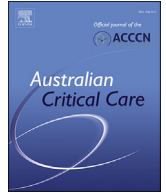




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Review paper

Arm cycle ergometry in critically ill patients: A systematic review

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ABSTRACT

Background: Intensive care unit (ICU) survivors face functional limitations due to ICU-acquired weakness. Arm cycle ergometry (ACE) introduced in the ICU may improve physical function. To our knowledge, there is limited evidence on the effectiveness of ACE and physical function outcomes in critically ill patients.

Objective: The objective of this systematic review was to examine the impact of ICU-based ACE on physical function, safety, and other clinical outcomes.

Review method used: Systematic Review.

Data sources: A search of seven databases was conducted from the inception to January 1, 2023: Medline Ahead of Print, Ovid MEDLINE(R), Allied and Complementary Medicine Database (AMED), Embase, Cochrane Central, Physiotherapy Evidence Database, and Cumulative Index to Nursing and Allied Health Literature (CINAHL).

Review methods: We included two arm studies of critically ill adults admitted to the ICU who received ACE and any comparator for our primary outcome, physical function. Our secondary outcomes included severe events. We included safety studies with or without a comparator group. Screening, data abstraction, and risk-of-bias assessments were completed independently, in duplicate. We used the Grading of Recommendations, Assessment, Development, and Evaluation approach to assess the overall certainty of evidence.

Results: We screened 651 citations and included eight studies that enrolled 183 patients. Due to heterogeneity, meta-analysis was not performed. For our primary outcome, one randomised controlled trial found significant improvements in physical function, measured by the Barthel Index with ACE, whereas a nonrandomised study showed no difference. Out of the six studies reporting safety, none reported any severe safety events. The overall certainty of evidence was very low.

Conclusion: ACE initiated in the ICU is a likely safe intervention. Based on the limited ACE studies and heterogeneity between studies, further research with more rigorous studies evaluating important outcomes for patients is needed.

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1. Introduction

Patients surviving their intensive care unit (ICU) stay are at risk of developing post-intensive-care syndrome (PICS), which is described as new or worsening impairments that persist beyond discharge from the ICU.¹ Surviving patients may experience poor quality of life due to their functional, mental, and cognitive

impairments from PICS.¹ At least 46% of ICU survivors will develop ICU-acquired weakness, defined as clinically detected weakness, with no other explanation than critical illness.² ICU-acquired weakness can impact both short- and long-term patient outcomes.

Early mobility is an important component of internationally designed early rehabilitation protocols for the ICU, which is included in an attempt to mitigate the physical function declines

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of PICS and ICU-acquired weakness.^{2,3} Early ICU mobility is associated with reduced ICU and hospital length of stay and number of days of delirium.^{2,3} It is safe with low adverse-event rates and is feasible with trained staff and collaboration for ICU protocol implementation.^{3–5} However, standardised dosage parameters such as exercise intensity, frequency, or duration are challenging, given the wide range of ICU admissions and severity of illness.^{3,6,7}

In-bed cycle ergometry of legs or arms has been introduced into ICUs and rehabilitation protocols as an early mobility strategy.^{8–10} Cycling can precisely quantify intervention volume and intensity, allowing incremental control for individualised programs.¹¹ Cycling with critically ill patients can also overcome commonly reported barriers to starting early mobility, including receipt of mechanical ventilation (MV), sedation, and patient tethers to multiple lines and tubes.^{5,7,12} Arm cycle ergometry (ACE) could address upper-extremity dysfunction and weakness. Upper limb muscle mass can decrease by 13.2–16.9% over 7 days of ICU stay.^{13,15} Thus, bathing, eating, and dressing may become impaired in ICU patients. Upper-extremity dysfunction can also impact gross motor skills, and declines have been observed at hospital discharge in the ability to roll in bed, transfer from sit to stand, and walk.¹⁵ Upper-limb strength is essential for walking due to its impact on arm swing, which has important roles in gait stability and balance.^{14–18} ACE may play a critical role in ICU physiotherapy treatment to promote functional independence.²¹

2. Objectives

To our knowledge, there is limited evidence on the effectiveness of ACE and physical function outcomes in critically ill patients. To address this gap, we conducted a systematic review to evaluate whether ACE in critically ill adults can improve physical function. Secondary objectives included the impact of ACE on safety, duration of MV, length of stay in the ICU and hospital, and mortality in the ICU and hospital.

