dv, kf, fx, dq, cw, tx, sh, ct, bt, nm, ox, px, rx, an, ui, sy, ux, mx] (1902269)

8 1 or 2 (331598)

9 3 or 4 (2064)

10 8 and 9 (1424)

11 5 or 6 or 7 (3719557)

12 10 and 11 (745)

13 limit 12 to english language [Limit not valid in Your Journals@Ovid; records were retained] (728)

14 limit 13 to human [Limit not valid in AMED,Global Health,Your Journals@Ovid; records were retained] (700)

15 limit 14 to humans [Limit not valid in AMED,Global Health,Your Journals@Ovid; records were retained] (700)

16 limit 15 to "therapy (best balance of sensitivity and specificity)" [Limit not valid in AMED,Global Health,Your Journals@Ovid; records were retained] (375)

17 remove duplicates from 17 (343)

18 from 18 keep 4-5,10,19,26,29-30,38,48,50,60,92,96,127,227,231,239,258,260,280,292,304,323,338,340,342 (26)

Abbreviations

ICU	Intensive care units
COVID-19	Coronavirus
RCT	Randomised control trial
FIM	Functional Independence Measure
HR	Heart rate
RPE	Borg rating of perceived exertion
5RM	Five-repetition maximum
HRR	Heart rate reserve
ICUAW	ICU-acquired weakness
QOL	Quality of life
SF-36	Short-Form Health Survey
AT	Anaerobic threshold
ERBI	Early Rehabilitation Barthel Index
FAC	Functional Ambulation Category
HADS	Hospital anxiety and depression scale
FSS-ICU	Functional Status Score for the Intensive Care Unit
HGD	Handgrip dynamometry
ISWT	Incremental shuttle walk
MRC	Medical Research Council Muscle Scale
MRCDS	Medical Research Council dyspnoea score
MoCA	Montreal Cognitive Assessment
NPRS	Numeric Pain Rating Scale
RASS	Richmond Agitation-Sedation Scale
RMI	Rivermead Mobility Index
PFIT-s	Physical Function in ICU Test–Scored
PWCFT	Physical working capacity of the fatigue threshold test
RPE	Rate of perceived exertion
SF-36	Short-form Health Survey
TUG	Timed up-and-go
10-MWT	10 Metre Walk Test
6-MWT	Six-minute walk test
AQoL	Assessment of Quality-of-Life instrument
AT	Anaerobic threshold
CPET	Cardiopulmonary exercise testing
RASS	Richmond Agitation-Sedation Scale
VO_2 peak	Peak oxygen consumption

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References

1. Herridge MS, Tansey CM, Matté A, Tomlinson G, Diaz-Granados N, Cooper A, et al. Functional disability 5 years after acute respiratory distress syndrome. New England Journal of Medicine. 2011;364(14):1293–304. Available from: https://f1000.com/prime/9789958.
2. Jimeno-Almazán A, Pallarés JG, Buendía-Romero Á, Martínez-Cava A, Franco-López F, Sánchez-Alcaraz Martínez BJ, et al. Post-COVID-19 syndrome and the potential benefits of exercise. International Journal of Environmental Research and Public Health. 2021 ;18(10). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8156194/.

