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When is it safe to exercise mechanically ventilated patients in the intensive care unit? An evaluation of consensus recommendations in a cardiothoracic setting

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ABSTRACT

Rationale: Consensus recommendations have been developed to guide exercise rehabilitation of mechanically ventilated patients in the intensive care unit.
Objective: This study aimed to investigate the safety of exercise rehabilitation of mechanically ventilated patients and evaluate the consensus recommendations.
Methods: This was a prospective, single-centre, cohort study conducted in a specialist cardiothoracic intensive care unit of a tertiary, university affiliated hospital in Australia.
Results: 91 mechanically ventilated participants; 54 (59.3%) male; mean age of 56.52 (16.3) years; were studied with 809 occasions of service recorded. Ten (0.0182%) minor adverse events were recorded, with only one adverse event occurring when a patient was receiving moderate level of vasoactive support.
Conclusions: The consensus recommendations are a useful tool in guiding safe exercise rehabilitation of mechanically ventilated patients. Our findings suggest that there is further scope to safely commence exercise rehabilitation in patients receiving vasoactive support.

Introduction

Mechanically ventilated (MV) patients in the Intensive Care Unit (ICU) can be subject to prolonged immobility, which can lead to complications such as ICU-acquired weakness.[1] ICU-acquired weakness is characterised by rapid muscle wasting in critically unwell patients, particularly those with multi-organ failure.[2] Prolonged weaning from mechanical ventilation (longer than 7 days) may have a role in the development of ICU-acquired weakness.[3] There is potential that ICU-acquired weakness can lead to prolonged ICU and hospital length of stay. Early exercise rehabilitation of MV patients has been shown to be safe and feasible.[4–6] Benefits of exercise rehabilitation in MV patients in the ICU include shorter ICU and hospital length of stay, reduced days on the ventilator, increased peripheral and respiratory muscle strength, and increased health-related quality of life.[7]

It can be difficult to determine when it is safe to begin exercise rehabilitation with a MV patient in the ICU. There may be concerns regarding the type and number of attachments, as well as existing haemodynamic or respiratory instability that may be exacerbated by exercise. Barriers to exercise in the ICU have been described as being structural, cultural or patient-related.[8] Pain, clinical stability and level of cooperation are examples of patient-related barriers; while structural barriers can include staff experience, time constraints or equipment issues. Cultural barriers relate to attitudes or protocols that may exist in the ICU.[8] Hodgson and colleagues found that the most commonly reported barriers to early exercise in MV patients were intubation with an endotracheal tube and sedation.[9] While consideration of potential risks versus the possible benefits of exercise rehabilitation of MV ICU patients is

Abbreviations: BSL, blood sugar level; ECMO, extra-corporeal membrane oxygenation; HR, heart rate; ICU, intensive care unit; IDC, in-dwelling catheter; LL, lower limb; MAP, mean arterial pressure; MOS, march on the spot; MV, mechanically ventilated; PEEP, positive end expiratory pressure; RASS, Richmond agitation and sedation scale; RR, respiratory rate; SOEOB, sitting on the edge of the bed; STS, sit to stand; UL, upper limb.

Conflicts of interest: None.

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Table 1
Summary of parameters for each consideration outlined in the consensus recommendations.[10]