3. Methods

3.1. Inclusion and exclusion criteria

This review was prospectively registered to the International Prospective Register of Systematic Reviews (CRD 42022326239) in May 2022. We included studies with critically ill adults, aged 18 years or older, admitted to an ICU for at least 24 h with any admitting diagnosis, who performed ACE in the ICU, compared to those who performed no ACE. The ACE could be delivered at any point during the ICU stay, by any personnel. Studies were included if the intervention involved ACE alone or combined with other interventions. We had no restriction on comparator groups, except patients in the control group could not receive any arm cycling interventions.

Our primary outcome of interest was physical function at ICU awakening, ICU discharge, or hospital discharge. Secondary outcomes included mortality (ICU and hospital), safety (reported safety/adverse events, or events leading to cycling termination as determined by the study protocol), length of stay (ICU and hospital), and duration of MV. We included published full texts of both randomised and nonrandomised study designs. Only studies with a control group were considered for outcomes of physical function, length of stay in the ICU or hospital, mortality, and length of MV. Studies with no control group were included to evaluate safety outcomes. Safety events were defined as severe (e.g., unplanned extubation, cardiac arrest during intervention) or serious (e.g., fall

to knees, transient changes in physiology or ICU support), based on prior cycling protocols.²²

We excluded abstracts due to the limited information typically provided. Studies not written in English were excluded due to a lack of multilingual research staff for translation. Non-peer-reviewed literature, grey literature, editorials, and letters were excluded due to the inability to perform risk-of-bias assessments on these documents.

3.2. Search strategy

In consultation with a research librarian, a comprehensive search was conducted in six electronic databases from inception to January 1, 2023, including Ovid Medline Epub Ahead of Print, in-process and other non-indexed citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R), AMED Allied and Complementary Medicine, Ovid EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Physiotherapy Evidence Database (PEDro), and EBS-COhost Cumulative Index of Nursing and Allied Health Literature (CINAHL). Citations of included articles were hand-searched for additional articles for potential inclusion. Full search strategies for all databases are presented in [Appendix A](#).

All studies were uploaded into Covidence Software (2020, Veritas Health Innovation, Melbourne, VIC, Australia) and duplicates were automatically removed.²³ All screening, reviews, and extraction occurred within the Covidence software.²³ Two reviewers independently screened titles and abstracts, and full-text in duplicate. If a reason for exclusion was not evident within the title and abstract by one reviewer, the full-text study was reviewed. All studies meeting inclusion criteria, with no exclusions, were included in the final review. Differences in full-text assessment screening were discussed between reviewers and were adjudicated by a third-party reviewer, if needed. The exclusion reasons are recorded in [Appendix B](#).

Two review authors performed data extraction independently and in duplicate for lead author, year of publication, study design, study population (sample size, sex, mean age, disease severity, admitting diagnoses), the delivered exercise intervention (frequency, intensity, time from ICU admission to start, duration, and type), comparators, outcome measures, and results.

