A FOUR-WEEK OBSERVATIONAL STUDY TO IDENTIFY CARDIOPULMONARY TRENDS IN CRITICALLY-ILL SEPSIS PATIENTS PARTICIPATING IN PHYSIOTHERAPY REHABILITATION IN THE VGH-ICU

by

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Abstract

Early mobilization (EM) has been an increasingly recognized tool in the intensive care unit (ICU) for critically ill patients. Advances in critical care medicine has led to the growth of the cohort of patients termed 'chronically critically ill'. These patients successfully stabilize from acute critical illness, however due to deterioration of physical and/or cognitive function become dependent on full time hospital care. ICU acquired weakness (ICUAW) is a spectrum disease characterized by symmetrical physical and/or cognitive impairments developed while admitted to an ICU. The development of ICUAW is a contributing factor that leads to chronic critical illness. EM has been proposed as a tool that can be used to prevent or slow down the onset of ICUAW. **PURPOSE**: The purpose of this thesis was to describe and quantify the rehabilitation practices and the cardiopulmonary trends in critically ill sepsis patients in the Vancouver General Hospital's ICU. **METHODS**: Patients (n = 21) who met the inclusion and exclusion criteria were observed during a four-week period, Monday to Friday. The chart notes were used for Saturdays and Sundays. Daily cardiopulmonary vitals (e.g. heart rate (HR), blood pressure (BP), respiratory rate, peripheral oxygen saturation etc.) were taken at three time points and the chart notes were used to record test results. Additionally, physiotherapy sessions were observed and described. **RESULTS:** Norepinephrine had a decreased median dose during EM compared to prophylactic management in the released to ward outcome group. Sequential Organ Failure Assessment (SOFA) score was significantly different between patients who achieved a mobility score of 0 compared to ≥ 3 ($p = 0.014$). Sitting on the edge of the bed (EOB) elicited a HR and BP response suggestive of exercise in some patients. Lastly, the cardiopulmonary trends were consistent with what was expected. **CONCLUSION:** Norepinephrine dose and SOFA score may independently be able to help predict the mobility score a patient is likely to achieve during physiotherapy. The HR and MAP response

observed during EOB in some patients participating in EM, presented a trend suggestive of exercise and warrants further investigation.

Lay Summary

A four-week observational study in the Vancouver General Hospital's intensive care unit (ICU) was conducted to investigate rehabilitation practices with critically ill sepsis patients. Admitted patients were observed three times daily and during physiotherapy sessions, Monday to Friday. On Saturday and Sunday, the records were consulted. Measurements and physiotherapy sessions that were observed were part of standard of care. The results suggest that a higher dose of blood pressure medication and/or a higher score of organ failure may be associated with decreased exercise capabilities in critically ill sepsis patients. Additionally, some exercises for critically ill patients produced a response that is suggestive of what occurs when healthy adults exercise. It can be speculated that physiotherapy in ICU's may elicit an exercise response in some patients and that outside factors may play a role in predicting who is more likely to be able to participate in structured exercise in this setting.

Preface

This thesis was designed by myself, Kayla Johnston, with the support of my supervisor and the support of intensive care unit staff members at Vancouver General Hospital. All observational data was collected by myself, with analysis assistance from UBC Faculty of Education and Simon Fraser University Statistics Department. All methods and protocols were reviewed by the Clinical Research Ethics Board at the University of British Columbia and approved (REB#H20-03695).

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List of Abbreviations

ATP	Adenosine triphosphate
BMI	Body mass index
BP	Blood pressure
Ca_{O_2}	Concentration of arterial oxygen
CIM	Critical illness myopathy
CIP	Critical illness polyneuropathy
CO_2	Carbon dioxide
COPD	Chronic obstructive pulmonary disease
CPR	Cardiopulmonary resuscitation
$C\bar{v}_{O_2}$	Concentration of mixed venous oxygen
EEG	Electroencephalography
EM	Early mobilization
EOB	Edge of bed
FiO_2	Fraction of inspired oxygen
GCS	Glasgow coma scale
HR	Heart rate
ICU	Intensive care unit
ICUAW	Intensive care unit acquired weakness
IL-10	Interleukin 10
IL-6	Interleukin 6
ILD	Interstitial lung disease
Kg	Kilograms
LE	Lower extremity
m	Meters

MAP	Mean arterial pressure
MV	Mechanical ventilation
O_2	Oxygen
P/F	Pressure of arterial oxygen divided by the fraction of inspired oxygen
$PaCO_2$	Pressure of arterial carbon dioxide
PaO_2	Pressure of arterial oxygen
PEEP	Peak end expiratory pressure
PM	Prophylactic management
PT	Physiotherapy
$\dot{Q}$	Cardiac output
RR	Respiratory rate
SaO_2	Arterial oxygen saturation
SIRS	Systemic inflammatory response system
SOFA	Sequential organ failure assessment
SpO_2	Peripheral oxygen saturation
SV	Stroke volume
TNF-α	Tumor necrosis factor alpha
UBC	University of British Columbia
UE	Upper extremity
V_A	Alveolar ventilation
$\dot{V}CO_2$	Volume of carbon dioxide
$\dot{V}_E$	Expiratory volume
VGH	Vancouver General Hospital
$\dot{V}O_2$	Volume of oxygen uptake
$\dot{V}O_{2\ max}$	Maximal volume of oxygen uptake
WOB	Work of breathing

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Lastly, the help/support of Dr. Bill Sheel for his guidance and continued perseverance with helping me to see this study through to completion during a pandemic.

Chapter 1: Introduction and Background

1.1 Overview

Early mobilization (EM) in the intensive care unit (ICU) has become increasingly recognized as a therapeutic tool with the potential to improve functionality and long-term prognosis of critically ill patients.[1–3] It has been shown to be safe and feasible to implement, including with mechanically ventilated patients.[4,5] However, the evidence to support the use of EM is, to date, inconclusive owing to issues related to the heterogeneity of the population(s) admitted to the ICU, high patient mortality and a wide range of research designs.[3,6–8]

In addition, a broad range of definitions of 'early mobilization' in the ICU has made interpretation of the collective literature difficult.[9] For example, the following definitions have been used:

- Critically ill patient mobilization that begins within 72 hours of their ICU admission.[10,11]
- Patient mobilization that begins when contraindications are absent and a set of systems-based safety criteria are met.[12]
- Mobilizations that are initiated as soon as possible following critical care unit admission.[13]
- Any activity beyond range of motion performed by a care provider (nurse, physical or occupational therapy) occurring within 48 hours of initiation of mechanical ventilation.[14]
- A planned series of exercises for a patient in a sequence that begins at a patient's current mobility and returns the patient to their baseline mobility status.[15]
- Progressive physiotherapy and acute rehabilitation initiated as soon as possible following admission to the ICU. It includes a progression of exercises from range of motion to ambulation that may begin while they are still receiving life support (i.e. mechanical ventilation).[16,17]

- A progression of mobilization interventions applied to patients in phases ranging from range-of-motion in bed exercises to walking out of bed. These are the physical activities that patients begin as early as possible after ICU hospitalization.[18]

For the purposes of this thesis, ICU EM will be defined as progressive physiotherapy and acute rehabilitation initiated as soon as possible following admission to the ICU, through a serious of exercises from range of motion to ambulation that may begin while they are still receiving life support. This definition addresses when EM should begin, the progressive nature of the physiotherapy and that it can begin while the patient is still on life support. 'As soon as possible' is assumed to denote that mobilization should begin when it is safe for the patient and that it should start while they are still in the ICU. The definition does not exclude patients who are unable to participate in the first 48-72 hours and it includes range of motion (ROM) as a mobilization. ROM is the first stage of mobility as identified by Hodgson et al[19]. This definition is also commonly used by Canadian research groups.[6,13,14]

With the continual advancement of critical care medicine a new cohort of patients has been termed 'the chronically critically ill'.[20] Chronically critically ill patients successfully stabilize from acute critical illness, however, due to deterioration of physical and/or mental functioning they often remain dependent on full time care.[20] A key contributor to becoming chronically critically ill, is ICU-acquired weakness (ICUAW). ICUAW is a spectrum disease that includes physical and cognitive impairments that are developed during the period of critical illness.[21] A predominant characteristic is skeletal muscle atrophy and dysfunction, in part due to the sedentary nature of an ICU setting.[1,22] The incidence of ICUAW is associated with length of ICU stay. With higher incidence reported with increased length of stay.[23]

The respiratory musculature and in particular the diaphragm are commonly negatively affected within the ICU environment.[24] Diaphragm weakness can result from the following: mechanical ventilation, neuropathies, myopathies (e.g. sepsis associated myopathy, ventilator-associated respiratory muscle injury, disuse atrophy etc.), metabolic abnormalities and decreased

oxygen (O_2) delivery.[25] A key point of concern is mechanical ventilation exacerbating diaphragm weakness resulting in difficulty weaning the patients off the ventilator.[24,26] Early implementation of aerobic type exercise, such as bed side cycle ergometry, in the ICU with mechanically ventilated patients has been suggested to help promote weaning and prevent dependency.[1,24]

The health-related benefits of regular physical activity are well-documented in the context of disease prevention for healthy individuals as well as for the management of those with chronic disease (e.g., heart failure, diabetes, among others).[27,28] Structured aerobic or endurance-type exercise training is also a common strategy with which to improve athletic performance. Here, the goal is to provide a training overload stimulus to those organ systems involved with O_2 transport and utilization in order to elicit a physiological adaptation that results in improved function. In addition, resistance training is utilized to increase muscle cross-sectional area and improve muscular strength for health-related outcomes as well as athletic performance.[29–31] In the critically ill, exercise is increasingly being utilized to prevent or slow the deterioration of the cardiorespiratory and musculoskeletal systems which is associated with a loss of functional independence. During periods of bedrest, such as that associated with the ICU environment, it is accepted that there is a decline in function across organ systems in both healthy and diseased populations.[1–3,22,32] There is growing support that targeted exercise rehabilitation has the potential to slow down or prevent the ICU-related decline in function and reduce mortality.[19,22,33] In patients diagnosed with septic shock in North American and Europe, a systematic review and meta-analysis published in 2019, estimated ICU mortality at 37.3% and 28-30-day mortality near 36.7%.[34]

The purpose of this review is three-fold. First, to summarize existing knowledge of exercise physiology as it pertains to performance, disease prevention and treatment of chronic disease. Second, to identify aspects of critical illness that have the potential or have been shown to benefit from EM. Lastly, to present an overview of the existing research that has been conducted on exercise with critically ill populations.

1.2 Exercise Physiology

1.2.1 Fundamentals of exercise physiology

Rhythmic muscular exercise represents a disruption to homeostasis. With dynamic exercise a number of physiological adjustments occur in an attempt to 'operate' at close to basal conditions. For example, skeletal muscle, the heart and lungs, vascular system, nervous system, endocrine system and the processes of thermoregulation all interact in a complex and highly coordinated fashion to meet the demands of exercise. This section will focus on the exercise physiology of the cardiopulmonary system and the role of the oxygen cascade in exercise performance and prevention and treatment of chronic diseases. Respiration, oxygen uptake and utilization and the acute and chronic adaptations of training will be discussed. Oxygen uptake is the ability of the lungs to take the O_2 inhaled during ventilation, transport it systemically bound to haemoglobin and extract it to be utilized at the tissue level.[35] During dynamic exercise, the increased demand for O_2 can be expressed by the Fick equation;

$$\dot{Q} = \frac{\dot{V}O_2}{Ca_{O_2} - C\bar{v}_{O_2}}$$

Where $\dot{Q}$ is cardiac output, $\dot{V}O_2$ is the volume of O_2 per unit of time and $Ca_{O_2} - C\bar{v}_{O_2}$ is the difference in O_2 concentration of arterial and mixed venous blood.[36] $\dot{V}O_2$ provides an estimate aerobic fitness and the maximal value ($\dot{V}O_{2\max}$) reflects the upper most capacity of the ability to integrate systems related to the intake, distribution and utilization of O_2.[29] At the onset of dynamic exercise there is an immediate increase in pulmonary ventilation, heart rate (HR), stroke volume (SV) and cardiac output ($\dot{Q}$). The cardiopulmonary adjustments serve to increase $\dot{V}O_2$ in proportion to metabolic demand.[29,37] The values stabilize at sub-maximal exercise intensity in what is known as steady-state. A point when the systems are in equilibrium and the O_2 transport system is able to meet the demands of the metabolically active tissue.[38]

What follows is a brief summary of each component of the Fick Equation.

1.2.2 Pulmonary ventilation

Effective pulmonary ventilation is the act of inhaling and exhaling air in order to deliver O_2 to the alveoli and remove carbon dioxide (CO_2). At rest, a healthy adult will have a breathing frequency near 10 breaths per minute and a tidal volume (V_T) of roughly 500 ml.[36] The diaphragm drives the breathing process with assistance from the accessory breathing muscles (e.g. sternocleidomastoid, internal intercostals, scalene etc.).[36] On the initiation of exercise, breathing frequency and tidal volume will rise as $\dot{Q}$ increases to meet the O_2 demands of the system and maintain Ca_{O_2} blood homeostasis. In a healthy adult Ca_{O_2} is held constant, despite the increased demand for O_2.[39] The Ca_{O_2} is maintained due the O_2 having significantly more time than it needs to bind to hemoglobin when the erythrocyte travels through the pulmonary capillaries at rest, allowing for room to increase the velocity of flow during exercise. The process requires a high saturation of arterial oxygen (SaO_2). The result is a higher volume of blood successfully undergoing gas exchange in the pulmonary capillaries and a higher rate of oxygenated blood being pumped systemically.[29,35,40]

Ventilation acts to remove metabolically produced CO_2 and maintain pH homeostasis near resting levels during submaximal exercise.[29] The volume of CO_2 ($\dot{V}CO_2$) being produced is analysed relative to the volume of expired gas ($\dot{V}_E$) as a measure of health; $\dot{V}_E/\dot{V}CO_2$. The ratio naturally increases with age, however in populations with cardiopulmonary diseases it will be significantly higher due to ventilation inefficiency.[41]

1.2.3 Cardiac response

The cardiac system responds to the onset of exercise to maintain O_2 homeostasis. Cardiac output is determined by HR multiplied by SV. Both increase during exercise, directly increasing $\dot{Q}$ linearly until near maximal effort to meet the O_2 demand. The response allows for a higher volume of oxygenated blood to be pumped into systemic circulation by the left ventricle of the

heart.[29,35] At rest, $\dot{Q}$ in a healthy adult is roughly 5 L/min and can increase to 20-40 L/min during maximal exercise depending on the individuals fitness.[39,42] Systolic blood pressure (BP) rises with increased exercise intensity as a function of $\dot{Q}$, diastolic BP remains relatively unchanged due to the fall in vascular resistance. The overall result is an increase in mean arterial pressure (MAP) during exercise in healthy populations.[35] This slight increase in MAP is governed by total peripheral resistance multiplied by $\dot{Q}$. To maintain MAP during exercise as $\dot{Q}$ is increased, the total peripheral resistance must decrease.[35] In a healthy adult this is done by prioritizing blood flow to skeletal muscles through vasoconstriction.[29]

1.2.4 Oxygen utilization

The ability of contracting skeletal muscle to extract and utilize O_2 from arterial blood for the purposes of metabolic work is expressed as: $Ca_{O_2} - C\bar{v}_{O_2}$. With increases in exercise intensity there is a widening of the $Ca_{O_2} - C\bar{v}_{O_2}$ which is indicative of a higher extraction/utilization at the tissue level. In healthy adults, Ca_{O_2} is maintained at near-resting values during exercise, including heavy or maximal intensities.[39] The maintenance of arterial oxygenation can be interpreted to mean that the cardiopulmonary system is well suited to ensure appropriate O_2 delivery to contracting muscle. As such a widening of the $Ca_{O_2} - C\bar{v}_{O_2}$ reflects a lowering of O_2 in the mixed venous blood and the metabolic usage of O_2 for adenosine triphosphate (ATP) turnover.