Respiratory considerations	Cardiovascular considerations	Neurological considerations	Other considerations
Intubation with ETT or tracheostomy tube	Blood pressure	Level of consciousness	Surgical (unstable major fracture, large open surgical wound)
Respiratory parameters (FiO_2, SpO_2, RR)	MAP‖	Delirium	Medical (known or suspected active/ uncontrolled bleeding or increased bleeding risk, febrile despite active cooling management, active hypothermia management)
HFOV mode	Known or suspected pulmonary hypertension	Intracranial pressure	Other considerations (ICU-acquired weakness, continuous renal replacement therapy, venous and arterial femoral catheters, femoral sheaths, all other drains and attachments)
PEEP	Cardiac arrhythmias (bradycardia, tachyarrhythmias, transvenous or epicardial pacemaker)	Other neurological considerations (craniectomy, open unclamped lumbar drain, subgaleal drain, acute spinal cord injury, subarachnoid haemohorrhage with unclipped aneurysm, vasospasm post-aneurysmal clipping, uncontrolled seizures and spinal precautions (pre-clearance or fixation))	
Ventilator dysynchrony	Cardiac devices (Femoral IABP, ECMO, VAD, pulmonary artery catheter or other continuous cardiac output monitoring device)		
Rescue therapies (nitric oxide, prostacyclin and prone positioning)	Other cardiovascular considerations (shock of any cause with lactate >4 mmol/L, known/suspected acute DVT/PE/severe aortic stenosis, cardiac ischemia)		

HFOV, High frequency oscillating ventilation; IABP, Intra aortic balloon pump; PEEP, Positive end expiratory pressure; ECMO, Extra-corporeal membranous oxygenation; MAP, Mean arterial pressure; VAD, Ventricular assist device.

important, undue concerns regarding adverse events may lead to exercise rehabilitation being withheld or delayed unnecessarily.[10]

International consensus recommendations for exercising MV patients in the ICU were developed in 2014[10] by a group of 23 ICU experts. These consensus recommendations have not yet been evaluated in a clinical setting. The recommendations comprise of four considerations: respiratory, cardiovascular, neurological and other. The considerations consist of multiple parameters. Respiratory considerations, for example, consist of parameters such as fraction of inspired oxygen (FiO_2), positive end expiratory pressure (PEEP) and respiratory rate, and neurological considerations consist of parameters such as level of consciousness, intracranial pressure and delirium. The parameters that comprise each consideration are further summarised in Table 1. The recommendations employ a "traffic-light" colour coding system (green, yellow, red) and classify each parameter into a corresponding colour when considering exercise rehabilitation, as illustrated in Figure 1.[10]

The panel members who formulated the recommendations and classified each parameter with a corresponding colour were unable to reach consensus regarding the dose of vasoactive drugs (and combinations of these drugs) at which it is considered safe to commence exercise rehabilitation.[10] Views about the dose, unit of measurement and combinations of these drugs were variable across the panel members of the consensus group. To our knowledge, there is no literature regarding the safety profile of exercise rehabilitation with MV patients on vasoactive support in the ICU.

Therefore, the study aims were to investigate the safety of exercise in patients within a predominately cardiothoracic intensive care unit and relate this to the current consensus recommendations.[10] We aimed to describe any adverse events that occurred while exercising MV patients and to observe if there was a relationship between any adverse events and if a patient was receiving vasoactive medications.

We hypothesised that the consensus recommendations[10] are a useful tool to help guide safe exercise rehabilitation of MV patients in a cardiothoracic ICU and in predicting the risk of adverse events.

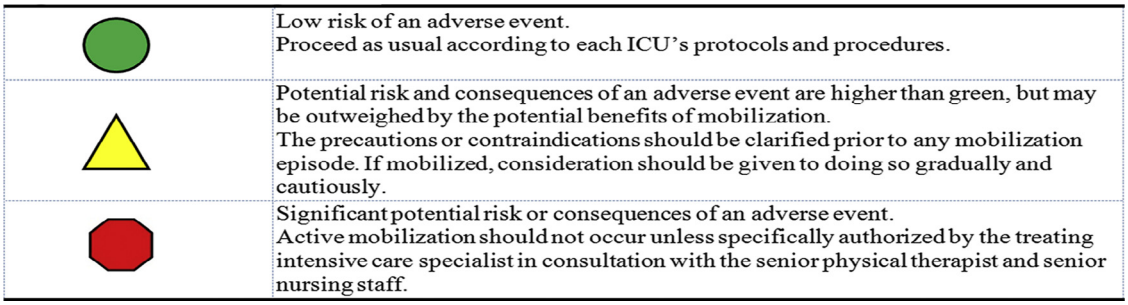

Fig. 1. Colour coding system of recommendations.[10] Permission to use this image has been obtained.