Risk of bias was assessed for all studies, using two tools.^{24,25} The Cochrane risk-of-bias tool 2 (ROB-2) assessed studies with a control group (i.e., randomised controlled trials (RCTs) and nonrandomised controlled trials (non-RCTs)).²⁴ The Cochrane risk-of-bias tool for nonrandomised studies (ROBINS-I) assessed bias in studies without a control group.²⁵

3.3. Analysis

Heterogeneity was assessed to determine if data were appropriate for pooling and meta-analysis. If there was significant heterogeneity, the data would be described narratively. For the outcomes of interest, we calculated the difference between groups. Difference scores (d) for outcomes of interest were calculated by subtracting the mean score for the control group from the ACE intervention group mean score. The overall quality of the evidence across outcomes was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation approach.^{25–27}

4. Results

4.1. Search results

After removing duplicates, we identified 651 citations, reviewed 68 full texts, and included eight studies.^{7,10,19,20,28–31} [Fig. 1](#) shows

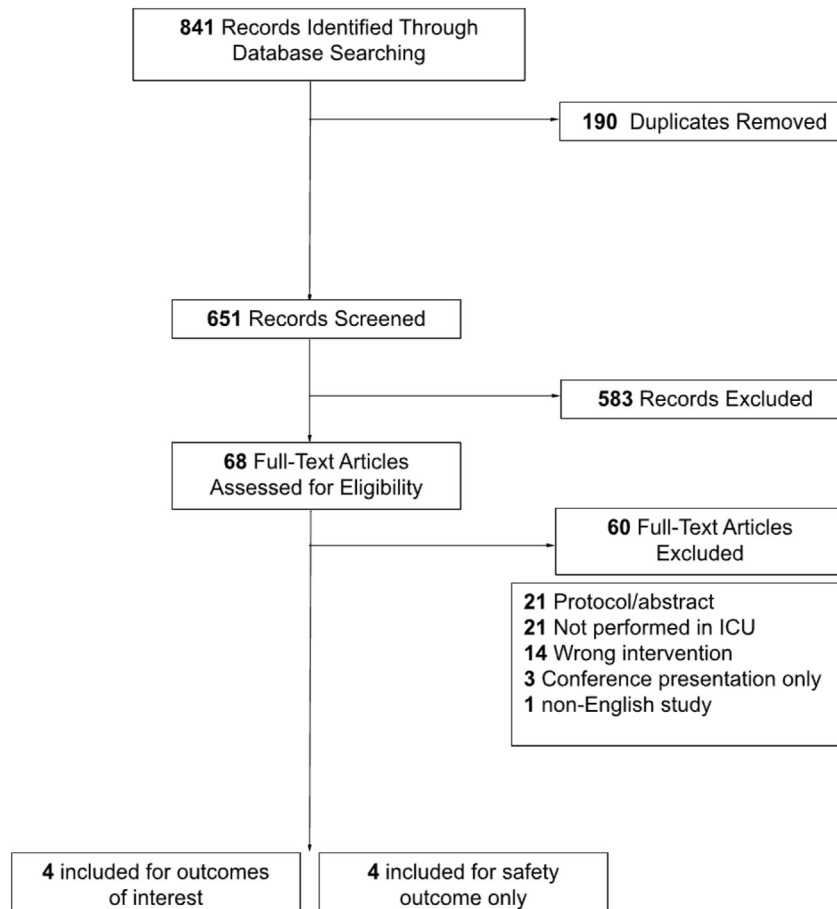


Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram. We display the process of screening and selecting studies for inclusion in the review.

the process of screening and study selection for inclusion in the review. During the assessment of the included studies, we identified two distinct applications of ACE. Studies using ACE as a method of exercise in the ICU were used to examine all study outcomes.^{10,28–30} Studies using ACE as an assessment tool were only included to assess safety outcomes.^{7,19,20,31}

4.2. Study characteristics

The eight studies included 183 critically ill patients.^{7,10,19,20,28–31} All studies performed ACE in an upright position, either in the bed or in a chair. Four studies included patients with longer MV (>15 days),^{10,19,29,31} and two studies performed ACE relatively early in the ICU stay (<5 days).^{7,28} Four studies including 118 patients used ACE as a physiotherapy treatment in the ICU.^{10,28–30} These study designs included two RCTs, one non-RCT, and one observational study. The participants' mean ages ranged from 56 to 72 years. In the three comparison groups, 45 patients in two studies received standard physiotherapy care.^{10,28} In the remaining studies, 15 patients received standard medical care only.²⁹ Four observational studies including 65 patients used ACE as an exercise test.^{7,19,20,31} The participants' ages ranged from 20 to 89 years. [Tables 1 and 2](#) describe characteristics of included studies.