Muscles utilize three metabolic pathways to generate ATP to power movements; phosphocreatine, anaerobic and aerobic pathways.[43] The first pathway is a single reaction catalyzed by creatine phosphokinase creating a rapid, but short lived supply of ATP that can be utilized on the immediate onset of exercise.[44] The second pathway breaks down glucose first through glycolysis, before further degrading the carbon skeleton products into lactate in the absence of O_2. The glycolytic system is fast and is utilized for shorter periods (e.g. seconds to minutes) of high intensities bouts of strength or power. It's limited by the availability of glucose and the accumulation of lactate that leads to metabolic acidosis.[29] Lastly, aerobic metabolism

utilizes the products of glycolysis to fuel the citric acid cycle and substrate level phosphorylation, producing the highest ratio of ATP per one glucose molecule. Substrate level phosphorylation requires O_2, it is slower to activate upon the initiation of exercise and it is the predominate form of energy production during lower intensity exercise. The oxygen reliant pathway can sustain exercise for long periods of time (e.g. minutes to hours).[29,43] The continued generation of ATP is necessary to excite the membrane and power the formation and contraction of the actin-myosin cross bridges. With training, an athlete has a higher ability to extract and utilize O_2 which typically results in increased exercise capacity.[29,45]

1.2.5 O_2 uptake – an integrated physiological variable

The VO_2 is determined by $\dot{Q}$ and $Ca_{O_2} - C\bar{v}_{O_2}$ and represents the amount of O_2 that can be consumed as a unit of time. The $\dot{V}O_{2max}$ is the uppermost ability of the system and is limited by the ability to transport oxygenated blood and the capacity of tissue to extract O_2 from the blood. During exercise, at the peripheral tissue, there is increased O_2 extraction causing a decreased $C\bar{v}_{O_2}$. The result is an increase in the $Ca_{O_2} - C\bar{v}_{O_2}$ difference and is combined with the increased $\dot{Q}$ to elevated VO_2.[39]

Measurement of $\dot{V}O_2$ provides a general measurement of the three main steps of the O_2 transport when we consider the Fick Equation rearranged; $VO_2 = \dot{Q} \times (Ca_{O_2} - C\bar{v}_{O_2})$. The first is the efficiency of alveolar ventilation, Ca_{O_2}. A healthy system can hold the Ca_{O_2} constant, despite the challenges faced by the pulmonary system for alveolar-capillary gas equilibrium during exercise. The second part is $\dot{Q}$ which reflects the cardiovascular system's capacity to transport the oxygenated blood through systemic circulation to the working musculature. The third step is shown by $C\bar{v}_{O_2}$. During exercise in a healthy adult the $C\bar{v}_{O_2}$ will decrease, giving us a measure of the tissues ability to extract the O_2 from the blood.[46]

In a laboratory setting, $\dot{V}O_2$ is measured by the participant completing an incremental exercise test and exhaled gasses collected and analysed. The maximal value is obtained by

exercising the participant to the point of volitional exhaustion and identifying when O_2 uptake has plateaued. The system plateaus when the circulatory systems ability to transport O_2 and the ability of the lungs to extract O_2 have reached their upper limit.[42]

1.2.6 Adaptations to aerobic and muscular exercise training

Repeated aerobic exercise training bouts completed consistently over weeks to months are associated with long-term adaptations in multiple physiological systems including cardiovascular, pulmonary and metabolic.[31,39] Aerobic adaptations include an increase in SV, a decrease in resting and submaximal exercise HR levels and an increase in $\dot{Q}$ at maximal intensity exercise. An increase in $\dot{Q}$, in part drives the increase in $\dot{V}O_{2max}$ seen in trained athletes. Additionally, blood pressure will decrease at rest and submaximal intensities, while blood volume will increase overall, putting less strain on the cardiovascular system. Gas exchange in skeletal muscle is increased owing to a greater capillary density which allows for increased O_2 extraction and as such an increased $Ca_{O_2} - C\bar{v}_{O_2}$ difference. Lastly, trained skeletal muscle has an increase in volume and density of mitochondria which permits greater O_2 mediated generation of ATP.[39]

Resistance exercise provides a training stimulus to the musculoskeletal system by performing concentric, eccentric, and isometric contractions under load.[30,47] Following resistance exercise, microtrauma can be present which elicits a remodeling response that over time increases the cross sectional area of the muscle provided the exercise intensity is progressively overloading.[30] Progressive training overload is the practice of consistently increasing either the intensity, volume or duration of a specific exercise to continually stress the muscular system.[47] When the muscle is not progressively overloaded, resistance training helps retain muscle mass and tone. Other chronic adaptations of resistance training include changes in connective tissue stiffness and potential for increased bone mineral density if the training is weight bearing.[30,47] In aging populations it promotes the retention of the strength needed to complete the activities of daily living and prevents the onset of frailty.[48]

An athlete will train to maximize cardiovascular efficiency and increase muscular strength accomplished by optimizing the pathways previously discussed.[28] In contrast, exercise is used with the critically ill patient in order to minimize the progression of ICU-related muscle degeneration and loss of cardiovascular function.[28] These complications can result from sedentary bed rest and lead to ICUAW and other negative health consequences.[22] EM exercises have the potential to slow down or reverse ICU-related decline by enabling the patient to use their skeletal musculature. When the movement or change in position is enough to increase skeletal muscle demand for O_2, the demand will require the cardiopulmonary system to adjust the RR, HR and/or SV to supply the O_2. Muscular contraction through mobilization will require an increase in $\dot{V}O_2$ and $\dot{Q}$ beyond what is needed for basal resting conditions[35]. Muscular contraction and the increased metabolic demand – even to a modest degree – is the first step in trying to mitigate muscle weakness and cardiopulmonary decline associated with critical illness and bedrest.[8,22]

1.3 Critical Illness: Intensive Care Unit Acquired Weakness

1.3.1 Pathophysiology

Patients admitted to an ICU are in critical condition suffering from life threatening illness or injury that require immediate intervention in order to prevent the loss of life. For patients who survive critical illness, secondary complications can arise, a common example being ICUAW.[20,21,49] ICUAW is defined as a condition that occurs after the onset of critical illness and results in symmetric weakness of the extremities and the respiratory breathing muscles characterized by muscle atrophy and dysfunction.[50]

ICUAW has three commonly identified pathologies including, critical illness polyneuropathy (CIP), critical illness myopathy (CIM), and severe muscle atrophy. They can present alone or they can coexist.[21,50,51] ICUAW pathologies become apparent with no alternative causal explanation other than the patient's underlying critical illness and the concurrent treatments that are receiving because of the illness.[51]

CIP is a well defined neuromuscular complication that can explain some cases of ICUAW.[52] The muscle weakness is caused by sensory-motor axonal polyneuropathy, decreased muscle tone and a loss of sense that usually starts distally, including to pain, temperature and vibration.[51] The end result of CIP is distal axon degeneration of both sensory and motor nerve fibers that leads to muscle weakness from denervation.[50] CIM is a primary acute muscle disease that is unrelated to denervation and is characterized by a decrease in muscle membrane excitability, a loss of myosin filaments, muscle fiber atrophy and necrosis.[50] Lastly, severe muscle atrophy is the result of increased muscle protein catabolism induced by sedentary behaviour, mechanical ventilation or functional denervation. Over time severe muscle atrophy results in a detrimental reduction in myofibril cross-sectional area.[23,50]

Clinically, there is no known pharmacological intervention for ICUAW. The lack of treatment options to treat ICUAW has contributed to the increased use of EM, a tool that is feasible to implement and can be provided without additional harm to the patient.[4,53]

1.3.2 Diaphragm atrophy and dysfunction

The diaphragm, (the primary inspiratory muscle) often becomes dysfunctional and atrophied in patients suffering from ICUAW.[26] Diaphragm atrophy is especially apparent in mechanically ventilated patients.[24] Mechanical ventilation (MV) is a life-saving tool and it is utilized when the patient can no longer sustain sufficient alveolar ventilation. Despite the benefits, there are known complications that include infection, respiratory muscle atrophy and injuries to the trachea, lungs and diaphragm.[54]

During MV, positive pressure is used to inflate the lungs and can be calibrated to either partially or fully assist the patient's breathing. When ventilation is fully assisted, the patient breathes without any active respiratory muscle contractions.[55] One mechanism of ventilator-induced injury is spontaneous ventilation by the patient that can result in elevated transpulmonary pressure swings and overinflation.[56] The impacts on the diaphragm include atrophy, weakness and

contractile dysfunction. The damage to the diaphragm caused from a mechanical ventilator has been termed ventilator-induced diaphragmatic dysfunction.[54] Patients who suffer from ventilator-induced diaphragmatic dysfunction often experience difficulty being weaned from the ventilator due to inspiratory muscle weakness which worsens with prolonged ventilator usage.[24,54] Changes in the ultrastructure of the diaphragm and muscle wasting after MV have been documented in animal studies (e.g. rats and rabbits) and are different than the changes seen after controlled inactivity in similar species.[57–59] Successfully being weaned from a mechanical ventilator is key to the individual being released from an ICU and regaining their autonomy.[1,54]

1.3.3 Bedrest

Bedrest has been shown to not only have detrimental effects on sick populations, but also in healthy persons and is believed to play a role in ICUAW.[22,33,60,61] For example, the 1966 Dallas Bed Rest study took five, 20-year-old healthy males and confined them to bed rest for three weeks with no weight bearing, followed by an eight-week training program. At the end of the bed rest period, on average, their VO_{2max} and $\dot{Q}$ had decreased by 27% and 26% respectively. Following the training period they experienced on average a 45% increase in VO_{2max} and a 40% increase in $\dot{Q}$.[33,61] Thirty years after the Dallas Bed Rest study was completed the five original participants were followed up with and it was found that the three weeks of bedrest had a more significant negative effect on their capacity compared to 30 years of aging.[33]

Historically, intensive care patient management strategies were designed to respond to and prevent all immediate threats to life.[62] Keeping patients sedated was common practice and thus bedrest was standard.[22,63] Today the negative implications associated with bedrest are well known and critical care medicine now routinely incorporates physiotherapy into the standard of care.[22]

1.4 Critical Illness: Sepsis

1.4.1 Pathophysiology

A common critically ill population are patients with a primary or secondary diagnosis of sepsis.[64] Sepsis is defined in the recently revised definition, 'Sepsis-3,' as 'life-threatening organ dysfunction caused by a dysregulated host response to infection'.[65] Sepsis can progress to septic shock, defined as persistent hypotension not corrected with adequate fluid resuscitation.[65] Sepsis syndrome involves both pro and anti-inflammatory responses in addition to significant modification of nonimmunologic pathways. The pathways affected can include cardiovascular, metabolic, autonomic, hormonal and neuronal.[65] It can arise from almost all organisms that cause human infection, allowing for a wide range of pathways that result in the syndrome.[66] Sepsis is also influenced by patient characteristics including underlying co-morbidities, age, sex, race and the presence of additional injuries, making it a complex syndrome to understand, diagnose and effectively treat. Successful treatment of sepsis increases with early recognition.[65]

The exact mechanism of cell injury during the hosts response to infection leading to sepsis induced organ failure is not completely understood. One early hypothesis is that the initial hyperinflammatory response is followed closely by the anti-inflammatory response that suppresses the immune system.[67] A more recent hypothesis, theorizes that both responses happen simultaneously.[66] The pro-inflammatory response results in the release of cytokines that activate the complement and clotting cascades. There is subsequent cell damage and increased risk of creating microthrombi. The anti-inflammatory response results in impaired T-cells and B-cells that can leave the host susceptible to infection from organisms that are not considered pathogenic in those who are immunocompetent.[66] Tissue ischemia due to failure of the oxygen cascade to meet the demands of the metabolically active tissue may also play a role in cell injury leading to organ failure. The failure of the oxygen cascade may be partially attributed to the characteristic hypotension caused from vasodilation that septic patients experience. Hypotension can interfere with systemic blood distribution to organ systems.[66] Lastly, mitochondrial dysfunction has been

implicated in sepsis causing organ dysfunction and resulting in impaired O_2 extraction and hypoxia.[68]

Patients who survive sepsis often suffer from long-term physical and/or cognitive impairments that reduce quality of life and increase dependency on the healthcare system.[69,70] Survivorship has become increasingly recognized as an area requiring attention, estimates show that the incidence of sepsis is increasing in high income countries, most likely due to the growing age of the populations.[71,72]

1.4.2 Operational definition of sepsis

Sepsis is operationally defined as (1) the presence of infection and (2) an acute change in the Sequential Organ Failure Assessment (SOFA) score of greater than or equal to 2 points from baseline. When there is no known history of organ failure, the baseline SOFA score is considered to be zero.[66]

1.4.3 Exercise interventions with sepsis patients

There is a severe lack of EM research on sepsis patients.[73] One exercise intervention completed with patient population showed improvement in self-reported physical function and possible attenuation of some of the negative long-term effects of sepsis.[74] In a pilot randomized control trial, they enrolled diagnosed sepsis patients who had been mechanically ventilated for at least 48 hours. One group participated in an individualized rehabilitation program that included electrical muscle stimulation (EMS), passive and active range of motion, sitting and ambulation. The second group received standard care. There was no difference in physical functioning between the groups at the end of the intervention, however group one had significantly increased self-reported physical function scores six months post discharge.[74]

Secondly, the inflammatory biomarkers interleukin-6 (IL-6), interleukin-10 (IL-10) and tumor necrosis factor alpha (TNF-α) were measured and compared between the exercise group and

the intervention group. Pro-inflammatory biomarkers are involved in muscle degradation, myocyte degeneration, muscle atrophy and inhibition of protein synthesis and includes IL6 and TNF-α. There was no change in TNF-α. The concentration of IL-6 was decreased in the exercise group and trending towards significance. Il-10, an anti-inflammatory biomarker and its presence promotes the inhibition of proteolysis. In the exercise group there was a significantly increased concentration. The findings suggest that exercise may affect the pathology of sepsis. Due to logistical reasons the target sample size was not reached before the completion of the study. Of the patients recruited, 6-month follow up data was also heavily reduced due to mortality.[74]

1.5 ICU Early Mobilization Literature

1.5.1 Summary

EM in the ICU has been studied to investigate both aerobic and muscular strength training.[75] In a study done by Porta and colleagues (2005), they investigated arm ergometry training on recently weaned mechanically ventilated patients. The treatment group had their general exercise physiotherapy augmented with 15 sessions of arm ergometry. Results found improved exercise capacity at the end of treatment compared to their baseline. The improvements included increased respiratory muscle strength measured by maximal inspiratory pressure and when exercising at the same intensity, the patient reported a reduced rate of perceived exertion on the Borg Scale.[76]

In a study conducted by Chiang and colleagues (2006), they investigated the effects of physical muscular training on patients who had been on mechanical ventilators for greater than 14 days in a post-intensive care unit. The physical training administered by a physiotherapist involved five sessions per week focused on upper and lower body exercises and diaphragm breathing training that could be done on or beside the bed. Whenever possible, the patients were progressed to the retraining of functional movements. The results found a significant increase in strength of the limbs and the respiratory muscles at three and six weeks compared to the baseline

measurements. The patients gained higher scores of functional independences and their ability to complete the activities of daily living. One limitation is the absence of a control group.[77]

In a recent study, cycle ergometry training was compared to resistance training in patients with ICU-acquired weakness.[32] The patients either performed recumbent cycle ergometry or a resistance training intervention that consisted of five session per week, 20 minutes each, administered over a four-week period. The cycle ergometry sessions were set at a patient determined intensity of 'somewhat hard'. The resistance training focused on major muscle groups. Resistance increased as patient strength increased. The results found that both groups had enhanced walking ability, lower limb muscular strength and cardiorespiratory function at the end compared to baseline. Although not conclusive, the researchers suggested that in critically ill populations, ergometry training may be the superior choice, further research is needed before more concrete conclusions can be drawn.[32]

The limited research available on the topic of EM in the ICU suggests that exercise may be beneficial to some critically ill populations.[32,76] What the research does not tell us, is which sub populations of critically ill patients actually benefit, what modality or modalities are best suited for using with critically ill populations and if the administration of arm or cycle ergometry in the ICU is feasible. Cycle ergometry has garnered more attention and one study has suggested that it is superior to resistance training.[32] However, cycle ergometry is quite time expensive compared to resistance training. It requires a complicated set up to get it adjusted for the patients use. The feasibility of using cycle ergometry and its ability to be implemented and utilized in ICU's has not been discussed.