Methods

Design

This was a prospective, single-centre, cohort study conducted at a specialist cardiothoracic ICU of a tertiary, university affiliated hospital in Australia. The Prince Charles Hospital's Human Research Ethics Committee approved this study with patient or next of kin written informed consent being obtained prior to study commencement (HREC/14/QPCH/218).

Recruitment

From February 2015 to December 2016, a sample population of 91 subjects was obtained by convenience sampling. As a result, the time between date of ICU admission and date of recruitment varied between subjects.

Inclusion and exclusion criteria

Patients were eligible for inclusion if they were >18 years of age and MV in the ICU. Patients were excluded if they were <18 years, not MV or if death was deemed imminent by the medical team.

Protocol

For each day that a participant remained ventilated, one physiotherapy occasion of service was recorded. The most advanced form of exercise rehabilitation intervention undertaken was recorded per day. This was defined as the exercise rehabilitation involving greatest amount of muscle activation from the participant and was determined by the treating physiotherapist. Exercise rehabilitation was defined as active in-bed or out of bed exercise. Passive range of motion, as well as ventilation or airway clearance techniques, were not considered exercise rehabilitation.[10] In-bed exercise included active-assisted upper limb (UL) or lower limb (LL) exercises. It also included in-bed cycling ergometry using the MOTOmed Letto™ (Reck, Germany). Out-of bed exercise was defined as tilt table (passively standing via plinth with tilt-in-space function up to 90 degrees), Moveo™ (DJO Global, Vista, CA, USA) which is a table that tilts up to 30 degrees and has a leg press function. Additionally, sitting on the edge of the bed (SOEOB), sit to stand (STS), marching on the spot (MOS) or mobilising away from the bedside.

Measures

Demographic data was collected, including age, sex, reason for ICU admission, and medications. Data was collected on a daily basis regarding clinical parameters specific to the 4 separate considerations (respiratory, cardiovascular, neurological and other) of the recommendations that were being evaluated.

The ICU Mobility Scale[11] was used to quantify the participant's mobility status after the exercise rehabilitation had occurred. This is a scale that is used to measure an adult ICU patient's maximum level of mobility. It has been shown to have strong inter-rater reliability[11] and is easy to use. It ranges from 0 to 10, where 0 indicates the patient has no active movement and is passively moved into positions, and 10 applies to patients who can mobilise independently without a mobility aid. Reasons why exercise rehabilitation was not performed or was ceased were recorded.

For the purpose of this study, inotropes and vasopressors were collectively called vasoactive medications and categorised as low, moderate or high doses with the classifications described in Table 2.

Table 2
Classification of vasoactive medication dosage for this study.

Vasoactive medication	Low (mcg/kg/min)	Moderate (mcg/kg/min)	High (mcg/kg/min)
Dopamine	<3	3–10	>10
Dobutamine	<3	3–10	>10
Adrenaline	<0.05	0.05–0.2	>0.2
Noradrenaline	<0.05	0.05–0.2	>0.2
Vasopressin	0.01	0.02–0.03	0.04
Levosimendan	0.05	0.1	0.2
Milrinone	0–0.15	0.15–0.5	0.5

Subjects receiving multiple (2 or more) vasoactive medications were categorised into either low, moderate or high level of support, depending on the highest level of an individual medication.

Prior to commencing any in-bed or out of bed exercise rehabilitation for patients with identified yellow or red parameters, careful consideration and discussion with senior physiotherapy and medical staff occurred.

Adverse events during or resulting from exercise rehabilitation were communicated to the researchers by documenting on the data collection form and were defined as the following[12]:

1. Removal, dislodgement, disruption or dysfunction of attachments (including airway, feeding tube, chest tube, vascular access, cardiac devices, wound or dressing).
2. Cardiovascular or haemodynamic instability
   - Hypotension (change in mean arterial pressure (MAP) to <55 mmHg).
   - Hypertension (change in MAP > 140 mmHg).
   - Desaturation (change in peripheral oxygen saturation to <85%).
   - Cardiac arrest.
   - New arrhythmia.
   - Death.
3. Other event considered clinically important by clinicians and not listed.
4. Fall.