4.3. Effects of interventions

Two studies assessed physical function,^{28,29} three studies assessed mortality,^{10,28,29} one study assessed length of ICU stay,²⁸

one study assessed length of MV,²⁹ and six studies assessed safety.^{7,19,20,28,30,31} No included studies examined length of hospital stay. Please see [Table 3](#) for more details.

4.3.1. Primary outcome- physical function

Two studies enrolling 62 patients (one RCT and one non-RCT; very-low certainty-evidence) examined physical function using the Barthel Index.^{28,29} The RCT found a higher Barthel Index score between ACE ($n = 12$; 19.3 ± 18.6) and the control group ($n = 15$; 13.4 ± 16.6 , $p = 0.01$) at study cessation ($d = 5.9$).²⁹ A higher score on the Barthel Index indicates greater functional independence. However, the non-RCT, which assigned sicker patients to ACE, found lower Barthel Index scores between groups (ACE [$n = 15$; 44.66 ± 38.05] and standard physiotherapy [$n = 20$; 51.75 ± 38.19 ; $p = 0.957$] [$d = -7.09$]).²⁸ Physical function was also measured with the Functional Independence Measure in one RCT, which reported higher group scores for ACE ($n = 12$; 44.6 ± 10.0), indicating greater functional independence; however, it did not report control-group scores ($p = 0.024$).²⁹ In the nonrandomised study, no difference was found in Ambulation Score at ICU discharge between ACE (mean \pm standard deviation) ($n = 15$; 3.20 ± 2.18) and standard physiotherapy ($n = 20$; 3.75 ± 2.22 , $p = 0.096$) ($d = -0.55$).²⁸

4.3.2. Secondary outcomes

4.3.2.1. Safety. Six studies including 86 patients evaluated safety.^{7,19,20,28,30,31} One study enrolling 30 patients evaluated safety events but did not explicitly report any safety outcomes.²⁰ Out of the remaining five studies ($n = 56$ patients; one non-RCT, four

Table 1
Table of included studies that used ACE as an intervention.

Author(s), year	RCT vs non-RCT	Study site	Inclusion Criteria	Participants		Intervention (frequency, intensity, time, type)	Comparator (frequency, intensity, type, time)	Outcome of interest
				Intervention (n), age [mean (SD)] or [range], female [n (%)], APACHE II [mean (SD)], ICU LOS to intervention start [mean]	Control (n), age [mean (SD)] or [range], female [n (%)], APACHE II [mean (SD)], ICU LOS to intervention start [mean]			
Chen YH, et al., 2012	RCT	Department of Respiratory Care, Chang Gung Memorial Hospital, Tao-Yuan, Taiwan	Subacute RRC adult patients undergoing prolonged mechanical ventilation at >6 h/day for >21 days; alert and cooperative; medically stable	Intervention: 12 Age: 64.9 ± 21.3 Female: 5 (41.7%) APACHE II: NA ICU LOS to start: NA	Control: 15 Age: 66.5 ± 18.7 Female: 8 (53.3%) APACHE II: NA	F: 4–6 sessions per week for 10 sessions; each session lasting 30–40 min; 15–25 min session of ACE I: ACE 60–80% age-predicted max, or Bourg rating: 3–5 T: when the patient is able to tolerate upright positions T: active, upright arm cycling plus stretching and strengthening exercises	Medical care only	Physical function (Barthel Index, Functional Index Measures) Mortality Length of MV
Cinar et al., 2020 (16)	Non-RCT	Medical ICU of Hacettepe University Faculty of Medicine, Ankara, Turkey	Critically ill, ages 18–80, clinically stable	Intervention: 15 Age = 63 (20.50) yrs Female = 7 (47%) APACHE II: 21.92 (7.80) ICU LOS to start: 3	Control: 20 Age = 56 (24.81) yrs Female = 11 (55%) APACHE II = 18.80 (9.45) ICU LOS to start: 2	F: 5 days/week, 20 min I: passive and/or active, active resistance individually adjusted (L1-L10) T: not reported T: in-bed arm cycling and standard PT (as per control)	F: 5 days/week I: Not reported T: Not reported T: respiratory physiotherapy, range of motion of upper limb, mobilisation in and out of bed	Length of stay (ICU) Physical function (Ambulation score, Barthel Index) Mortality Safety
Porta et al., 2005	RCT	RIICUs of Salvatore Maugeri Scientific Institutes of Gussago and Montes-cano and Gaiato Onlus Villa Pineta Italy	Weaned from mechanical ventilation for 48–96 h	Intervention: 25 Age: 70 (5.6) Female = 10 (40%) APACHE II: NA ICU LOS to start: 28	Control: 25 Age = 72 (5.2) Female = 11 (44%) APACHE II: NA ICU LOS to start: 24	F: daily, 15 sessions total, 20 min I: active, increasing 2.5 W/session T: within 96 h following weaning T: arm ergometry at shoulder level plus standard PT (as per control)	F: 6x/week, 45 min I: not reported T: started within 96 h following weaning T: ROM upper and lower limb, chest PT, assisted deambulation, functional and strength exercise, reinforcement techniques for head and trunk control, sitting and standing balance, gait training	Mortality