1.5.2 Limitations

There are inherit limitations with completing and interpreting the results of ICU EM literature.[3,6,7] First, there can be no control group that does not participate in any form of EM. All ICU patients must receive standard of care treatment. To assign a patient group to receive no EM intervention cannot be done. EM is considered to be a part of best practice and has been robustly

shown to be safe and feasible to implement.[8,11,12] Second, 'standard of care' does not have a commonly used definition and the use of 'standard of care' is frequently used as a substitute for a control group. In some cases it is possible that in an EM intervention study that the standard of care offered to one group is similar to what is being offered to the intervention group making it difficult to draw conclusions on between group differences.[9,32,76,77]

Other issues include the heterogeneity of the population admitted (e.g. age, sex, ethnicity, the number of critical illness present, underlying co-morbidities etc.) to the ICU. Heterogeneity makes it difficult for researches to isolate a specific population. Patient recruitment and obtaining informed consent from the patient or their legal decision makers is difficult and has contributed to small sample sizes in the research.[3] There is a necessity to utilize a wide variety of research designs when studying EM of critically ill populations. Executing real world research is difficult and the protocols need to adapted to accommodate different locations. The result has been a substantial lack of reproducibility.[8] Lastly, there a high mortality associated with critical illness. The high mortality limits gathering longitudinal follow-up data and result in low sample sizes when participants are not able to complete the experimental protocol.[3]

Overall, due to the limitations listed above, the evidence available on the topic of EM in critically ill populations is of poor quality.[8,75,78]

1.6 Purpose

The purpose of this thesis was to describe and quantify the physiotherapy rehabilitation practices and identify cardiopulmonary trends in critically ill sepsis patients admitted in the VGH-ICU.

1.7 Research Question

1. What are the current rehabilitation practices in the VGH-ICU for critically ill sepsis patients?
2. How can the current rehabilitation practices in the VGH-ICU be quantified?
3. What are the cardiopulmonary trends of the critically ill sepsis patients admitted to the VGH-ICU who are undergoing rehabilitation with a physiotherapist?

1.8 Hypothesis

This is an exploratory descriptive analysis, with the objective of describing and quantifying trends in the VGH-ICU. VGH is a tertiary, teaching hospital. A formal hypothesis is not being tested in this thesis.

Chapter 2: Methods

2.1 Protocol

2.1.1 Participants

All patients admitted to the VGH-ICU during the four-week observation period who met the inclusion and exclusion criteria were included in the study. There was no recruitment. Waived consent was utilized. The study was non-experimental, minimal risk and was designed to observe the patients who were admitted and being treated during the study time frame. All measurements and practices that were observed, were routine care and were performed by the usual practitioners. Without waived consent it would have been impractical to answer the research question. All patients admitted during the four-week time who met the inclusion and exclusion criteria needed to be included immediately in order to properly quantify the current practices and cardiopulmonary vital signs. The inclusion and exclusion criteria were as follows:

Inclusion criteria:

- Admitted to the VGH-ICU during the four-week observational period
- Male or Female
- Ages 18 and over
- Admitted with a diagnosis of sepsis
- Gained a diagnosis of sepsis during ICU admission
- Sepsis was suspected during ICU admission, but not yet confirmed
- Had or gained a diagnosis of shock, sepsis suspected, during ICU admission

Exclusion criteria:

- Admitted to the VGH-ICU greater than two weeks prior to the start of the four-week observational study window
- Had or gained a COVID-19 diagnosis

- Admitted due to major trauma
- Admitted due to large burns
- Admitted with or because of a spinal cord injury
- Gained a spinal cord injury during ICU admission
- Patient put onto extracorporeal membrane oxygenation

2.1.2 Recruitment

There was no recruitment for this observational study. In order to answer the research question, all patients who met the inclusion and exclusion criteria needed to be observed.

2.1.3 Consent

Waiver of consent was utilized in order to answer the research question (Appendix A, Table 11). The study involved no more than minimal risk to the participants. The goal was to capture the rehabilitation practices of the physiotherapy team in the VGH-ICU with the admitted sepsis patient population in a four-week time frame. All measurements that were collected, including the physiotherapy sessions that were observed, were part of routine care and performed by the usual practitioners with no influence from the research team.

The alteration to consent requirement is unlikely to adversely affect the welfare of the patients because this study was strictly observational. The researcher present was a silent observer. The predominant risk to participation was patient confidentiality and great effort went into ensuring that it was maintained. Confidentiality was maintained by de-identifying all data stored electronically using a randomized identification. In addition, all digital files did not include identifiers such as name, date of birth, medical record number and personal health number. Hard copies of original data collection forms were kept in a locked filing cabinet in the principal investigator's office.

Lastly it was impractical to answer and address the research questions if prior consent from patients was required. The study relied on observations starting immediately when the inclusion and exclusion criteria was met. Physiological measurements that were being constantly monitored in the ICU are recorded into the Flowsheet on set intervals, however they were not recorded during physiotherapy sessions. The measurements during physiotherapy needed to be captured in real time during the physiotherapy sessions and could not be taken from the Flowsheet or archived medical charts. The decline of consent by one patient or family will make the project less scientifically valid.

2.1.4 Experimental overview

Protocols were sent to the Clinical Research Ethics Board at the University of British Columbia (UBC) and they were approved (REB#H20-03695). UBC research personnel had formal written approval to conduct observational research in the VGH-ICU. Additional operational approval was obtained from Vancouver Coastal Health Research institute. All patients identified by the lead researcher, with the aid of the ICU physiotherapy team were observed three times a day; (1) 08:00-09:00 (2) 11:30-12:30 and (3) 17:00-17:30. The times were modified as necessary to coordinate observation of physiotherapy sessions and be flexible around the timing of all medical interventions planned for the patient (e.g. scans, surgery, testing etc.). All information was written by hand into tracking Form A from the 'Flowsheet', monitor and mechanical ventilator. All measurements that were observed were being collected with no influence from the researcher and obtained with no patient interaction. The variables collected include; HR, blood pressure (BP), respiratory rate (RR), fraction of inspired O_2 (FiO_2), positive end expiratory pressure (PEEP) and peripheral oxygen saturation (SpO_2).

Additionally, once a day, relevant medications were on were recorded from the Medical Anaesthesia Record (MAR) and the dosage for intravenous administered medications, if needed, taken from the Flowsheet for each patient. The results of all blood gas analysis tests were recorded

from the Flowsheet. The test results included the partial pressure of arterial oxygen (PaO_2) and the partial pressure of arterial CO_2 ($PaCO_2$). The severity of sepsis of each patient was approximated by tracking organ failure and inflammation. The Sequential Organ Failure Assessment (SOFA) score and the Systemic Inflammatory Response Syndrome (SIRS) Score were calculated. The former included, PaO_2/FiO_2 (P/F) ratio, platelet count, bilirubin concentration, MAP and related vasopressors, Glasgow Coma Scale (GCS), concentration of creatine and daily urine output. The latter included, white blood cell (WBC) count, temperature, RR and HR. All values were recorded from the Flowsheet. On Monday, weekend measurements were obtained from the Flowsheet if the patient was still admitted to the ICU. Once the patient was released from the ICU, their charts were no longer accessible to the researcher.

Patients who were participating in EM, prophylactic management (PM) or a visual assessment with a chest check with a physiotherapist were observed during each of their sessions and all information was written by hand into tracking Form B. During the observations, HR, BP, MAP and RR were recorded. This included one pre-session measurement and additional measurements during mobilizations that had potential to elicited a cardiopulmonary response. The date and duration of the session was recorded and the mobilizations and/or exercises performed described. Lastly, each mobilization was graded against the VGH mobility scale (6-pt scale) and the Early Progressive Mobility Scale (11-pt scale). Descriptions of EM sessions that are conducted on Saturdays and Sundays were obtained through the physiotherapy chart notes and briefly clarified by the physiotherapist if needed.

When patients met the inclusion and exclusion criteria during their ICU admission, they were included in the study once identified, regardless of how long they had already been admitted. All measurements recorded that are noted to be before their date of inclusion were collected retroactively from the Kardex, Flowsheet and Physiotherapy Charts.

All forms were de-identified with randomized ID’s and inputted into encrypted digital spreadsheets.

2.1.5 Data collection forms

2.1.5.1 Demographics form

Demographics included the patients age, sex, height, weight, body mass index (BMI) presence of pre-existing conditions, relevant medical history and tobacco use. It was taken from the Kardex admission form.

2.1.5.2 Form A: daily tracking

General physiology tracking of variables that included BP (e.g. systolic, diastolic and MAP), HR, RR, FiO_2, PEEP, and SpO_2. Also included are the blood gas analysis results for PaO_2, $PaCO_2$ and the calculated P/F ratio, vasopressor dosage, SOFA score measurements, SIRS score measurements and relevant medications.

2.1.5.3 Form B: observed physiotherapy description

Physiotherapy rehabilitation session tracking form includes time of day, length of session, number of healthcare practitioners present and cardiopulmonary measurements. The physiological measurements include HR, systolic and diastolic BP, MAP and RR. They will be taken within five minutes of the start of the physiotherapy session, and during the following mobilizations; (1) supine bed exercises, (2) passively sitting in bed chair, (3) active or active assisted EOB for longer than one minute, (4) sitting in a chair, (5) sit to stand, (6) immediately post active assisted patient transfer from either supine or bed chair to EOB. Additionally, descriptions of mobilizations and/or exercises performed, including the mobility scores (VGH-ICU Mobility Score and Early Progressive Mobility Score) were recorded. The highest score achieved on the Early Progressive Mobility Score was used to classify the sessions of EM (≥1), PM (=0) or visual assessment (no mobility score could be assigned).

2.1.5.4 Form C: retroactive physiotherapy description

Descriptions derived from chart notes of physiotherapy sessions that occurred on Saturday and Sunday. Any clarifications made by the physiotherapist will be noted.

2.1.6 Measurements

2.1.6.1 SOFA score – sequential organ failure assessment

In critical care research the SOFA score is commonly used as an assessment tool to classify the severity of organ dysfunction (Appendix A,Table 12). It utilizes lab tests that are commonly performed in intensive care and standard clinical measurements to identify abnormalities in the following organ systems; respiratory, coagulation, liver, cardiovascular, central nervous system and renal. An increasing score represents an increase in organ dysfunction on a scale of 0 to 24.[65] It will be calculated using a validated online calculator.[79] When PaO_2 has not been measured, it will be approximated using SpO_2. SOFA scores calculated with either PaO_2 or the SpO_2 estimation have been shown to be highly correlated.[80]

2.1.6.2 SIRS score – systemic inflammatory response syndrome

The assessment tool characterizes the presence of inflammation looking at the following variables; temperature, HR, RR and WBC count (Appendix A, Table 13).[65]

2.1.6.3 VGH-ICU mobility pathway (6pt)

A six-stage progressive pathway that includes patient description, goals of care and mobility goals starting from bedrest to stable ambulation (Appendix A, Table 14).[81]

2.1.6.4 Early progressive mobility scale (11pt)

An 11-stage progressive pathway that includes patient classification and descriptions of mobility milestone (Appendix A, Table 15).[82]

2.1.6.5 Cardiopulmonary vital signs

BP was measured with an arterial line or a non-invasive blood pressure cuff and HR was recorded with electrocardiographic monitoring, both are reported directly onto the monitor. The mechanical ventilator monitors RR, PEEP and $FiO2_2$. FiO_2 was also recorded during Optiflow™ nasal high flow therapy. When FiO_2 was not directly measured, the flow in L/min was used to estimate the value based on the scale provided by the SOFA score calculator.[79] SpO_2 was measured by pulse oximeter and was used to approximate SaO_2. SpO_2 is used as an approximation for SaO_2 in critically ill populations, however there is potential that it is less accurate than when used as a comparison in healthy adults.[80]

2.1.7 Data collection and processing

All observational data were collected by Kayla Johnston and hand written into either the Demographics Form or Form A, B or C during the four-week observational window. All forms were de-identified with randomized identifications and transferred to an encrypted digital spreadsheet on an ongoing basis. All data that could not be directly observed were recorded from the Kardex, Flowsheet, physiotherapy chart notes and MAR.

2.1.8 Data analysis

The recorded measurements were transferred into excel spreadsheets. Day one for each patient was the day they were admitted to the VGH-ICU, regardless of when they met the inclusion and exclusion criteria. In-person observations of the patient did not start until they met the inclusion and exclusion criteria. All data recorded from before the inclusion date, were collected retroactively if time allowed.

2.1.8.1 ICU patient characteristics

The sample population of patients that met the inclusion and exclusion criteria were analyzed in multiple ways. The first was a demographic analysis taken from the Kardex. Descriptors including mean, standard deviation, median, minimum and maximum were used to analyze the following; age, sex, height, weight, body mass index (BMI), SOFA and SIRS scores. The most prevalent pre-existing co-morbidities in this sample were noted and the frequency of the underlying conditions each patient were calculated.

2.1.8.2 ICU admission characteristics

Characteristics of each stay were analyzed using the descriptors, mean, standard deviation, median, minimum and maximum. Length of stay in days, number of PT sessions, length of MV and the percent of stay MV were looked at. Duration of sessions were considered and the sessions were compared in the following three groups; EM, PM and visual assessment with a chest check.

2.1.8.3 Descriptions of early mobilization and prophylactic management

Mobilizations that were identified during the four-week window were grouped to consider if they occur in both PM and EM or only one. They will be described based on what the researcher observed. The gross frequency each mobilization occurred and the percent was reported.

2.1.8.4 Barriers to performing physiotherapy

All barriers identified by the physiotherapist who performed each session included in the study were described using gross frequency and percent.

2.1.8.5 Exploratory findings

The following variables were collected for the exploratory analysis; SOFA score, SIRS score, norepinephrine dose, mobility scores, daily cardiopulmonary vitals and vitals during early mobilization sessions. The data was grouped in different ways including by norepinephrine dose, mobility score and type of mobilization being performed. Boxplots and categorical scatterplots

were used to visualize the data and compare different variables looking for potential evidence of correlation or differences between means.

2.1.8.6 Statistical analysis

Interval variables that have previous known relations were analyzed using a Pearson correlation test. Mean values between identified groups based on outcome, norepinephrine dose or mobility score were compared using a two-tailed statistical test where unequal variance was assumed. Statistical analysis and generation of all descriptive statistics was done using IBM SPSS. Significance was set at $P \leq 0.05$. Graphs were generated using IBM SPSS, R and Python.

Chapter 3: Results

3.1 Patient Enrollment and Analysis

The observational window ran July fifth to 30th, 2021 and all patients admitted to the ICU June 21, 2021 or later were considered for enrollment. During the four-week time frame, 23 ICU patients met the inclusion and exclusion criteria. Of the initial 23 patients who met the study criteria, two were later deemed ineligible. One patient had a retropharyngeal abscess that resulted in a non-traumatic C2 spinal cord injury on day three and a second patient diagnosed with shock, at risk of becoming septic passed away before a concrete diagnosis was made. Lastly, one patient was excluded from the cardiopulmonary and physiotherapy analysis. The patient was not admitted to the VGH-ICU long enough to garner any cardiopulmonary or physiotherapy measurements. The total number of included ICU stays was 24; one patient had two ICU admissions and a second had three ICU admissions (Appendix B, Figure 9).

3.2 Patient Characteristics

The patient characteristics of the sample admitted to the VGH-ICU are reported in Table 1 and Table 2. All patients were either admitted to the ICU with sepsis or septic shock as the primary cause for admission or while admitted to the ICU they gained a sepsis diagnosis or a strongly suspected sepsis diagnosis. Four patients were current smokers, two patients were previous smokers and one patient did not have a recorded smoking history. The most common underlying or pre-existing conditions in descending order included hypertension (n=11), type 2 diabetes mellitus (n=8), dyslipidemia (n=4), chronic kidney disease (n=3) and osteoporosis (n=3). The frequency of pre-existing conditions the patient sample had is show in Appendix B, Figure

10. No trend was found between length of stay and the number of underlying pre-existing conditions (Appendix B, Figure 11).