3. Torres-Castro R, Vasconcello-Castillo L, Alsina-Restoy X, Solis-Navarro L, Burgos F, Puppo H, et al. Respiratory function in patients post-infection by COVID-19: a systematic review and meta-analysis. Pulmonology. 2020.
4. Connolly B, Salisbury L, O'Neill B, Geneen LJ, Douiri A, Grocott MP, et al. Exercise rehabilitation following intensive care unit discharge for recovery from critical illness. Cochrane Database of Systematic Reviews. 2015 Jun 22.
5. 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(12):e008828.
6. Mehrholz J, Pohl M, Kugler J, Burridge J, Mückel S, Elsner B. Physical rehabilitation for critical illness myopathy and neuropathy. Cochrane Database of Systematic Reviews. 2015.
7. Batterham AM, Bonner S, Wright J, Howell SJ, Hugill K, Danjoux G. Effect of supervised aerobic exercise rehabilitation on physical fitness and quality-of-life in survivors of critical illness: an exploratory minimized controlled trial (PIX study). Br J Anaesth. 2014;113(1):130–7.
8. McDowell K, O'Neill B, Blackwood B, Clarke C, Gardner E, Johnston P, et al. Effectiveness of an exercise programme on physical function in patients discharged from hospital following critical illness: a randomised controlled trial (the REVIVE trial). Thorax. 2016;72(7):594.1-595.
9. Veldema J, Bösl K, Kugler P, Ponfick M, Gdynia H, Nowak DA. Cycle ergometer training vs resistance training in ICU-acquired weakness. Acta Neurol Scand. 2019;140(1):62–71.
10. Denehy L, Skinner EH, Edbrooke L, Haines K, Warrillow S, Hawthorne G, et al. Exercise rehabilitation for patients with critical illness: a randomized controlled trial with 12 months of follow-up. Critical Care. 2013;17(4):R156. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4056792/.
11. McWilliams DJ, Benington S, Atkinson D. Outpatient-based physical rehabilitation for survivors of prolonged critical illness: a randomized controlled trial. Physiother Theory Pract. 2017;32(3):179–90.
12. Herridge MS, Chu LM, Matte A, Tomlinson G, Chan L, Thomas C, et al. The RECOVER program: disability risk groups and 1-year outcome after 7 or more days of mechanical ventilation. American Journal of Respiratory and Critical Care Medicine. 2016 Oct;194(7):831–44. Available from: http://europepmc.org/abstract/MED/26974173.
13. Berney S, Haines K, Skinner EH, Denehy L. Safety and feasibility of an exercise prescription approach to rehabilitation across the continuum of care for survivors of critical illness. Phys Ther. 2012;92(12):1524–35.
14. Staron RS, Karapondo DL, Kraemer WJ, Fry AC, Gordon SE, Falkel JE, et al. Skeletal muscle adaptations during early phase of heavy-resistance training in men and women. J Appl Physiol. 1994;76(3):1247–55.
15. Adams WC, McHenry MM, Bernauer EM. Long-term physiologic adaptations to exercise with special reference to performance and cardiorespiratory function in health and disease. Am J Cardiol. 1974;33(6):765–75.
16. Ferrari R, Fuchs SC, Kruel LFM, Cadore EL, Alberton CL, Pinto RS, et al. Effects of different concurrent resistance and aerobic training frequencies on muscle power and muscle quality in trained elderly men: a randomized clinical trial. Aging Dis. 2016;7(6):697.
17. Kuisma R. A randomized, controlled comparison of home versus institutional rehabilitation of patients with hip fracture. Clin Rehabil. 2002;16(5):553–61.
18. Borg GAV. Psychophysical bases of perceived exertion. Med Sci Sports Exerc. 1982;14(5):377–81.
19. Whaley MH, Woodall MT, Kaminsky LA, Emmett JD. Reliability of perceived exertion during graded exercise testing in apparently healthy adults. J Cardpulm Rehabil. 1997;17(1):37–42.
20. Morishita S, Tsubaki A, Nakamura M, Nashimoto S, Fu JB, Onishi H. Rating of perceived exertion on resistance training in elderly subjects. Expert Rev Cardiovasc Ther. 2019;17(2):135–42.
21. Zourdos MC, Klemp A, Dolan C, Quiles JM, Schau KA, Jo E, et al. Novel resistance training–specific rating of perceived exertion scale measuring repetitions in reserve. J Strength Cond Res. 2016;30(1):267–75.