Definition of abbreviations: ACE = arm cycle ergometry; APACHE II = Acute Physiology and Chronic Health Evaluation II; h = hours; ICU = intensive care unit; I+V = intubation and ventilation; L = level; LOS = length of stay; MV = mechanical ventilation; PT = physiotherapy; RCC = respiratory care centre; RCT = randomised controlled trial; RCT = randomised control trial; RIICU = respiratory intermediate ICU; ROM = range of motion; SD = standard deviation; W = watts.

Table 2

Table of included studies for safety outcome only.

Author(s), year	Study type	Goal of the study	Study site	Inclusion criteria	Participants	ACE as assessment/ treatment method (FITT/parameters of test)	Outcomes
					Intervention (n), age [mean (SD)] or [range], female [n (%)], APACHE II [mean (SD)]		
Chen YH, et al., 2015	Observational	To examine the impact of additional PSV during exercise (ACE) in those with prolonged MV	Department of Respiratory Care, Chang Gung Memorial Hospital, Tao-Yuan, Taiwan	Subacute RICU adult patients undergoing prolonged mechanical ventilation at >6 h/day for >21 days	Intervention: 15 Age: 73.1 ± 11.2 Female: 11 (73%) APACHE II: - NA	F: 3 sessions I: 10 W T: upon medical stability and MV settings PSV T: upright, in-bed ACE	Safety
de Beer, et al., 2018	Observational	To determine if strength and endurance (measured by ACE) are predictive of successful extubation	Steve Biko Academic Hospital, Pretoria, South Africa	Adult ICU patients eligible for their first spontaneous breathing trial (SBT)	Intervention: 30 Age: NA Female: 18 (60%) APACHE II: - NA	F: 1 ACE session, 5 min I: passive, and active at 1 gear (0.85 kg) T: following eligibility for a spontaneous breathing trial T: semi-Fowler's 45° of flexion, in-bed arm cycling	Safety
Deluzio S et al., 2018	Observational	To examine the safety and feasibility of ACE in a NCCU	NCCU, John Hopkins Hospital, Baltimore, Maryland, USA	Adults admitted to NCCC with upper-limb weakness and/or incoordination	Intervention: 6 Age: 67.7 (12) Female: 2 (33%) APACHE II: NA ICU LOS to start: NA	F: 13 sessions I: % of time passive and active ACE as capable T: not reported T: in-bed or chair level arm cycling	Safety
Vitacca M et al., 2006	Observational	To examine the effects of ACE with or without MV on a variety of physiological and reported measures in difficult-to-wean patients with COPD	RIICUs of Salvatore Maugeri Scientific Institutes of Gussago and Montescano and Gaiato Onlus Villa, Pineta, Italy	Adult, tracheostomized, difficult-to-wean COPD on mechanical ventilation for ≥15 days, admitted to RIICU	Intervention: 8 Age: 68 ± 8 Female: 3 (37.5%) APACHE II: 13 ± 1	F: 4 ACE tests (incremental and endurance on 2 consecutive days, with and without pressure support ventilation) I: Incremental test—0 Watts, then add +2.5 W/min every minute until exhaustion. Endurance test- 50% peak workload on incremental test T: >15 days of MV after admission to RIICU T: upright arm ergometer at patient's shoulder level	Safety
Wilkinson et al., 2021	Observational	To examine the safety and feasibility of measuring metabolic demand in ACE, early in ICU stay	University Teaching Hospital ICU, United Kingdom	Admitted to the ICU with medical diagnosis requiring I + V for at least 48 h	Intervention: 12 Age: 20–89 Female: NA APACHE II: 18.33 (6.30)	F: 1 session, 30 min I: passive T: no reported T: semirecumbent in-bed arm cycling	Safety