Table 1. Patient characteristics.

Sex		Age (years)	Weight (Kg)	Height (m)	BMI (Kg/m^2)
Women	Mean ± SD	70 ± 18	70 ± 24	1.60 ± .05	26 ± 8
	Median	74	64	1.60	26
	Minimum	44	35	1.52	13
	Maximum	87	105	1.67	38
	N	8	8	8	8
Men	Mean ± SD	64 ± 15	79 ± 19	1.75 ± 0.13	26 ± 4
	Median	65	75	1.74	26
	Minimum	27	53	1.50	19
	Maximum	83	124	1.95	33
	N	13	12	12	12
Combined	Mean ± SD	66 ± 16	74 ± 21	1.69 ± 0.13	26 ± 6
	Median	66	70	1.68	25
	Minimum	27	35	1.50	13
	Maximum	87	124	1.95	38
	N	21	20	20	20

Age in years, weight in kilograms (kg), height in meters (m), body mass index (BMI) in kg/m^2, standard deviation (SD), number (N).

Table 2. Admission and release SOFA and SIRS score characteristics.

Outcome		SOFA score (Day 1)	SIRS score (Day 1)	Last recorded SOFA score	Last recorded SIRS score
Death	Mean ± SD	9 ± 4	1 ± 1	7 ± 5	2 ± 2
	Median	10	2	5	2
	Minimum	4	0	4	0
	Maximum	12	2	13	3
	N	3	3	3	3
	Missing	2	2	2	2
Released to ward	Mean ± SD	11 ± 3	2 ± 1	6 ± 3	1 ± 1
	Median	11	3	7	2
	Minimum	5	0	1	0
	Maximum	16	4	10	2
	N	14	14	18	18
	Missing	5	5	1	1
Combined	Mean ± SD	11 ± 3	2 ± 1	6 ± 3	1 ± 1
	Median	11	2	6	2
	Minimum	4	0	1	0
	Maximum	16	4	13	3
	N	17	17	21	21
	Missing	7	7	3	3

Sequential organ failure assessment (SOFA), systemic inflammatory response syndrome (SIRS), standard deviation, number (N).

3.3 ICU Admission Characteristics

During the observational period there were a total of 24 ICU admissions that met the criteria for analysis, their characteristics are reported in Table 3. All but one patient received a physiotherapy assessment and the average time to the initial assessment was 2.5 days. The outcomes, when separated by ICU admission, include 17 patients being released to ward and four deaths on their first ICU admission, two patients being released to ward after their second ICU admission and one death after their third ICU admission (Appendix B, Figure 12). There was a statistically significant association between length of stay and number of days being mechanically ventilated ($r = .934$; $p < 0.001$) (Appendix B, Figure **13**).

Table 3. ICU admission characteristics.

Sex		Length of stay (days)	Number of PT sessions	Length of MV (days)	Length of stay on MV (%)
Women	Mean ± SD	8 ± 8	3 ± 3	6 ± 9	47 ± 44
	Median	5	4	3	55
	Minimum	2	0	0	0
	Maximum	29	7	28	100
	N	10	10	10	10
Men	Mean ± SD	11 ± 8	5 ± 6	7 ± 7	59 ± 42
	Median	9	4	7.5	78
	Minimum	2	0	0	0
	Maximum	36	25	25	100
	N	14	14	14	14
Combined	Mean ± SD	10 ± 8	4 ± 5	7 ± 7	54 ± 42
	Median	7.5	4	4	72
	Minimum	2	0	0	0
	Maximum	36	25	28	100
	N	24	24	24	24

Length of stay in days, number of physiotherapy (PT) sessions, length of mechanical ventilation (MV), the percent of stay they were on MV, standard deviation (SD), number (N).

3.4 General Physiotherapy Session Characteristics

Over the four-week observational window, 80 physiotherapy sessions were observed. The observations included direct observation (n=64) or the chart notes were analyzed with a supplemental interview with the physiotherapist for clarifications (n=16). The duration of the sessions are detailed in Table 4. The recorded time includes the time the physiotherapist spent with the patient, it does not include the time spent checking in with the patients charts and bedside clinicians at the start of the day or their time spent charting after the session is complete. The sessions were broken down into three categories; EM, PM and visual assessment that included checking the chest.

Table 4. Physiotherapy session duration characteristics

Session Type	Mean ± SD	Median	Minimum	Maximum	N
Early Mobilization	22 ± 10	20	5	50	45
Prophylactic Management	9 ± 4	10	4	20	24
Visual Assessment	12 ± 3	10	10	15	3
Total	**17 ± 10**	**15**	**4**	**50**	**72**

The duration of each session is recorded in minutes. Eight sessions were excluded from analysis due to the physiotherapist not recording the length of the session in the chart notes. Standard deviation (SD), number (N).

The number of bedside clinicians present during the sessions varied; 57.5% of the sessions were conducted with just one physiotherapist present, 37.5% had one additional clinician present and 5% required two additional clinicians. The additional clinicians could include a physiotherapist, nurse, respiratory therapist, rehab assistant and/or doctor. Mechanically ventilated patients with endotracheal tubes accounted for 52.5% of the sessions and 46.3% of sessions were with non-mechanically ventilated patients. For 1.3% of sessions, it was not apparent if the session occurred before or after the patient being extubated in the notes. Bedside visitors were present at

16.3% of sessions, absent from 71.3% of sessions and there was no record from 12.6% of session. Lastly, 18.8% of the time the physiotherapist reported the session ending early due to barriers outside of their control.

3.5 Description of Prophylactic Management Physiotherapy

There were 80 physiotherapy sessions observed in the ICU and 37.5% of the sessions met the definition of PM (n=30). The mobilizations used during these sessions are described in Appendix B, Table 18 and an analysis of the Gross frequency and percent in Table 5.

Table 5. Gross frequency and percent of prophylactic mobilizations.

	Frequency	Percent
Fully assisted edge of bed	1	0.9
Repositioned in bed	1	0.9
Overhead lift	2	1.7
Passive roll in bed to both right and left side	4	3.4
Passive Bed Chair Exercises	5	4.3
Asked to complete a physical action	12	10.3
Suction	22	19
Chest auscultations	25	21.6
Passive bed exercises, UE and/or LE	44	37.9
Total	**116**	**100.0**

Prophylactic management (PM) includes mobilizations, assessment tools and interventions. The frequency is the number of times observed during PM sessions (n=28) in the four-week time frame, it was possible for a mobilization to be observed twice in one session. Two sessions did not have the specific mobilizations listed in the chart and were excluded. Upper extremity (UE), lower extremity (LE).

3.6 Descriptions of Early Mobilization Physiotherapy

EM was the second type of physiotherapy session that was observed. Of the 80 sessions, 60% met the criteria (n=48). Note, 2.5% of the sessions did not meet the classification of either EM or PM and have not been described. Descriptions of the EM sessions are detailed in Appendix B, Table 18 and Table 19. Mobilizations that are commonly used in PM can also be used during EM.

The gross frequency and percent each exercise was analyzed during the observed EM sessions is shown in Table 6. The most commonly utilized mobilizations include asking the patient to complete a physical action such as squeezing their hand or wiggling their toes (11%), physiotherapist assisted transfers of patients to and from sitting on the edge of the bed (EOB) and lying supine (10.1%) and sitting on the edge of the bed for greater than one minute (7.9%). In addition, any form of active or active assisted upper extremity (UE) or lower extremity (LE) exercises accounted for an accumulative of 21.1% compared to passive exercises which were only utilized 3.5% of the time.

Table 6. Gross frequency and percent analysis of early mobilizations.

	Frequency	Percent
Trying to communicate	1	0.3
Standing weight transfer right and left	2	0.6
Orientate patient (where/why)	3	0.9
Standing march	3	0.9
Vibrations to chest and coughing	3	0.9
Sitting in modified bed chair	5	1.6
Unassisted transfer	5	1.6
Shuffle while standing	6	1.9
Sit to stand	7	2.2
Active UE exercises	11	3.5
Chair sitting	11	3.5
Passive exercises	11	3.5
Suction	11	3.5
Overhead Lift	14	4.4
Active assisted LE exercises	16	5.0
Roll in bed right and left	16	5.0
Sitting in bed chair	16	5.0
Diaphragm breathing	17	5.4
Active assisted UE exercises	20	6.3
Active LE exercises	20	6.3
Edge of Bed (> 1 min)	25	7.9
Chest auscultations	26	8.2
Lie/EOB transfer	32	10.1
Asked to complete a physical action	35	11.0
Total	**317**	**100.0**

Early mobilization (EM) includes mobilizations, assessment tools and interventions. The frequency is the number of times observed during EM sessions (n=48) in the four-week time frame. Lower extremity (LE), upper extremity (UE), edge of bed (EOB).

3.7 Barriers to Performing Physiotherapy in an ICU

The physiotherapists were presented with barriers to performing care. The barriers that occurred during the four-week observational window that resulted in no physiotherapy session occurring are listed in Table 7.

Table 7. Frequency and percent analysis of identified barriers to physiotherapy.

	Frequency	Percent
Fevered	1	1.3
Haemodynamic instability	1	1.3
High WOB based on RR	1	1.3
Late admission; no time to see	1	1.3
Pain limited	1	1.3
Patient actively seizing when not sedated	1	1.3
Patient did not want to participate in physio	1	1.3
Comfort care - no physio	2	2.6
Ribs broken from CPR	2	2.6
Cardiovascular instability	4	5.2
Patient not following directions	4	5.2
Intervention(s) scheduled	6	7.8
Physio not advised by doctor	8	10.4
Aggressive towards bedside practitioners - safety concerns	9	11.7
PIC score of 4 or 5	35	45.5
Total	77	100.0

The frequency at which each barrier the contributed to a physiotherapy session from occurring was observed during the four-week time frame and the percent breakdown. Work of breathing (WOB), Respiratory rate (RR), priority intervention criteria (PIC), cardiopulmonary resuscitation (CPR).

The most common barrier was the patient prioritization that is detailed in the Critical Care Priority Intervention Criteria (PIC) Protocol (Appendix A, Table AB). [83] Low PIC rankings were often not seen due to limited staff or because they were not suitable for EM. This presented 45.5% of the time for why a session did not occur. The next most common reasons for physiotherapy

sessions not occurring were safety concerns for the bedside clinicians (11.7%), the patient not being cleared for physiotherapy by a doctor (10.4%) and other medical interventions scheduled (7.8%). Scheduled medical intervention barriers also presented as a barrier to physiotherapy sessions that that did happen. The timing of 16 of the 80 (20%) observed sessions had to change to accommodate other interventions that were planned for the patient.

Barriers that occurred during the physiotherapy sessions, that made it more difficult for the physiotherapist to complete their goals of care are detailed in Table 8. The most common barrier identified by the physiotherapists to delivering care includes patient fatigue (12.2%), a language barrier being present (9.5%), safety concerns for bedside practitioners (6.8%) and the patient not following directions (6.8%).

Table 8. Frequency and percent analysis of barriers during physiotherapy.

	Frequency	Percent
Acute pulmonary edema	1	0.7
Bloody secretions	1	0.7
Bowel movement	1	0.7
Dizziness	1	0.7
Fevered	1	0.7
Hands and feet going necrotic	1	0.7
High FiO_2	1	0.7
High RR	1	0.7
Limited hearing	1	0.7
Not enough bedside practitioners	1	0.7
Restless	1	0.7
SpO_2 decreased during mobilizations	1	0.7
Anxiety	2	1.4
Arterial line	2	1.4
EEG running	2	1.4
Global weakness	2	1.4
Ribs broken from CPR	2	1.4
Cardiovascular instability	3	2.0
ICU delirium	3	2.0
Limited by airborne precautions	4	2.7
Patient did not want to participate	5	3.4
Physio not advised by doctor - prophylactic management only	5	3.4
Unresponsive, not on sedatives - prophylactic management only	5	3.4
Drowsiness	7	4.8
Haemodynamic instability	8	5.4
Movement risks harming patient	8	5.4
Pain limited	8	5.4
Patient at risk of harming themselves	8	5.4
Sedated	9	6.1
Aggressive towards bedside practitioners - safety concerns	10	6.8
Patient not following direction	10	6.8
Language barrier	14	9.5
Fatigued	18	12.2
Total	**147**	**100.0**

Electroencephalogram (EEG), fraction of inspired oxygen (FiO_2), respiratory rate (RR), intensive care unit (ICU) cardiopulmonary resuscitation (CPR), saturation of peripheral oxygen (SpO_2).

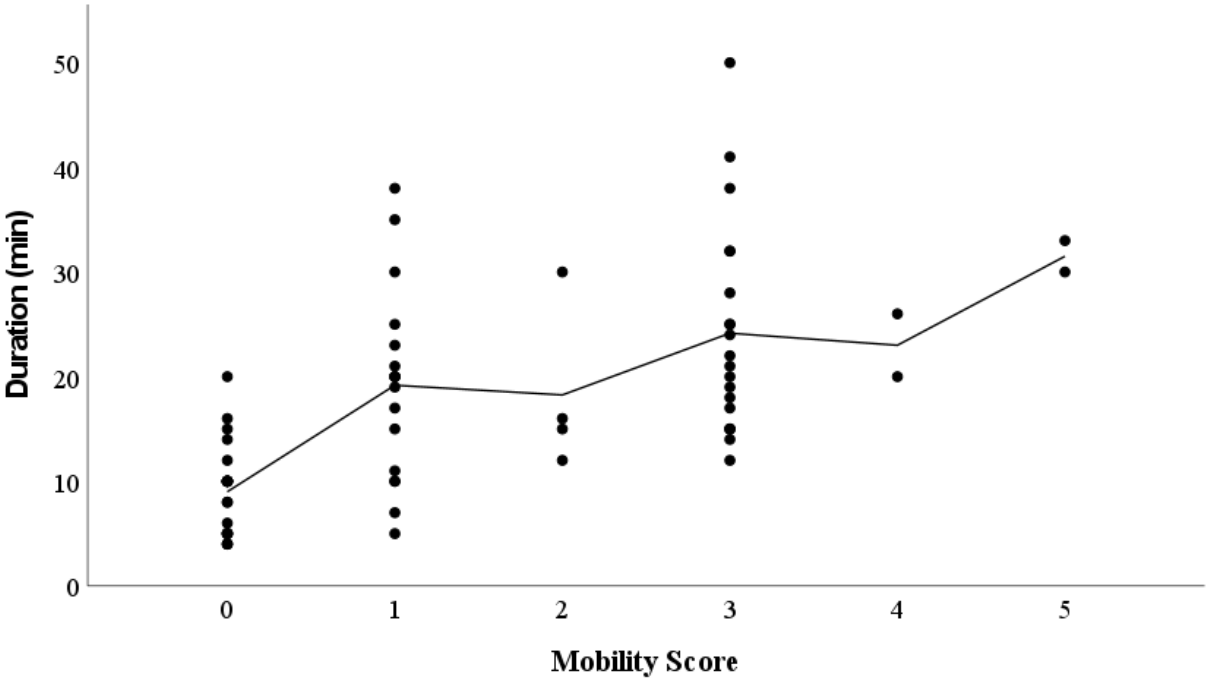
3.8 Exploratory Findings

The exploratory analysis identified trends in this sample of critically ill sepsis patients. The sample size of this study was quite small and heterogeneous. The findings need to be considered with these limitations. The 11-pt mobility scale was used for all result analysis due to its increased sensitivity over the 6-pt scale, the 6-pt scale will not be referenced further.