Statistical analysis

Statistical analyses were performed using SPSS 24 (IBM Corporation, Somers, NY, USA). Vasoactive medication doses were categorised into low, medium or high categories (Table 1), which allowed statistical analyses to be conducted. We originally planned to investigate the relationships between variables, however the low number of adverse events precluded further formal analysis and therefore the results are largely descriptive.

Results

Patient characteristics

Ninety-one mechanically ventilated participants; 54 (59.3%) male; mean age of 56.52 (SD16.3) years; were studied. The participant's reasons for their ICU admission were: 41 (45.1%) post-cardiothoracic surgery (including heart and lung transplantations), 20 (22%) cardiac-related illness, 14 (15.4%) respiratory-related illness, and the remaining 16 (17.6%) participants were admitted for other reasons including complications post-cardiothoracic surgery, abdominal- or metabolic-related illness or infection.

In total, 809 occasions of service were documented, in which a physiotherapist decided whether or not a patient was appropriate for in or out of bed exercise rehabilitation. On 260 (32.1%) occasions, exercise rehabilitation did not occur. One hundred and

Table 3
Details of adverse events recorded during exercise rehabilitation of MV ICU patients.

Exercise type	Adverse event description	Number yellow parameters identified	Which yellow parameters	Number red parameters identified	Which red parameters	Patient on vasoactive medication
In-bed LL cycling	Other-Disruption of IDC	2	SpO2, respiratory rate	0		No
Tilt	Other-increased heart rate and low flow alarm on ECMO	3	Stable ventricular rate (120–150 bpm), PEEP > 10, respiratory rate > 30	1	ECMO-femoral or subclavian	No
Tilt	CV instability	2	RASS –2 to +2, respiratory rate > 30	1	Pacemaker-dependent rhythm	No
Tilt	CV instability	2	Respiratory rate > 30, MAP > lower limit target range while receiving moderate level support	1	Pacemaker-dependent rhythm	Yes .15 mcg/kg/min Noradrenaline
Moveo	CV instability	1	Stable ventricular rate (120–150 bpm)	0		No
Tilt	CV instability	0		1	Pacemaker-dependent rhythm	No
STS	CV instability	0		0		No
STS	CV instability	0		0		No
Moveo	Other-PaO_2 decreased post	0		0		No
Moveo	Other-BSL decreased post	0		0		No

IDC, In-dwelling catheter; ECMO, Extra-corporeal membrane oxygenation; PEEP, Positive end expiratory pressure; RASS, Richmond agitation and sedation scale; MAP, Mean arterial pressure; BSL, blood sugar level.

one (12.5%) of the 809 occasions of service consisted of in-bed exercise, 448 (55.4%) consisted of out-of-bed exercise. The mean ICU Mobility Scale score was 2.52.

Exercise rehabilitation

Forty-six (45.5%) of the 101 in-bed exercise interventions consisted of active-assisted UL and/or LL exercises, 31 (30.7%) consisted of active UL and/or LL exercises, while 24 (23.8%) consisted of in-bed cycling. One hundred and eighty-nine (42.2%) of all 448 out of bed exercise interventions consisted of tilt table, and 55 (12.3%) included the use of the tilt table with leg press function. 60 (13.4%) out-of bed interventions included mobilising away from the bedside, 46 (10.3%) sitting on the edge of the bed, 92 (20.5%) STS practice, and 6 (1.3%) MOS. A total of 10 (0.0182%) adverse events were reported over the total 549 occasions of in- or out-of-bed exercise rehabilitation. All of the adverse events were minor and led to no further complications or clinically significant issues. Details regarding these adverse events are illustrated in Table 3.