Definition of abbreviations: ACE = arm cycle ergometry; APACHE II = Acute Physiology and Chronic Health Evaluation II; COPD = chronic obstructive pulmonary disease; h = hours; ICU = intensive care unit; I + V = intubation and ventilation; L = level; LOS = length of stay; NCCU = neurocritical care unit; MV = mechanical ventilation; PSV = pressure support ventilation; PT = physiotherapy; RCT = randomised control trial; RICU = respiratory intensive care unit; RIICU = respiratory intermediate ICU; ROM = range of motion; SD = standard deviation; W = watts.

observational studies),^{7,19,28,30,31} no severe safety events occurred during any ACE sessions (very-low-certainty). Due to limited reporting, we could not determine the number of patients who experienced serious safety events.

4.3.2.2. Duration of mechanical ventilation. One study enrolling 27 patients reported the duration of MV.²⁹ No difference was found in the length of MV (one RCT; very-low-certainty) between ACE (mean ± standard deviation) (n = 12; 32.7 ± 23.4) and control (n = 15; 54.6 ± 46.2, p = 0.15).

4.3.2.3. Length of stay. One study enrolling 35 patients reported ICU length of stay.²⁸ We found no differences (one non-RCT; very-low-certainty) between interventional ACE (median days) (n = 15;

8.5) and control groups (n = 20; 8.50; p = 0.169) (d = 9.5). No studies reported hospital length of stay.

4.3.2.4. Mortality. Three studies including 112 patients reported mortality.^{10,28,29} There were three deaths in total, which all occurred in a control group (one non-RCT, two RCT; very-low-certainty).

We summarise available outcome comparisons in a Grading of Recommendations, Assessment, Development, and Evaluation evidence table (Table 3).²⁵ All outcomes were of very low certainty.

4.4. Risk of bias

For studies evaluating physical function, Cinar et al. had an overall high risk of bias primarily due to concerns with

Table 3
Table of results by outcome.