3.8.1 Mobility score

Mobility score achieved during each physiotherapy session was plotted against the session's duration. The higher the mobility score achieved during a session, the longer the mean duration of the session when considering a score of 0 (n=24), 1 (n=17) and 3 (n=20) (Figure 1). There was a statistical significance found using a two-tailed test for duration of physiotherapy session between a mobility score of 0 and 1 ($p<0.001$) and mobility score of 0 and 3 ($p <0.001$). There was no statistical significance between a mobility score of 1 and 3 ($p=0.128$). Mobility scores of 2 (n=4), 4 (n=2) and 5 (n=2) were excluded from analysis due to low numbers.

Figure 1. Scatterplot of duration of physiotherapy sessions.



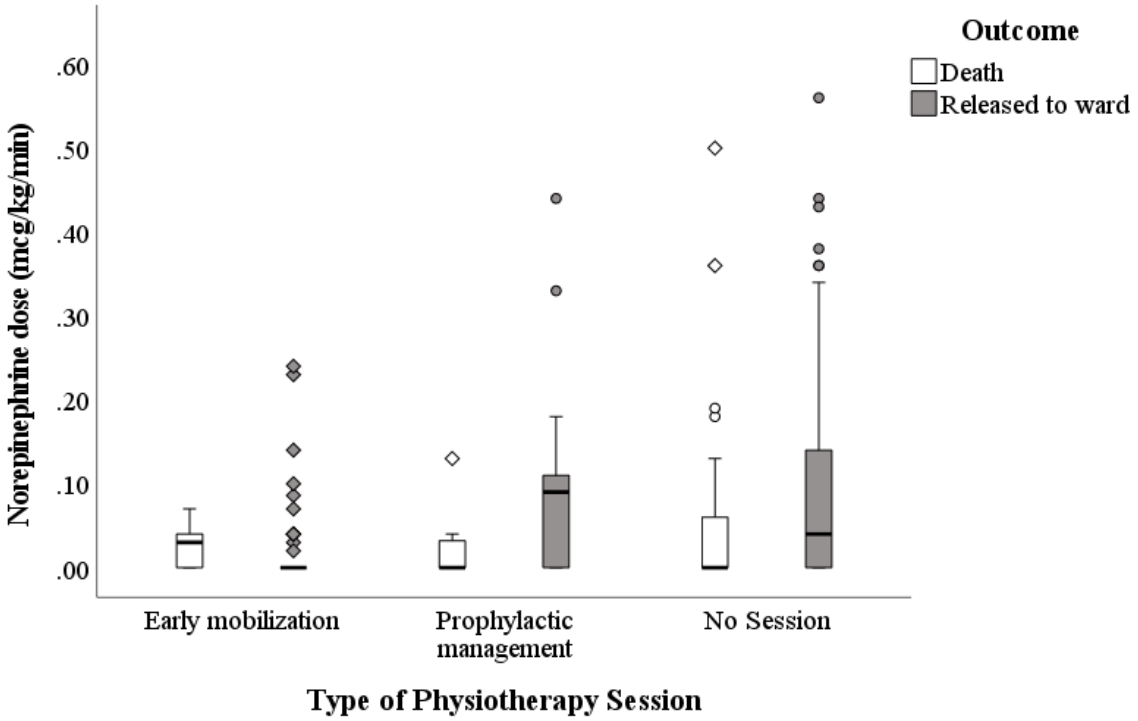
The patients' highest mobility score achieved during a physiotherapy session and the length of the physio session in minutes. The black line denotes the mean values. 70 sessions were included. The two visual assessments were excluded from analysis.

3.8.2 Vasopressor dosage

Norepinephrine was used as a vasopressor; the common drug name is Levophed. The dose recorded was compared to Physiotherapy session type (Figure 2) and the characteristics of the 'released to ward' group are in Table 9. The 'death' group was not analysed further due to small sample size. The observations shown in Figure 2 suggests that the dosage of vasopressor might typically be higher in patients that do not receive physiotherapy compared to those that participate in EM. It also suggests that the dose during PM might also tend to be higher than during EM when

looking at the group that was released to ward. Norepinephrine dose is often high in the first 48 hours of admission (Figure 3) and this can help explain the outliers in Figure 2.

Figure 2. Cluster boxplot of norepinephrine dose.



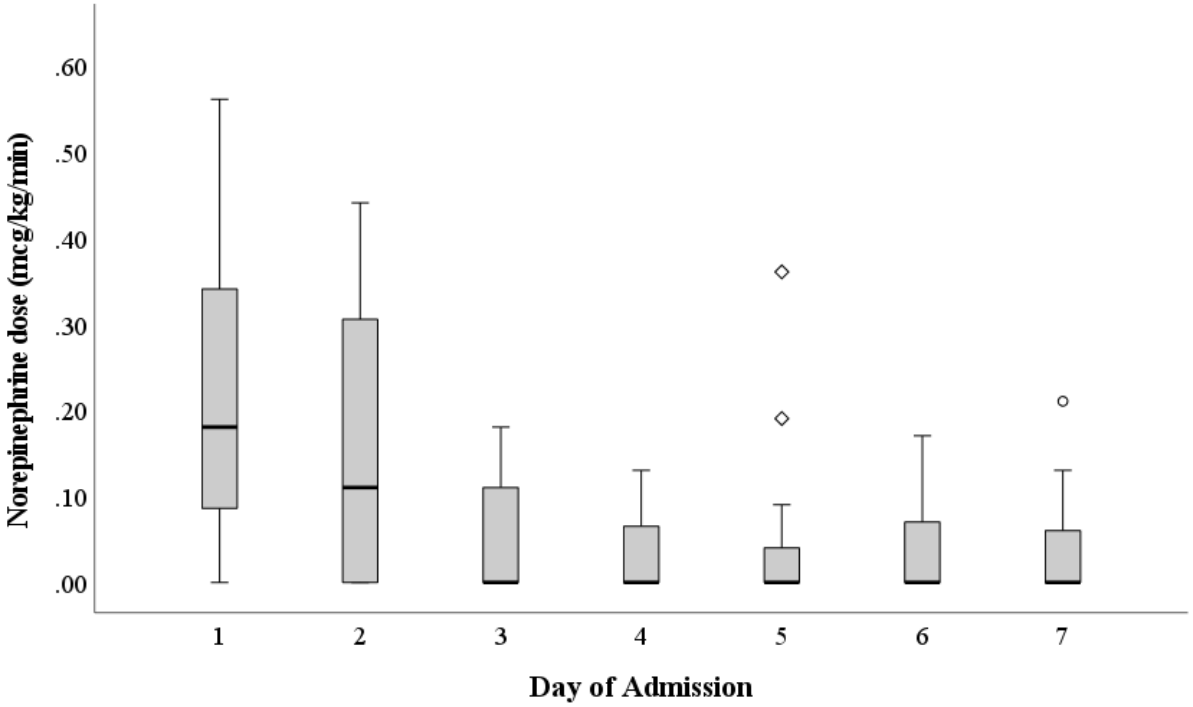
Dose of norepinephrine administered in mcg/kg/min, on days when physio did and did not occur, the thick blackline represent median. Early mobilization was defined as achieving a mobility score of ≥1 on the 11-pt mobility scale and prophylactic management was a mobility score of 0 on the same scale. Patients are grouped by outcome, death (white) and released to ward (grey). ○ Represents outliers and ◊ represents extreme outliers.

Table 9. Characteristics of norepinephrine dose in the outcome group, 'released to ward'.

	Mean ± SD	Median	Minimum	Maximum	N
Early mobilization	.03 ± .06	.00	.00	.24	55
Prophylactic management	.09 ± .10	.09	.00	.44	28
No session	.12 ± .18	.07	.00	1.11	96
Total	**.09 ± .15**	**.02**	**.00**	**1.11**	**179**

Norepinephrine dose in mcg/kg/min, standard deviation (SD), number (N).

Figure 3. Boxplot of norepinephrine administered during first seven days.

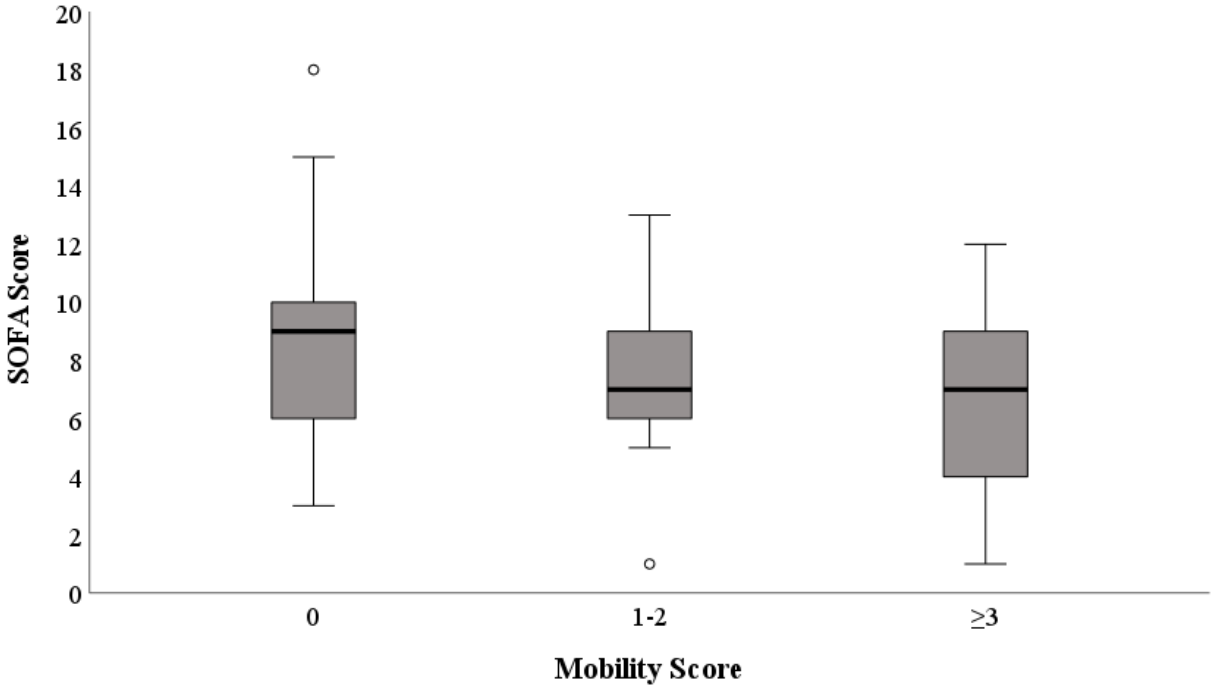


Norepinephrine dose in mcg/kg/min administered on the first seven days of intensive care unit admission for all outcome groups. The thick black line represents median, ○ represents outliers, ◊ represents extreme outliers.

3.8.3 SOFA score

Daily SOFA score, grouped based on the highest mobility score achieved during their physiotherapy session is shown in Figure 4 and Table 10. There was no significant difference between a mobility score mean of 0 and a score of 1-2 (p=0.125) or a score of 1-2 and 3 (0.268). There was a significant difference found between a mobility score mean of 0 and a score greater than or equal to 3 (p=0.014).

Figure 4. Boxplot of SOFA score.



Sequential organ failure assessment (SOFA) score, grouped by the highest mobility score achieved during a physiotherapy session. The thick black line represents median. ○ represents outliers.

Table 10. Characteristics of the SOFA scores recorded based on mobility score.

Mobility Score	Mean ± SD	Median	Minimum	Maximum	N
0	9 ± 3	9	3	18	28
1-2	8 ± 3	7	1	13	22
≥ 3	7 ± 3	7	1	12	25
Total	8 ± 3	8	1	18	75

Sequential organ failure assessment (SOFA, 11-point mobility score, standard deviation (SD), number (N).

3.8.4 Daily cardiopulmonary trends

The daily averages have been reported for each patient for the first seven days of admission. Daily HR, systolic BP, diastolic BP and MAP can be seen in Appendix B, Figure 14. Daily PaO_2, $PaCO_2$, FiO_2, P/F and SpO_2 can be seen in Appendix B, Figure 15. The trends are consistent with

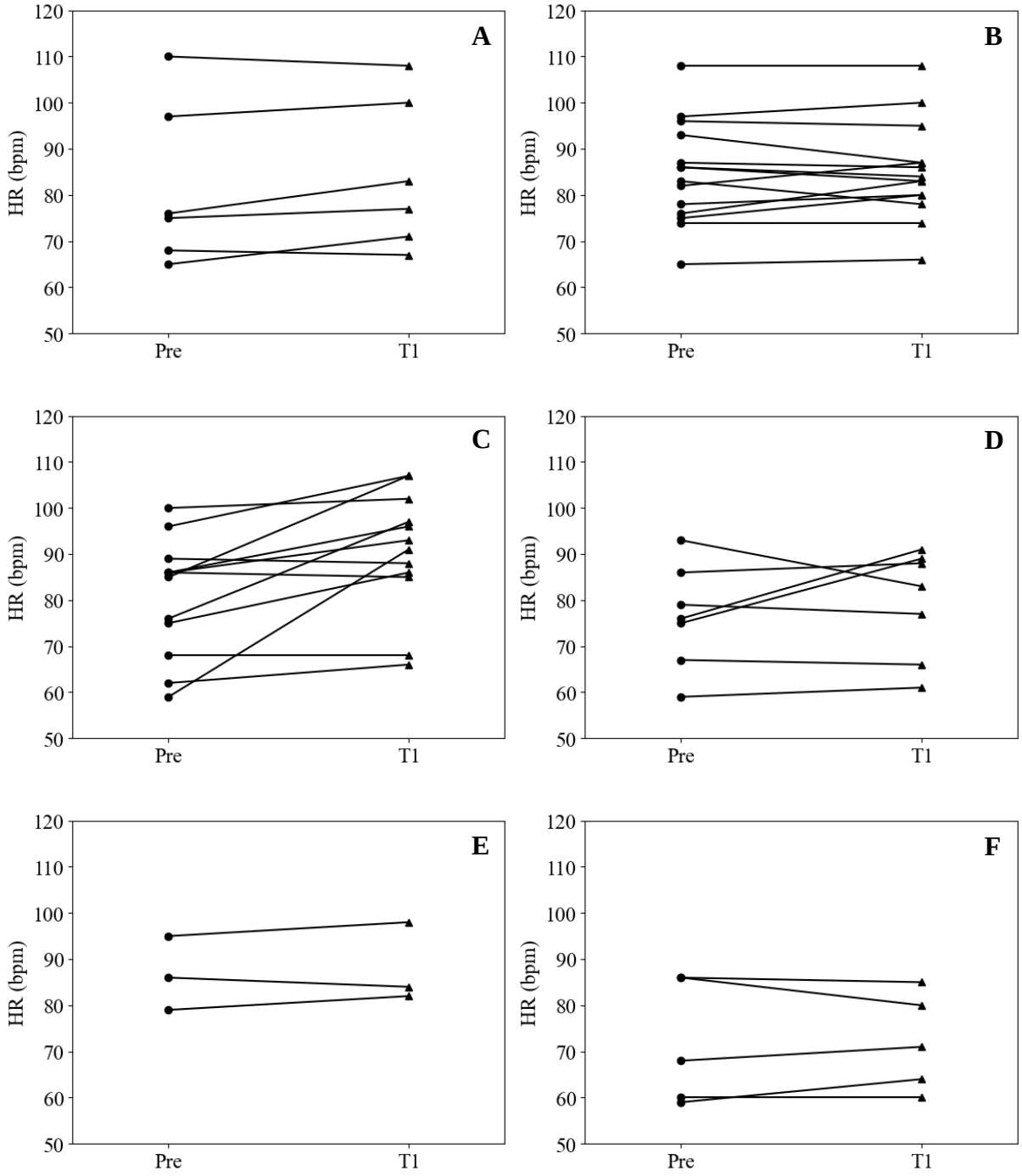
what you would expect given this sample is primarily being mechanically ventilated, provided supplemental oxygen, medicated to adjust vital signs and the inherent cardiopulmonary instability associated with critical illness. Common instabilities observed include, increased FiO_2 requirement after extubation, an example is show in Appendix B, Figure 16. Increased BP when the patient is weaned off norepinephrine (Appendix B, Figure 16. Recorded HR, Systolic BP, MAP and FiO2 for patient 01-01. and Figure 17) and in some cases BP remains unstable despite norepinephrine being administered (Appendix B, Figure 18).