Identification of yellow and red parameters

Despite identification of red parameters, in bed exercise occurred on 2 of 101 occasions (1.98%). In these cases, no adverse events occurred. Despite the presence of yellow parameters, in bed exercise occurred on 72 of 101 occasions (71.28%). Of these cases, 1 adverse event occurred (1.38%). This was disruption of an in-dwelling urinary catheter during in-bed cycling and was not considered significant, as it did not result in any clinical consequences.

Out of bed exercise occurred despite yellow parameters having been identified on 189 of 448 occasions (42.18%). Out of bed exercise occurred despite red parameters having been identified on 43 of the 448 (9.59%) occasions with 4 (9.30%) adverse events documented. On one occasion (0.52%), an adverse event occurred with a yellow parameter (and no red) having been identified.

A chi-square cross tabs found that the occurrence of an adverse event during out of bed exercise was significantly higher if a red parameter had been identified compared to yellow and green parameters ($p < 0.01$). Three events were classified as cardiovascular (CV) instability, and 1 "other" adverse event (Table 2). Adverse events occurred following 1/189 (0.5%) identification of yellow parameters and on 4/216 occasions (1.9%) when neither yellow nor red parameters were identified.

Exercise rehabilitation and vasoactive medications

In total, 299 occasions of service occurred where the participants were receiving inotropes or vasopressors. Active exercise rehabilitation did not occur on 144 (48.16%) of these 299 occasions. In-bed exercise occurred on 41 (13.71%) occasions. 15 patients (36.58%) were classified as being on low, 24 (58.53%) moderate and 2 (4.87%) on high level of vasoactive support. No adverse events occurred during in-bed exercise on patients on inotropes or vasopressors.

Out-of-bed exercise occurred on 114 (38.12%) occasions when patients were receiving inotropes or vasopressors, with 67 (58.77%) participants classified as being on low, 46 (40.35%) on moderate and 1 (0.87%) on a high dose of vasoactive support.

In total, one adverse event occurred during exercise rehabilitation when a patient was on vasoactive support (0.87%). Specifically, this adverse event was defined as cardiovascular instability, and occurred whilst using the tilt table on a patient who was classified as receiving a moderate level of inotropic support (0.15 mcg/kg/min Noradrenaline). Prior to exercise occurring, two yellow parameters were identified (RR > 30, MAP >lower limit target range while receiving moderate level support) and one red parameter identified (pacemaker-dependent rhythm) when referring to the recent consensus recommendations.[10]

A chi-square crosstabs ($p < 0.001$) found that the likelihood ratio of an adverse event was increased when patients were not receiving inotropic support.

Discussion

In this study, despite yellow and red parameters being identified, exercise rehabilitation of MV ICU patients was frequently conducted after careful consideration and discussion with senior staff members and the medical team, and a comprehensive assessment of haemodynamic stability. It was observed that the risk of

an adverse event occurring when exercising a MV patient on vasoactive support was minimal. While previous studies[13] and recommendations[10] looking at critically ill patients have suggested a cautious approach recommending limiting exercise rehabilitation for patients on vasoactive support, our findings indicate that dependency on vasoactive medication alone should not be considered a reason for withholding exercise rehabilitation. The consensus recommendations[10] are a useful tool in guiding exercise rehabilitation of patients on vasoactive support and should be used in conjunction with a thorough assessment of the patient's haemodynamic stability and consultation with senior medical and physiotherapy staff.

There was a significantly increased risk of an adverse event if a red parameter was present. Interestingly, the likelihood ratio of an adverse event was increased when patients were not receiving inotropic support. However, our findings do not prove causality. Of note is that half of the adverse events described as cardiovascular instability occurred in patients who were not receiving vasoactive medications while they were undertaking interventions involving passive standing up (i.e. tilt table +/– leg press function).