Outcome of interest	Study	Study design	Absolute effect		Difference score (d)	Certainty
			Arm ergometry	Controls		
Physical function Barthel Index	Cinar et al., 2020	Non-RCT	Mean \pm SD Barthel Index at ICU discharge (n = 15) 44.66 \pm 38.05	Mean \pm SD Barthel Index at ICU discharge (n = 20) 51.75 \pm 38.19	-7.09	Very low
	Chen et al., 2012	RCT	Mean \pm SD Barthel at study end (n = 12) 19.3 \pm 18.6	Mean \pm SD Barthel at study end (n = 15) 13.4 \pm 16.6	5.9	
Physical function Ambulation Score	Cinar et al., 2020	Non-RCT	Mean \pm SD Ambulation Score at ICU discharge (n = 15) 3.20 \pm 2.18	Mean \pm SD Ambulation Score at ICU discharge (n = 20) 3.75 \pm 2.22	-0.55	Very low
Physical function FIM	Chen et al., 2012	RCT	Mean \pm SD FIM at study end (n = 12) 44.6 \pm 10.0	Mean \pm SD FIM at study end (n = 15) not reported	Unable to calculate	Very low
Length of stay, ICU	Cinar et al., 2020	Non-RCT	Mean (days) (min-max; n = 15): 18 (3-70)	Mean (days) (min-max; n = 20): 8.50 (3-44)	9.5 days	Very low
Length of stay, Hospital	No studies reported	N/A	N/A	N/A	N/A	N/A
Duration of MV	Chen et al., 2012	RCT	32.7 \pm 23.4	54.6 \pm 46.2	-21.9	Very low
Mortality	Chen et al., 2012	RCT	0/12	3/15	-3	Very low
	Cinar et al., 2020	Non-RCT	0/15	0/20	0	
	Porta et al., 2005	RCT	0/25	0/25	0	
Safety	Cinar et al., 2020	Non-RCT	9 of 45 sessions terminated early (20%; n = 15) Fatigue n = 2; Shortness of breath n = 1; Heart rate: >130 bpm n = 2; Decrease in blood pressure >20% n = 2; Oxygen saturation: <90% n = 1; Blush and sweat n = 1	Not reported	Unable to calculate	Very low
	Wilkinson et al., 2021	Observational	1 of 12 session terminated early (8.3%; n = 12) Desaturation n = 1	NA	Unable to calculate	
	Dezulio et al., 2018	Observation	No safety events (0/13; n = 6)	NA	Unable to calculate	
	Debeer et al., 2018	Observational	Not reported (n = 30)	NA	Unable to calculate	
	Vitacca et al., 2016	Observational	2 of 36 sessions had desaturation requiring oxygen titration, no termination (5.6%, n = 6)	NA	Unable to calculate	
	Chen et al., 2015	Observational	4/45 sessions terminated for serious safety events (8.9%, n = 15) Arrhythmia n = 1 Desaturation n = 3	NA	Unable to calculate	

Abbreviations: ICU = intensive care unit; FIM = Functional Index Measure; MV = mechanical ventilation; RCT = randomised controlled trial; SD = standard deviation.

nonrandomisation and lack of blinding overall, lack of allocation concealment, and no blinded assessors.²⁸ This study allocated people to treatment groups, based on their illness severity.²⁸ The study by Chen et al. in 2012 was also deemed to be high risk of bias due to missing data regarding safety.²⁹ Further risk-of-bias details of the remaining studies are in Figs. 2 and 3.

5. Discussion

5.1. Summary of evidence

This systematic review included eight studies that collectively enrolled 183 critically ill patients. There were no deaths and no severe safety events during ACE sessions across the studies. This suggests the potential for ACE to be a safe early intervention in the ICU. When examining the impact of ACE on physical function, we assessed very-low-quality evidence due to heterogeneity in the study design and limitations in study conduct. We identified no difference between groups on ICU length of stay or length of MV. However, all of these results are limited by few studies, very-low-certainty evidence, and further research could change these results.

The findings from this review examined the safety of ACE in the ICU. The included studies reported no severe safety events or deaths in ACE participants. This finding was consistent with previous research on early mobility and leg cycling in the ICU, where

there were few safety events, suggesting that leg cycling was safe for mechanically ventilated ICU patients.^{32,33} The results of our review were limited by inconsistent reporting across studies of safety-related outcomes.