3.8.5 Daily cardiopulmonary trends during mobilization

All patients had their HR, systolic and diastolic BP and MAP recorded before the start of observed sessions. During the session, when the values were being recorded, the same measurements were taking during specific mobilization. There were 47 mobilizations that captured potential change in vital measurements during six mobilizations; bed exercises while supine, sitting in bed chair, EOB, sitting in a chair, standing and immediately after active assisted patient transfers. BP measurements were only taken when there was an arterial line inserted and there were no obvious signs it was reading incorrectly.

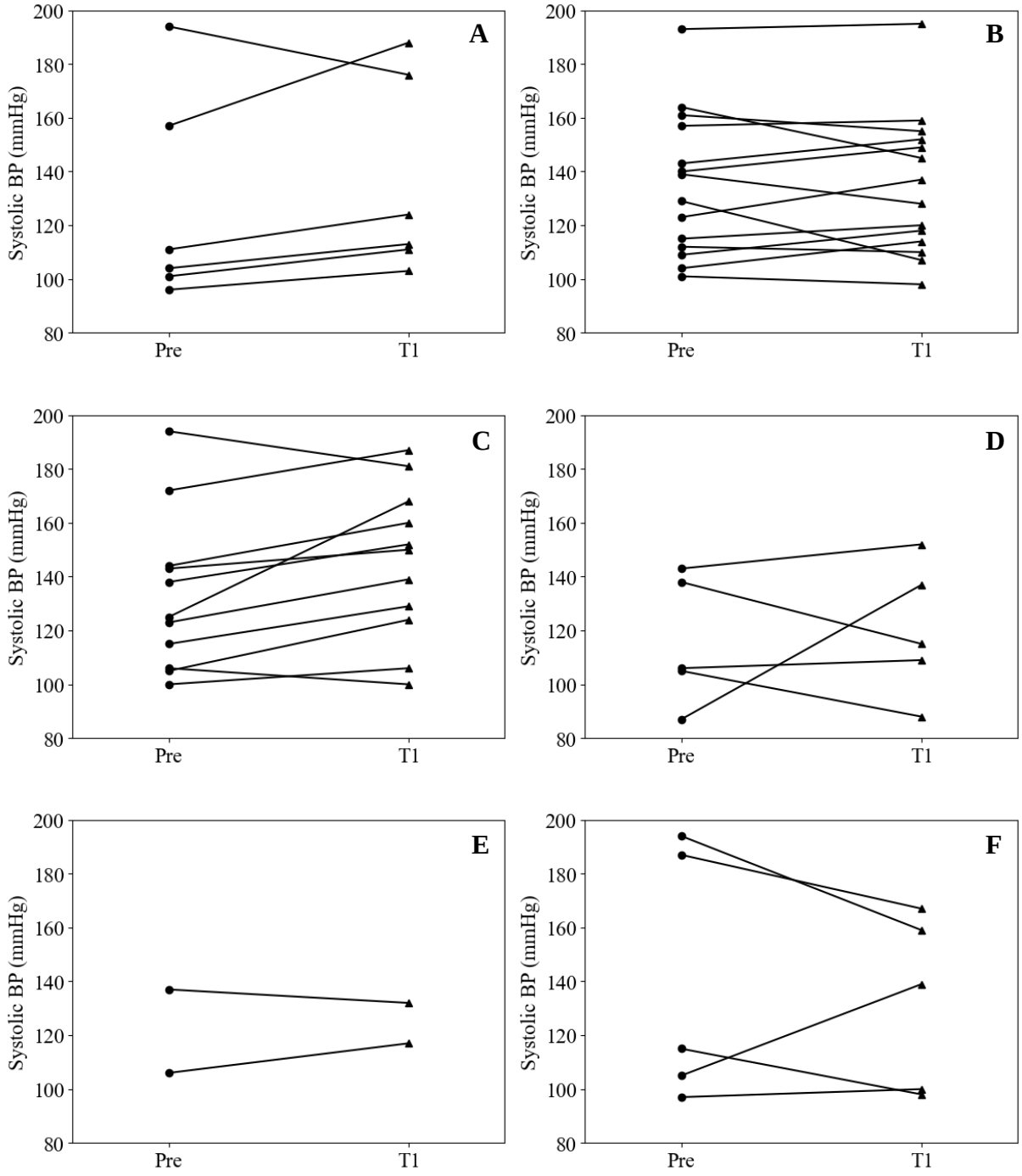
The values reported include HR (Figure 5), systolic BP (Figure 6) and MAP (Figure 7) plotted to show change from pre-physiotherapy to during specified mobilization.

Figure 5. Heart rate pre and during mobilizations.



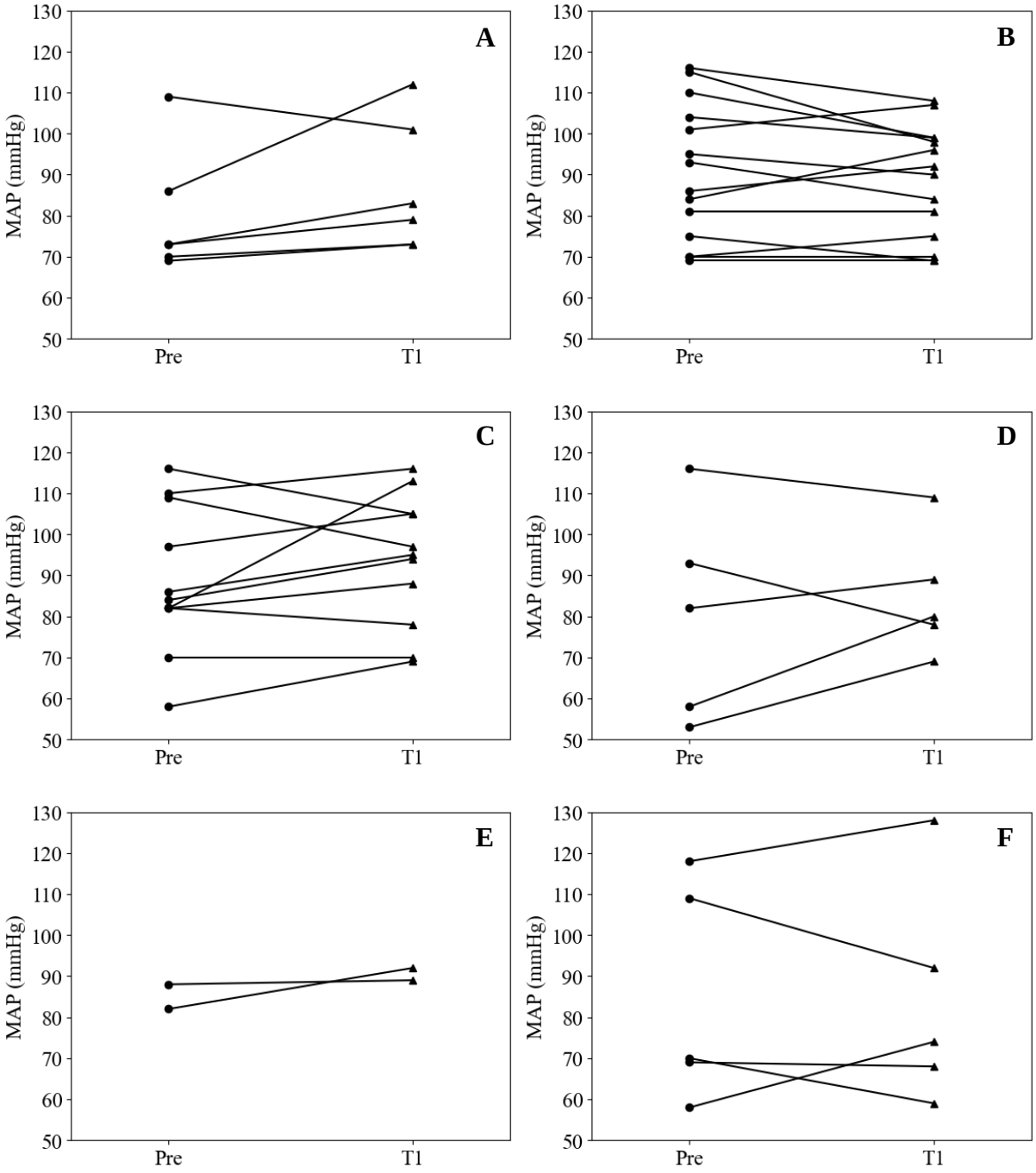
Heart rate (HR) in beats per minute (bpm) pre (Pre) and at time point one (T1) during specific early mobilizations. Pre (●) and T1 (▲) are plotted. The solid line connects paired values. (A) Bed exercises, (B) sitting in bed chair, (C) sitting on the edge of the bed, (D) sitting in a chair, (E) sit to stand, (F) immediately post active assisted patient transfer.

Figure 6. Systolic blood pressure pre and during early mobilizations.



Systolic blood pressure (BP) in mm of mercury (mmHg) pre (Pre) and at time point one (T1) during specific early mobilizations. Pre (●) and T1 (▲) are plotted. The solid line connects paired values. (A) Bed exercises, (B) sitting in bed chair, (C) sitting on the edge of the bed, (D) sitting in a chair, (E) sit to stand, (F) immediately post active assisted patient transfer.

Figure 7. Mean arterial pressure pre and during early mobilizations.



Mean arterial pressure (MAP) in millimetres of mercury (mmHg), pre (Pre) and at time point one (T1) during specific early mobilizations. Pre (●) and T1 (▲) are plotted. The solid line connects paired values. (A) Bed exercises, (B) sitting in bed chair, (C) sitting on the edge of the bed, (D) sitting in a chair, (E) sit to stand, (F) immediately post active assisted patient transfer.

Chapter 4: Discussion and Conclusion

4.1 Discussion

The purpose of this thesis was to quantify and describe cardiopulmonary trends and physiotherapy rehabilitation of admitted sepsis patients during four weeks of observations in the VGH-ICU. This thesis does not inform on clinical practices. The primary findings include an association between increased vasopressor dosage and achieving a decreased mobility score during physiotherapy sessions. In addition, a second association was observed between increased SOFA score and a decreased mobility score. Lastly, this thesis provides some evidence to suggest the cardiopulmonary responses that are present during certain mobilization maneuvers, for some of the patients are similar to those seen during exercise. Collectively, the results can be used to help inform future research projects on the current mobilization practices occurring with sepsis patients and identify the barriers that will need to be overcome to design a study to work and be successful in the VGH-ICU environment. Secondly, the results have the potential to quantify the existing measurements being recorded in the ICU and report on trends, that at the time of the study, were unknown to the physiotherapy team. The results have the potential to reaffirm current practices and identify areas that warrant review.

4.1.1 Vasopressor dosage

The vasopressor, norepinephrine, was recorded daily from the patients Flowsheet. The pharmacological effect of norepinephrine is arterial vasoconstriction resulting in increased systolic BP.[84] Norepinephrine is often a necessary intervention when dealing with sepsis induced hypotension that is not remediated by fluid resuscitation.[65] In the present study, norepinephrine was recorded daily from the patient's Flowsheet. MAP was used to monitor hypotension and norepinephrine was administered to maintain MAP goals (e.g. MAP $\geq$ 60 mmHg). The dosage of

all vasopressors were taken into account by the physiotherapists when considering the patients' suitability for mobilization each morning. A patient with a higher dose (mcg/kg/min) of norepinephrine required to maintain MAP was viewed to have increased hemodynamic instability and would be more difficult to mobilize safely.

Norepinephrine dose had a median of 0 mcg/kg/min during EM sessions and 0.09 mcg/kg/min during PM in the group that was released to ward. The outliers in the EM, 'released to ward' category can be in part explained by the unstable nature of critical illness. They do not belong to one patient, instead, many patients in the sample had one or two days where they required norepinephrine and still participated in EM. The low median and extreme outliers in the no session, 'released to ward' group can be partially explained in two ways. The first is stable patients who aren't on vasopressors and usually participate in EM are deprioritized on Saturday and Sunday due to low physiotherapy staff. Second, the average time to the first physiotherapy session is two and a half days. In the first 48 hours the median dose of norepinephrine is ≥ 0.1 mcg/kg/min, compared to a median of 0 mcg/kg/min for days three to seven (Figure 3).

A high vasopressor dosage does not preclude a patient from receiving physiotherapy and many still participated. However, vasopressor dosage may play a role in helping to predict the mobility score a physiotherapist can likely achieve safely when working with the patient.

4.1.2 SOFA score

The validated SOFA score is used to help classify the severity of sepsis.[85,86] Increased mortality is associated with a higher SOFA score in hospital settings.[85] The variables used to calculate the SOFA score are common to many ICU's,[65,85] making it a feasible tool to utilize when conducting research.

During the four-week observational window, SOFA score was calculated daily and a trend was identified. SOFA score was associated with the highest mobility score completed during physiotherapy (Figure 4 and Table 10). In the VGH-ICU, the mobility scores patients achieve when working with the physiotherapists typically range from zero to three. In the case where a mobility score of greater than or equal to four was achieved, the patient was released to ward soon after. The first four progressive stages of mobility take the patient from passive in bed ROM to sitting with or without support on the edge of the bed. Scores of zero were compared to scores of three and a significant difference in mean SOFA score was found between these two groups ($p=0.014$). No significant difference was found between a score of zero and a score of one or two, although these exploratory results trend towards statistical significance ($p=0.125$). The small sample size and heterogeneous population make it difficult to draw more definite conclusions.

4.1.3 Daily cardiopulmonary trends

The cardiopulmonary trends in the critically ill patient group studied in this thesis were variable. Between- and within-patient variability was expected based on previous investigations.[3,6–8] The daily average values over the first seven days of admission can be used to reflect the first week of admission for the sample of patients studied. On average, MAP was maintained over 60 mmHg, suggesting that the utilization of norepinephrine was effective in managing blood pressure. Norepinephrine has a greater effect on increasing systolic BP compared to diastolic BP[87] and as such, the relative maintenance of MAP can be attributed to increases in systolic BP. HR was consistently between 60-100 bpm (Figure 14.A). The resting HR of patients appears to be elevated, however the medication(s) that may have effected HR was not recorded.

Figure 15.A shows PaO_2 as a function of the first seven days of ICU admission. The relatively high PaO_2 values were particularly evident during the first two days of admission which is consistent with other work.[88] The high PaO_2 values can be attributed to the constant O_2 therapy ($FiO_2 \geq 0.25$) being administered. Only two patients were put on an FiO_2 of 0.21 at some point during the first seven days of admission (Figure 15.C). The FiO_2 was an important part of care and this is reaffirmed by the variability seen in the SpO_2 (Figure 15.E) and the calculated P/F ratios (Figure 15.D). The P/F ratio can be used to categorize acute lung injury (≤ 300) and acute respiratory distress syndrome (≤ 200)[89] further supporting the necessity to use MV and oxygen therapy.

4.1.4 Cardiopulmonary trends during exercise

Active exercise is known to elicit specific cardiopulmonary changes in healthy adult populations such as increased HR, a slight increase in MAP and increased RR. The magnitude of the response observed is influenced by the intensity of the exercise and level of cardiorespiratory fitness.[29,35] Changes in HR and hemodynamics during physiotherapy were obtained using a pre-physiotherapy measurement and a second measurement during specific early mobilization exercises. The purpose here was to monitor the responses among critically ill patients to determine if mobilization maneuvers currently being used by physiotherapists elicit a response comparable to dynamic exercise.

The exercise that appeared to elicit the most noticeable response was the EOB mobilization, which is described as a mobility score of three. The mobilizations of bed exercises (mobility score = 1), sitting passively in bed chair (mobility score = 1) and chair sitting (mobility score = 2) did not produce any noticeable trend. The mobilization of assisted standing, surprisingly, did not appear to elicit a measurable physiological change. Two possible explanations include the low

number (n=2-3) of observations and the possibility that the patients that completed the sit to stand action were not as ill and had retained their muscular strength. The sit-to-stand exercise was observed only 2.2% of the time, suggesting that standing mobilizations are infrequently used with sepsis patients while they are still in ICU.