22. Buskard ANL, Jacobs KA, Eltoukhy MM, Strand KL, Villanueva L, Desai PP, et al. Optimal approach to load progressions during strength training in older adults. Med Sci Sports Exerc. 2019;51(11):2224–33.
23. Harber MP, Konopka AR, Undem MK, Hinkley JM, Minchev K, Kaminsky LA, et al. Aerobic exercise training induces skeletal muscle hypertrophy and age-dependent adaptations in myofiber function in young and older men. Journal of Applied Physiology [Internet]. 2012 Nov 1;113(9):1495–504. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3524668/.
24. Künzell S, Gail S. Reliability of a 5-repetition maximum strength test in recreational athletes. Dtsch Z Sportmed. 2014;2014(11):314–7.
25. Borde R, Hortobágyi T, Granacher U. Dose–response relationships of resistance training in healthy old adults: a systematic review and meta-analysis. Sports Medicine . 2015 ;45(12):1693–720. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4656698/.
26. Jidovtseff B, Harris NK, Crielaard JM, Cronin JB. Using the load-velocity relationship for 1RM prediction. J Strength Cond Res. 2011;25(1):267–70.
27. Pérez-Castilla A, Jukic I, García-Ramos A. Validation of a novel method to assess maximal neuromuscular capacities through the load-velocity relationship. J Biomech. 2021;127:110684.
28. Sale DG. Neural adaptation to resistance training. Med Sci Sports Exercise. 1988;20(Sup 1):S135-45.
29. Lopez P, Radaelli R, Taaffe DR, Newton RU, Galvão DA, Trajano GS, et al. Resistance training load effects on muscle hypertrophy and strength gain. Medicine & Science in Sports & Exercise. 2020;Publish Ahead of Print(6).
30. Schefold JC, Wollersheim T, Grunow JJ, Luedi MM, Z'Graggen WJ, Weber-Carstens S. Muscular weakness and muscle wasting in the critically ill. J Cachexia Sarcopenia Muscle. 2020;11(6):1399–412.
31. Dirks Marlou L, Hansen D, Van Assche A, Dendale P, Van Loon Luc JC. Neuromuscular electrical stimulation prevents muscle wasting in critically ill comatose patients. Clin Sci. 2014;128(6):357–65.
32. Nyasavajjala SM, Low J. Anaerobic threshold: pitfalls and limitations. Anaesthesia. 2009;64(9):934–6.
33. Alison JA, Kenny P, King MT, McKinley S, Aitken LM, Leslie GD, et al. Repeatability of the Six-Minute Walk Test and relation to physical function in survivors of a critical illness. Phys Ther. 2012;92(12):1556–63.
34. Parry SM, Granger CL, Berney S, Jones J, Beach L, El-Ansary D, et al. Assessment of impairment and activity limitations in the critically ill: a systematic review of measurement instruments and their clinimetric properties. Intensive Care Med. 2015;41(5):744–62.
35. Libuy MH, Szita CP, Hermosilla PJ, Arellano SD, Rodríguez-Núñez I, Báez RC. Validez y confiabilidad de las escalas de evaluación funcional en pacientes críticamente enfermos. Rev Med Chil. 2017;145(9):1137–44.
36. Leone M, Duvergé S, Kalinova É, Bui HT, Comtois AS. Comparison of bioenergetics of walking during a multistage incremental shuttle walk test and a 6-min walk test in active older adults. Aging Clin Exp Res. 2016;29(2):239–46.
37. Chrispin PS, Scotton H, Rogers J, Lloyd D, Ridley SA. Short Form 36 in the intensive care unit: assessment of acceptability, reliability and validity of the questionnaire. Anaesthesia. 1997;52(1):15–23.
38. Scheunemann LP, White JS, Prinjha S, Hamm ME, Girard TD, Skidmore ER. Post–intensive care unit care. A Qualitative Analysis of Patient Priorities and Implications for Redesign. Ann Am Thorac Soc. 2020;17(2):221–8.
39. Ågård AS, Egerod I, Tønnesen E, Lomborg K. Struggling for independence: A grounded theory study on convalescence of ICU survivors 12 months post ICU discharge. Intensive Crit Care Nurs. 2012;28(2):105–13.
40. Righy C, Rosa RG, da Silva RTA, Kochhann R, Migliavaca CB, Robinson CC, et al. Prevalence of post-traumatic stress disorder symptoms in adult critical care survivors: a systematic review and meta-analysis. Critical Care. 2019;23(1). Available from: https://doi.org/10.1186/s13054-019-2489-3.

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