Our included studies used three different outcome measures to assess physical function. The results were inconsistent across outcome measures and studies, representing very-low quality evidence. We identified only two studies that had different designs, control groups, and outcome time points. Due to the quality and quantity of evidence limitations, we conclude that there is very low certainty that ACE and standard physiotherapy care are no different in promoting physical function. Therefore, it is unclear whether ACE impacts physical function at timepoints during ICU stay, or beyond; however, further research could change these conclusions. Promising evidence from other populations, such as people with spinal cord injuries, indicate that ACE can improve fitness, motor function, and quality of life.³⁴ We identified no differences between groups for length of ICU stay and length of MV; however, this was very-low-certainty evidence, and more research is required.

5.2. Strengths, limitations, and future directions

Strengths of our study include several strategies to reduce bias. Two reviewers independently assessed study eligibility, abstracted data, and assessed risk of bias. Our literature search was performed

Study	Risk of bias domains					Overall
	D1	D2	D3	D4	D5	
Chen, 2012	+	-	X	+	+	X
Cinar, 2020	X	+	+	X	+	X
Porta, 2005	+	+	-	+	+	-

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
X High
- Some concerns
+ Low

Fig. 2. Risk-of-bias assessments for studies with a control group, using Cochrane risk-of-bias assessment 2 (ROB2).

Study	Risk of bias domains							Overall
	D1	D2	D3	D4	D5	D6	D7	
Chen, 2015	+	+	?	?	+	+	+	+
deBeer, 2018	+	+	?	?	X	+	+	X
Deluzio, 2018	+	+	?	?	X	+	+	X
Vitacca, 2006	+	-	?	?	X	+	+	X
Wilkinson, 2021	+	+	?	?	+	+	+	+

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement
X Serious
- Moderate
+ Low
? No information

Fig. 3. Risk-of-bias assessments for studies with no control group, using Risk of Bias in Observational Studies of Interventions (ROBINS-I).

in consultation with a research librarian, and large topic-specific databases were searched to include all possible electronic sources of studies. Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines were implemented for transparent reporting of the included and excluded studies.

However, this review also has limitations. We could not utilise statistical methods to assess publication bias due to the few studies included in our review. We excluded one study not written in English due to lack of translation capacity. This review precluded patient and caregiver perspectives in determining patient-important outcomes; however, this selection was based on existing literature^{7,10,19,20,28–30} and consensus among our research team.

Future investigators are encouraged to further explore the effects of ACE on clinical and patient-important outcomes in all critically ill patient populations with rigorously designed RCTs. Due to the structure of the glenohumeral joint, participants with upper-limb weakness could be at risk of developing a shoulder pathology. The measurement of upper-extremity pain or the occurrence of a shoulder pathology during arm cycle ergometry was not reported in any of the included studies. Both pain and pathology of the upper extremity should be considered for measurement in future studies investigating the efficacy of ACE in the ICU. Larger sample sizes would aid in estimating the magnitude of association and generating more reliable results. Investigators are encouraged to focus on studying outcomes

at common timepoints both in the ICU and post discharge. Outcome-assessor blinding should be considered, given that blinding research personnel and participants to group assignment is impossible when administering arm-cycling intervention. Consistency in reporting safety events across ICU studies would be beneficial to better conclude the safety of ICU exercise interventions.

6. Conclusion

ACE can occur in ICU environments. We identified no deaths or serious safety events in the few ACE studies. Safety assessment measures varied across the studies and could not be pooled. However, our results are consistent with, and support pre-existing literature on the safety of early upper-limb exercise in the ICU if it is individualised and if patients are closely monitored. Our review was limited due to the few studies available on ACE in the ICU. However, its utility is promising, and more rigorous studies could examine its impact on short- and long-term physical function and other patient-important outcomes.

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Credit authorship contribution statement

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Conflict of interest

Michelle Kho received the loan of 3 RT300 in-bed cycle ergometers (Restorative Therapies, Baltimore, MD) for research unrelated to this study.

Registration of review

PROSPERO CRD 42022326239.

Data availability statement

Data are available by contacting the lead author upon reasonable request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.aucc.2024.01.008>.

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