With respect to the EOB measurements, there was a trend for increases in HR, MAP and systolic BP in many of the patients. Increases were observed in the patients who were able to successfully manage the orthostatic stress of sitting upright. The patient with the largest increases during EOB suffered from ICU delirium and became agitated during EOB, eliciting a response the physiotherapist described as anxious. The patient was transferred back into bed and monitored while their vital signs stabilized. In the observed EOB mobilizations, there were instances of decreases in MAP and systolic BP that can be explained by hemodynamic instability in response to an increase in metabolic rate (i.e., exercise). The change in position from supine to sitting on the edge of the bed requires increased cardiac work. Patients who experienced a decrease in BP during EOB are still potentially eliciting a response that is characteristic of exercise. To some degree the patients are adjusting to the orthostatic stress and they are not experiencing the dangerous drop in MAP that can end EOB prematurely. In the case of the measurements reported in this thesis, only patients who were sufficiently stable to remain sitting on the EOB longer than one minute had their vital signs recorded. Furthermore, it can be inferred that the patients who could sit on the EOB were still able to regulate their hemodynamic system enough to tolerate the orthostatic position in the short term.

All patients included had therapeutic and pharmacological interventions attempting to control their cardiopulmonary systems. The interventions prescribed were necessary to maintain cardiopulmonary function and thus preserve life. Despite the interventions controlling the

cardiopulmonary systems effectively, changes are seen during mobilizations. Further investigation is needed to draw parallels between what mobilizations elicit a response that can be used as a training stimulus and the potential distinction of who is likely to benefit. In critically ill populations, that are well documented to be heterogeneous,[3,6–8] it is assumed that not all mobilizations will elicit an exercise response in all critically ill patients.

4.1.5 Barriers to early mobilization in the VGH-ICU

Physiotherapy in an ICU are not always possible. There are several potential barriers to care that affect the number of patients that can be seen in a day. The first is all patients are screened daily and prioritized based on the PIC Protocol. There are five categories that range from patients who are category one and must be seen within the hour by a physiotherapist, to patients who are a category five, who are medically stable and are not due for chest physiotherapy or review of their ROM.[83] All patients in the ICU are prioritized and seen accordingly. Patients who require chest physiotherapy are prioritized over patients who require prophylactic management or early mobilization. PIC category four and five are deprioritized for physiotherapy when staffing limitations precludes all patients from being seen. The Richmond Agitation-Sedation Scale (RASS) score is used when making an informed decision on who can be seen (Appendix A, Table 17).[90] In the case of a medically stable, RASS minus five patient, they would be a low priority and would have their chest, ROM and level of consciousness monitored. Secondly, certain sessions require double staffing. The more complicated mobilizations, such as EOB, often require two physiotherapists present to manage the arterial line and/or the ventilator during the transfers and while the patient is in a position where a fall is possible. Physiotherapists manage the patient from the front and back to prevent a fall. The need for multiple physiotherapists to be present places further strain on the staffing and leads to the lower priority PIC patients not being seen.

Additionally, physiotherapists must plan their sessions to accommodate the patient's scheduled interventions. Interventions such as continuous positive airway pressure (CPAP) trials and dialysis leave the patient exhausted and a poor candidate for being able to participate actively in EM. In the cases of long CPAP trials, if there is a break in the middle, the physiotherapist will try to schedule their session then. It is possible that other interventions will take priority. When dialysis is scheduled (e.g. intermittent hemodialysis or continuous renal replacement therapy), due to patient fatigue, the physiotherapy sessions must occur before the intervention begins, leaving a limited window. Other interventions such as scans or imaging (CT-scan, X-rays, bronchoscopies etc.), surgical interventions and procedures such as chest tube insertion, intubation, extubation, dental work, echocardiogram, EEG and patient cleaning, must also be accommodated when trying to schedule physiotherapy sessions.

Barriers are presented to the physiotherapist during their sessions and should be anticipated as potential obstacles to executing an exercise trial with critically ill populations. Critically ill patients can be very complicated to move. In patients with haemodynamic or cardiopulmonary instability, simply changing positions can lead to dangerous changes in BP, HR, SpO_2 and RR. For example, a sudden drop in MAP below 65 mmHg regardless of the vasopressor support that had been previously maintain the MAP goals. In some instances, the opposite happens and the movement caused the BP to increase dangerously (e.g. systolic > 190 mmHg). Haemodynamic instability, particularly hypotension, is often noted in septic patients.[66] Movement can trigger anxiety, agitation or increased pain. However, the benefits of movement are notable and the reason EM is well accepted as a component of standard of care in critically ill populations.[1–3] Once the patient has been cleared for mobilization, the physiotherapist has to consider the entirety of the patient's medical status, including medications and chest X-rays before they can determine what

movement is safe for the patient and what the mobility goals are. After no contraindications to mobilization have been identified (e.g. active seizures, active bleeding etc.) there are additional barriers the physiotherapists face to providing the care to the patients.

A barrier to completion of a physiotherapy session that presents regularly is the patient's ability to participate (Table 8). Participation is influenced by motivation, fatigue, pain levels and medications. Fatigue is often exacerbated by the different interventions they partake in such as dialysis or CPAP breathing trials. During dialysis the patient experiences large changes in blood volume causing hypotension that can persist when dialysis is completed.[91] CPAP trials are used on severely deconditioned patients and they tend to be fatigued after due to the energy exertion that is required of them to breath during the trial. Dialysis and CPAP leave the patient fatigued and often unwilling to actively participate with the physiotherapist. Although less common, in some cases pain also contributed to a patient being less willing to participate. Examples include post transplant wounds on the abdomen being aggravated with movement or pain where the arterial-line had been inserted into the femoral artery limiting the patient's willingness to move that leg. Lastly, medications can leave the patient drowsy and, in some cases, confused and unable to consistently engage in what is being asked of them. Without patient participation, what the physiotherapist is able to do becomes more limited.

Language is one of the most commonly noted barriers by the ICU physiotherapy team (Table 8). Without the ability to communicate directly with the patient, guiding the patient through the set of exercises (e.g. deep breathing, coughing, arm and leg ROM and sitting on the EOB) becomes more difficult. Although translating phone applications are used and when fluent bedside clinicians are available, they were recruited to help, often the barrier is not fully overcome unless it is the physiotherapist who is fluent in the language. Additional considerations also need to be

made for cultural differences that often coincide with a language barrier being present. The belief that when you are sick, you are supposed to rest and move as little as possible still persists. In addition, some patients are only willing to listen to instructions if they are given to them by a doctor and are less inclined to listen to a physiotherapist. Especially, if physiotherapy does not play a role in medicine in their culture or country of birth.

Patient and physiotherapist safety can present as a barrier to providing care. In some cases, there may be dangers to the physiotherapist if they attempt to mobilize a RASS plus four patient. In cases where the patient is aggressive towards the bedside clinicians they are put into soft restraints (e.g. wrist, ankle and abdominal). The restraints prevent the patient from being able to assault the healthcare workers who are providing them care. However, the protection greatly limits what a physiotherapist is able to do for mobility, especially if they are conducting the session on their own. In these cases when the patient did not need chest physiotherapy, still retained their strength and did not have a ROM deficit, the patient is de-prioritized for physiotherapy and is monitored. Despite the patient being a candidate to benefit from EM, the physiotherapist must consider their own safety.

In other cases, the soft restraints are needed because the patient poses a risk to themselves (e.g. RASS plus three; agitation, confusion, discomfort or a lack of understanding of why the medical interventions are necessary). Examples include, trying to pull out lines (e.g. arterial line, mechanical ventilator tube, intravenous lines, nasogastric feeding tube etc.), attempting to get out of bed when they are physically incapable or pulling up bandages that are keeping wounds covered. Soft restraints are used to prevent patients from causing themselves harm. Pulling out an endotracheal breathing tube can lead to aspiration and further lung damage and open wounds are at high risk of infection. The soft restraints in this case are an obstacle to the physiotherapist. When

they can work together with another bedside clinician, they can often manage the patient to keep them safe and still perform all the mobilizations scheduled. When they do not have assistance and are working alone, they are limited to freeing one arm or leg at a time and managing the mobilization (e.g. active, active assistive or passive ROM) such that the patient is unable to cause themselves harm.

4.1.6 Barriers to investigation of early mobilization in the VGH-ICU

The dynamic nature of an ICU and the complexity of cases being treated makes it a challenging environment to execute quality research. A key to running a successful study in an ICU environment is that the research project must be able to adapt and work alongside the standard of care being provided by the bedside clinicians (e.g. ICU doctors, specialists, nurses, physiotherapists, respiratory therapists, occupational therapists, rehabilitation assistants, pharmacists, social workers, students etc.).

In the case of this observational study, it was difficult, if not impossible to adhere to a standardized timeline for data collection. The primary barrier was the medical interventions and investigations that the patient participated in throughout the day (e.g. surgical interventions, scans, imaging, tests etc.). The schedule changed as patient priorities were shifted by the attending ICU physician as their medical status fluctuated and new points of concern became apparent. Collecting general observations at specific set times was not possible. These observations often had to be postponed or collected retroactively from the charts due to patients being unavailable or not in the ICU at the time when measurement collection had been scheduled. It should be expected that there will be differences in the delivery of early mobilization care between physiotherapists. Additionally, due to the dynamic environment, it should be expected during observational ICU

research that there will be cases where multiple events will happen simultaneously and the research design must accommodate. Additionally,

All patients in the ICU had a number of lines connecting them to different machines producing a wealth of information on their physiology. However, what is being collected changes depending on the patient's status. An unstable patient admitted will likely will have more measurements being recorded. Once the patient has stabilized, less information is often needed to effectively monitor the patient. For example, upon admission, some patients had end tidal CO_2 being recorded, however after one to two days the feed was disconnected and only reconnected in the case of the patient's status deteriorating. Arterial lines, although common, were not left in all patients. Although a huge amount of information is being generated about a patient at any given time, it needs to be recognized that all measurements will not always be available and what is available will change day to day.

4.2 Limitations

Study limitations are inherent with real world research designs. This observational study attempted to quantify and describe physiotherapy practices and cardiopulmonary trends with critically ill sepsis patients over a four-week window in the VGH-ICU.

The data collected could not be observed on a standardized schedule. The ICU environment was dynamic and data collection had to adapt to reflect the individual patient schedules. The daily physiological measurements were collected when it was possible to collect them. In cases where the patient was away from the ICU for extended periods of time, the measurements could not be directly observed from the monitor or MV and had to be retroactively collected when the

handwritten Flowsheet was available. Despite retroactive collection, it was possible that the Flowsheet did not have the time required and the closest, next available time point was used.

The Flowsheet is maintained by the bedside nurse and the nurse changes day to day and can change during the day as nurses cover for each other to take breaks. It is hand written and the measurements are either observed from the monitors or mechanical ventilator, recorded from the test results or measured directly by the nurse (e.g. GCS and temperature). In the case of HR, systolic BP, diastolic BP and MAP, the numbers tend to fluctuate and it is assumed that there is discrepancy on how these values were recorded. In addition, the recorded chart requires interpretation as specific numbers are not recorded for HR, systolic BP and diastolic BP (Appendix A, Figure 8). Lastly, how measurements were collected, had multiple options. For blood pressure, both arterial lines and non-invasive blood pressure cuffs were utilized.

Tests were run on each patient throughout the 24-hour day. The timing was variable and tests were not always run. The BGA and blood draws looked at blood gases, bilirubin, creatinine, WBC count and platelet levels. The results of these tests were needed to calculate the SOFA score. However, at no point were all analysis points collected at the same time. In other cases, the tests needed for certain aspects of the score were not done at all leaving a variable missing and had to be approximated.

The collection of cardiopulmonary measurements during physiotherapy sessions had limitations. The first limitation was that there was only one researcher recording values and on multiple occasions two physiotherapy sessions overlapped and the researcher was therefore unable to record the measurements of one of them. Secondly, in some cases the physiotherapists forgot to alert the researcher to a change in session time. These sessions were often changed at the last minute to accommodate other investigations and interventions that were occurring. Again, in these

cases, records of the cardiopulmonary variables was missed. During sessions that were observed, non-critical lines were often disconnected to allow for easier mobilization of the patient, reducing the available measurements (e.g. the SpO_2 measurement was removed from tracking Form B). Non-invasive blood pressure cuffs were also disconnected. Lastly, during movement, the arterial line was not always producing a reliable BP measurement. The physiotherapist commented when the measurement did not seem correct. The error was characterized by extreme, erratic, fluctuations or values that were not possible. These limitations in collecting cardiopulmonary measurements during physiotherapy sessions led to a large amount of missing data.

Despite the strict inclusion and exclusion criteria, the sample was heterogeneous. There was a broad range of ages, many different underlying and pre-existing conditions and almost all the patients had a different primary reason for ICU admission. Although sepsis was present during some aspect of their ICU admission, sepsis was often a secondary diagnosis that occurred after the patient had been admitted and occurred after a variable amount of time. Sepsis is a very difficult syndrome to classify as it can present in many different scenarios. The short time frame limited the total number of people in the study creating a small sample that further contributed to sample heterogeneity.

4.3 Conclusion

The completion of this thesis demonstrates that observational research on early mobilization is feasible to complete in the VGH-ICU. The barriers to research can be addressed through a protocol that can adapt to the dynamic environment and be implemented without impacting the standard of care the patients must receive. This thesis also provides evidence to support further investigation into factors that predict the mobility score that critically ill sepsis patients are likely to achieve when working with a physiotherapist. These factors include

norepinephrine and SOFA score. An increased norepinephrine dose may be associated with a lower mobility score and a higher SOFA score may also be associated with a lower mobility score. In addition, EOB, compared to supine bed exercises or sitting in bed chair appears to have increased effect on changing the vital signs. During the orthostatic position mobilization, EOB, some patients experienced an increased HR, increased MAP and an increase systolic BP. The changes in vitals are suggestive of known training stimulus responses in healthy adults.[29] Longitudinal research studies are needed to understand if early mobilization in critically ill sepsis patients is able to elicit a physiological response that can help slow down or prevent the ICUAW pathology.

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Appendix A

Table 11. A copy of section 6.7.A detailing waived consent copied directly from the approved ethics application (REB#H20-03695).

6.7.A. Waiver/Alteration of Consent If you are asking for a waiver or an alteration of the requirement for participant informed consent, please justify the waiver or alteration and explain how the study meets all the criteria. CLICK on blue question mark. Ensure that you address each criteria individually. Include the corresponding letter (a, b, c, d, e) before each answer.	A. The research involves no more than minimal risk to the participants: This is an observational study designed to capture the rehabilitations practices of the physiotherapy team in the VGH-ICU with the admitted sepsis patient population in a 4 week window of time. It is designed to observe and track the patients who they are currently treating and who will be admitted during this time frame. It does not involve additional risk to the participants; no experimental design and no interventions. The measurements that are being collected and the physiotherapy sessions that are occurring are routine care and will be performed by the usual practitioners with no influence from the research team. B. The alteration to consent requirements is unlikely to adversely affect the welfare of participants: This study is strictly observational with no intervention and no experimental design taking place. The patients will be treated with routine care, by the usual practitioners. The research team will be silent observers, recording measurements that are already being taken and watching physio sessions. The predominant risk is patient confidentiality and great effort will go into ensuring that it is maintained. This will be done by de-identifying all data stored electronically using a randomized ID. In addition these digital records will not include identifiers such as name, date of birth, medical record number and personal health number. Hard copies will be kept in a locked filing cabinet in the principle investigators office (which is also locked). This level of de-identification has been used in prior studies, audits and other administrative databases that have been approved for waived consent. C. It is impossible or impracticable (see Glossary) to carry out the research and to address the research question properly, given the research design, if the prior consent of participants is required:

	It is impractical to answer the research question if prior consent is required. This is due to the short 4 week observational period and the goal to quantify the current rehabilitation practices in the sepsis patient population admitted to the VGH-ICU. All patients admitted during this time will be included if they meet the inclusion and exclusion criteria and the observations need to start soon after admission. Physiological measurements that are being constantly monitored in the ICU are not recorded long term and these measurements need to be captured in real time and can not be taken from the Flowsheet or archived medical charts. The decline of consent by one patient or family will make the project less scientifically valid. D. In the case of a proposed alteration, the precise nature and extent of any proposed alteration is defined The proposed alteration is described in A, B and C E. The plan to provide a debriefing (if any) that may also offer participants the possibility of refusing consent and/or withdrawing data and/or human biological materials, shall be in accordance with Article 3.7B. There is no plan to provide debriefing.