When performing a passive standing up movement (tilt table), the patients who are not dependent on vasoactive support do not receive the vasoconstrictive effects to assist them in maintaining cardiovascular stability. This could be related back to the Tilt Table test,[14] which is an orthostatic challenge in an upright tilt used to diagnose syncope with unknown origin. CV instability observed during the tilt table interventions in this study could be linked to the diagnoses described by this test.[14] Initial orthostatic hypotension is caused by the mismatch between cardiac output and systemic vascular resistance and manifests as a drop in blood pressure and dizziness.[15] Classic orthostatic hypotension is due to autonomic failure to increase the systemic vascular resistance in upright positioning leading to a drop in blood pressure.[15] Additionally, delayed orthostatic hypotension (which occurs between 3 and 30 minutes post upright positioning) is caused by a progressive fall in venous return, low cardiac output and reduced reflex vasoconstriction but no decrease in heart rate.[15] It may be safer to, where possible, have patients who are not dependent on vasoactive medications participate in exercises that involve more activation of the larger muscle groups rather than passively driven exercises to facilitate venous return. For example, using a tilt table with a leg press function or in-bed LL cycling.

However, of the recorded adverse events, 40% occurred when no yellow or red parameters had been identified prior to commencing the exercise rehabilitation. Specifically, these events were described as either CV instability or "other", in which one instance of low BSL and one occasion of low PaO_2 were recorded. This may suggest that physiotherapists should gather clinical information in a holistic and system based approach prior to conducting exercise rehabilitation, including checking peripheral circulation, urine output, mentation and blood sugar levels.

The very low incidence of adverse events when exercising patients dependent on vasoactive medications indicates that there may be further scope to exercise these patients earlier. The findings indicate that dependency on vasoactive medications should not be considered a reason to withhold exercise rehabilitation, and that a holistic assessment of the patient should occur in conjunction with consultation with senior medical and physiotherapy staff prior to commencing exercise rehabilitation.

In this study, we found that the recent consensus recommendations[10] are a useful tool in guiding safe exercise rehabilitation of MV patients and in predicting the risk for adverse events in a cardiothoracic ICU. We have found that there is further scope to commence early exercise rehabilitation in ICU patients on vasoactive support. Our findings suggest that dependency on vasoactive medication should not be considered a reason for withholding exercise rehabilitation.

Limitations

Some limitations to this study should be acknowledged. Firstly, as a specialist cardiothoracic hospital, the classification of vasoactive medication dosage cannot be generalised and will vary depending on the institution. The definition of adverse events[12] might be considered too general. Future studies should include a more thorough description of adverse events. The lack of detail surrounding adverse events that occurred during this study (most notably with regards to CV instability) makes it difficult to draw conclusions with regards to the physiological effect that exercise rehabilitation has on certain patients, particularly when considering whether or not they were receiving vasoactive medication. More in depth descriptions would allow a greater understanding of the physiology and potential reasons behind the CV instability, as described previously when discussing the Tilt Table test.

Furthermore, intensity and duration of the exercise rehabilitation performed was not recorded. These factors could be related to the likelihood of an adverse event occurring, particularly when considering whether or not patients were receiving vasoactive medications. Lastly, the results are only reflective of our institution, and further study is needed to determine if the results are transferrable to other ICUs.

Conclusion

We found the consensus recommendations[10] to be a useful tool in guiding safe exercise rehabilitation of MV patients and in predicting the risk for adverse events in a specialist cardiothoracic ICU. The risk of an adverse event occurring when exercising a MV patient on vasoactive support was minimal, as long as a comprehensive and holistic clinical assessment was performed prior to commencing the exercise rehabilitation. The findings indicate that there may be further scope to commence exercise rehabilitation in vasoactive medication dependent ICU patients and that dependency on these medications should not contraindicate exercise rehabilitation. This study highlights the remaining lack of consensus surrounding the safety for exercise rehabilitation of patients who are receiving vasoactive medications in the ICU. Future research should focus on more clearly defining this safety profile. This may lead to exercise rehabilitation commencing at an earlier time for ICU patients.

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