Table 12. Sequential Organ Failure Assessment Score, copied directly from Vincent et al.[92]

SOFA score	1	2	3	4
Respiration				
PaO_2/FiO_2, mmHg	<400	<300	<200	<100
			——— with respiratory support ———	
Coagulation				
Platelets $\times 10^3/mm^3$	<150	<100	<50	<20
Liver				
Bilirubin, mg/dl (μmol/l)	1.2 – 1.9 (20 – 32)	2.0 – 5.9 (33 – 101)	6.0 – 11.9 (102 – 204)	>12.0 (<204)
Cardiovascular				
Hypotension	MAP < 70 mmHg	Dopamine ≤5 or dobutamine (any dose)[a]	Dopamine >5 or epinephrine ≤0.1 or norepinephrine ≤0.1	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1
Central nervous system				
Glasgow Coma Score	13 – 14	10 – 12	6 – 9	<6
Renal				
Creatinine, mg/dl (μmol/l) or urine output	1.2 – 1.9 (110 – 170)	2.0 – 3.4 (171 – 299)	3.5 – 4.9 (300 – 440) or <500 ml/day	>5.0 (>440) or <200 ml/day

[a] Adrenergic agents administered for at least 1 h (doses given are in μg/kg·min)

Sequential organ failure assessment (SOFA), partial pressure of arterial oxygen (PaO_2), fraction of inspired oxygen (FiO_2), mean arterial pressure (MAP).

Table 13. Systemic Inflammatory Response Score, adapted from Singer et al. [65]

One point for each criteria met.	1. Temperature >38ºC or <36ºC 2. Heart rate >90beats/minute 3. Respiratory rate >20 breaths/minute or $PaCO_2$ <32mmHg 4. White blood cell count >12 000/mm^3 or <4000/mm^3 or >10% immature bands

Partial pressure of arterial carbon dioxide ($PaCO_2$).

Table 14: DD The VGH 6 stage mobility pathway.[81]

	Patient Description	Goals of Care	Mobility Goals
Stage 1 (Bedrest)	• Unstable • Unable to mobilize as per mobility screen.	• Optimize cardiopulmonary function. • Prevent pressure ulcers. • Prevent joint pain and stiffness.	• Q2h turns • Ensure functional positioning
Stage 2 (Bedrest)	• Stable • Unable to mobilize as per mobility screen	• All of the above • Increase/maintain limb strength • Encourage interaction and stimulation from environment.	• All of the above • Bed exercises • ROM
Stage 3 (AAT)	• Stable • Mobilize and progress to mobility goal as able. • Review RN/PT/RT notes. • **Bed chair, sitting at EOB, ceiling lift to wheelchair/chair.**	• All of the above • Increase trunk strength • Progress to standing	• All of the above • Progress sitting tolerance (i.e. up in chair 2/day, longer duration).
Stage 4 (AAT)	• Stable • Mobilize and progress to mobility goal as able. • Review RN/PT/RT notes. • **Able to stand or pivot to chair.**	• All of the above • Increase sitting and standing tolerance • Improve balance • Progress to walking	• All of the above • Progress standing tolerance to taking steps/marching.
Stage 5 (AAT)	• Stable • Mobilize and progress to mobility goal as able. • Review RN/PT/RT notes. • **Able to start ambulating away from the bedside.**	• All of the above • Increase tolerance to exercise and functional mobility • Improve dynamic balance and safety	• All of the above • Progress sitting to ≥ 2 times/day. • Progress ambulation.
Stage 6 (AAT)	• Stable • **Ambulating safely with supervision**	• Maximize mobilization and ADLs	• Ambulating and sitting for meals.

Vancouver General Hospital (VGH), activity as tolerated (AAT), Q2H is the turning standard for pressure ulcer prevention, registered nurse (RN), physiotherapist (PT), respiratory therapist (RT), activities of daily living (ADL).

Table 15. The 11-pt ICU mobility scale.[82]

SCORE	CLASSIFICATION	DEFINITION
0	Nothing (lying in bed)	Passively rolled or passively exercised by staff, but not actively moving
1	Sitting in bed, exercising in bed	Any activity in bed, including rolling, bridging, active exercises, cycle ergometry and active assisted exercises; not moving out of bed or over the edge of the bed
2	Passively moved to chair (no standing)	Hoist, passive lift or slide transfer to the chair, with no standing or sitting on the edge of the bed
3	Sitting over the edge of the bed	May be assisted by staff, but involves actively sitting over the side of the bed with some trunk control
4	Standing	Weight bearing through the feet in the standing position, with or without assistance. This may include use of a standing lifter device or tilt table
5	Transferring bed to chair	Able to step or shuffle through standing to the chair. This involves actively transferring weight from one leg to another to move to the chair. If the patient has been stood with the assistance of a medical device, they must step to the chair (not included if the patient is wheeled in a standing lifter device)
6	Marching on spot (at bedside)	Able to walk on the spot by lifting alternate feet (must be able to step at least 4 times, twice on each foot), with or without assistance
7	Walking with assistance of 2 or more people	Walking away from the bed/chair by at least 5 m (5 yards) assisted by 2 or more people
8	Walking with assistance of 1 person	Walking away from the bed/chair by at least 5 m (5 yards) assisted by 1 person
9	Walking independently with a gait aid	Walking away from the bed/chair by at least 5 m (5 yards) with a gait aid, but no assistance from another person. In a wheelchair bound person, this activity level includes wheeling the chair independently 5 m (5 years) away from the bed/chair
10	Walking independently without a gat aid	Walking away from the bed/chair by at least 5 m (5 yards) without a gait aid or assistance from another person

Intensive care unit (ICU).

Table 16. VGH Critical Care PIC Protocol, copied directly.[83]

Category	Description
1	**Must be seen within 1 hour** • Patient required on-call treatment the previous night • Experiencing acute desaturation or hypoxemia and it is not due to a pulmonary embolism or myocardial infraction • Patient requires 2 or more respiratory treatments in a day • Patient who requires immediate discharge planning
2	**Needs to be seen within 1-4 hours** • Newly admitted patient who meets one of the following criteria - A primary respiratory diagnosis - A history or respiratory disease (e.g. COPD, bronchiectasis, asthma, ILD, neuromuscular disease - Impaired gas exchange requiring an FiO2 of greater than or equal to 0.40 • Patients who have at least one of the following problems identified - Retained secretions - Delay of extubation or risk of re-intubation secondary to secretions - Loss of lung volume - $V_A/\dot{Q}$ mismatch, except in cases of pulmonary embolism and pulmonary edema - Respiratory pump failure - Ineffective cough with respiratory compromise • Burn ROM
3	**Seen within 8 hours** • Patients who are unable to have a hands-on assessment due to medical instability will be checked daily until assessed - Medical instability includes; active seizures, uncontrolled ICPs, significant cardiovascular instability (ventricular arrhythmias, fluctuating pressures or HR outside limits, ICU code that day not due to respiratory compromise) or significant bleeding • Patients at risk of significant functional decline without physiotherapy that day • Change in mobility orders • Patient due for chest physiotherapy and ROM review
4	**Seen 3-5 times per week** • Patients who have identified physical impairments requiring rehabilitation to achieve baseline function
5	**Monitor** • Medically stable intubated patients who are not due for chest physiotherapy or ROM review • Patients at baseline respiratory and mobility function

Vancouver General Hospital (VGH); Priority intervention criteria (PIC), chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), fraction of inspired oxygen (FiO2), alveolar ventilation (V_A), volume of blood ($\dot{Q}$), range of motion (ROM), intercranial pressure (ICP), heart rate (HR), intensive care unit (ICU).

Figure 8. Blank Flowsheet cardiovascular record.[93]

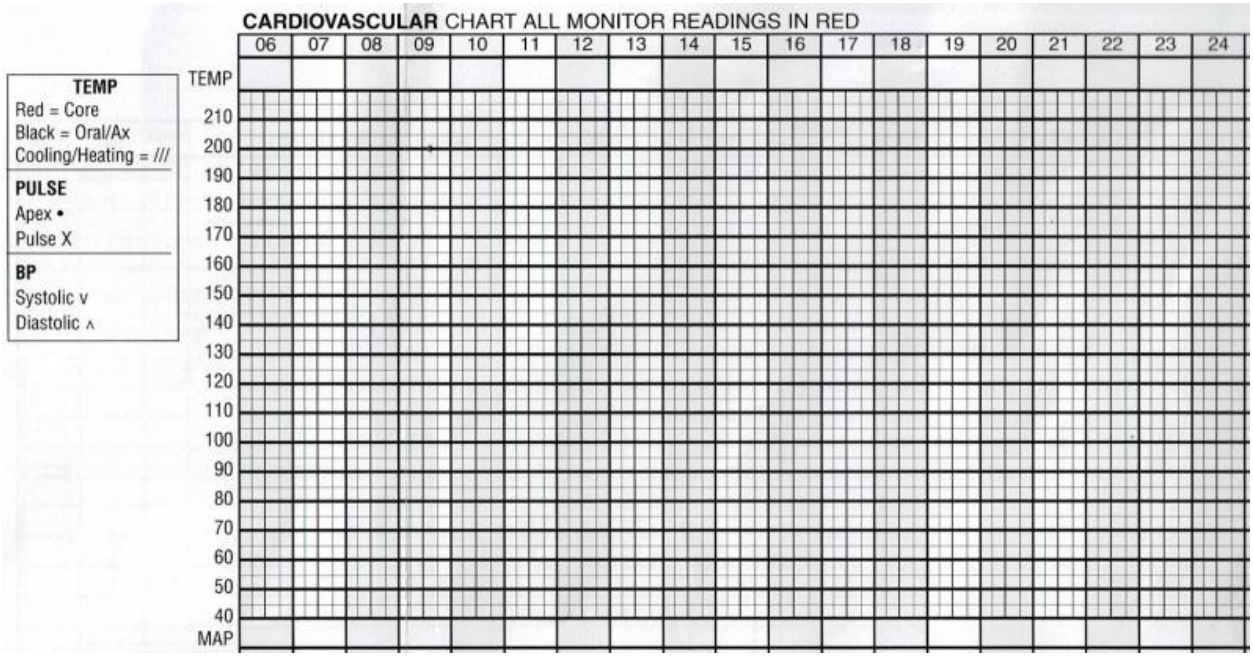


Table 17. Richmond agitation – sedation scale.[90]

SCORE	TERM	DESCRIPTION
+4	Combative	Overtly combative or violent; immediate danger to staff
+3	Very agitated	Pulls on or removes tube(s) or catheter(s) or has aggressive behavior toward staff
+2	Agitated	Frequent non-purposeful movement or patient–ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	
-1	Drowsy	Not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact, to voice
-2	Light sedation	Briefly (less than 10 seconds) awakens with eye contact to voice
-3	Moderate sedation	Any movement (but no eye contact) to voice
-4	Deep sedation	No response to voice, but any movement to physical stimulation
-5	Unarousable	No response to voice or physical stimulation

Appendix B

Figure 9. Flow Diagram.

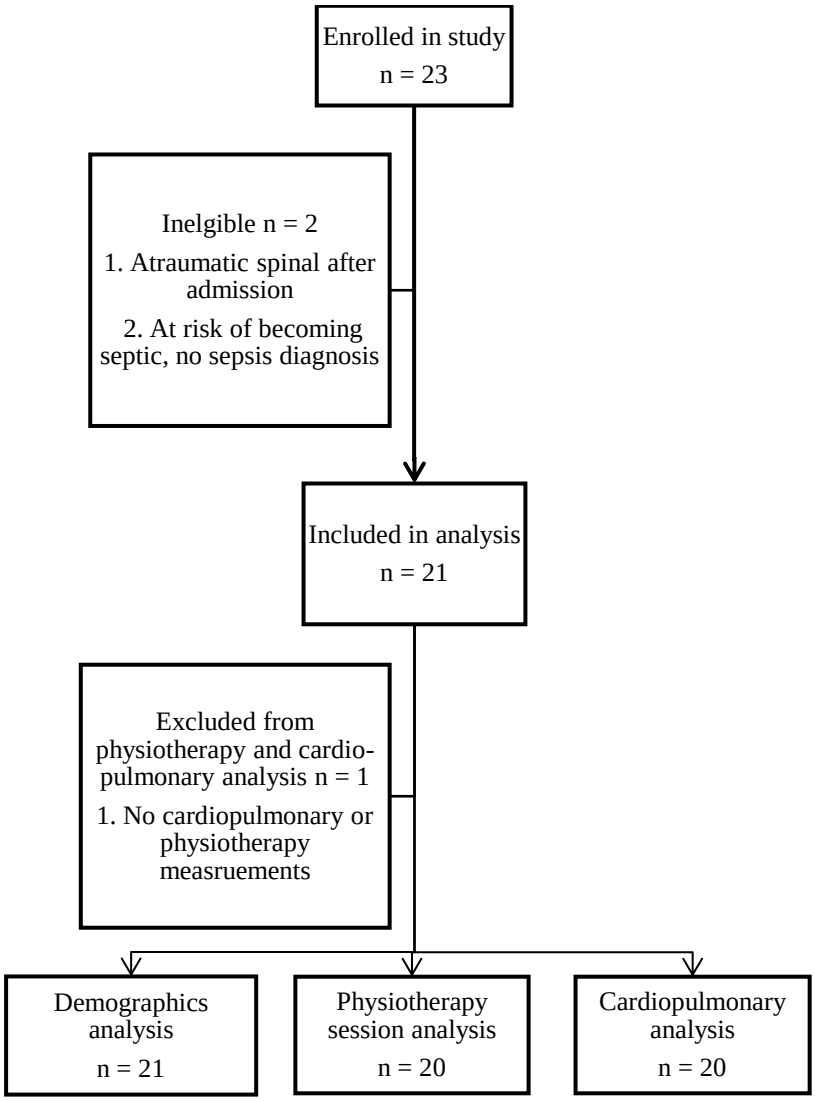


Table 18. Descriptions of intensive care physiotherapy part 1**.**

Patient Transfers	**Description**
Overhead lift	A hoist machine that can move the patient using a sling into different positions with no active participation from the patient
Investigations	**Description**
Chest auscultations	Listening to the lungs with a stethoscope looking for regions of low volume air flow in upper and lower quadrants.
Interventions	**Description**
Suction	The use of deep suction to remove secretions directly from the lung
Mobilizations	**Description**
Asked to complete a physical action	The patient is asked to respond to a question with a specific action (e.g. squeeze hands, wiggle toes, open eyes or cough). The physiotherapist often facilitates this question with sensory stimulus to the region being requested to move when it is the hands or feet.
Passive bed exercises	While in bed, the physiotherapist manipulates the joints of the upper and lower extremities through the entire range of motion that is possible while the patient remains in bed. The mobilization looks to identify the development of ROM deficits and maintain muscle length.
Passive bed chair exercises	Adjusting the bed position to allow the patient to sit in a more upright position of equal to or greater than 45 degrees, with both hips and knees in some degree of flexion. A modified bed chair would be the angle of incline being less than 45 degrees, while still maintaining some hip and knee flexion.
Passive roll right and left	Taking a prone patient and rolling them right and then left. Used to trigger spontaneous coughing, reposition the patient in the bed, aid in cleaning, put on an abdominal binder or put them into a sling for use with the overhead lift.
Repositioning in bed	Using pillows and adjusting the bed settings to reposition the patient to prevent bed sores.

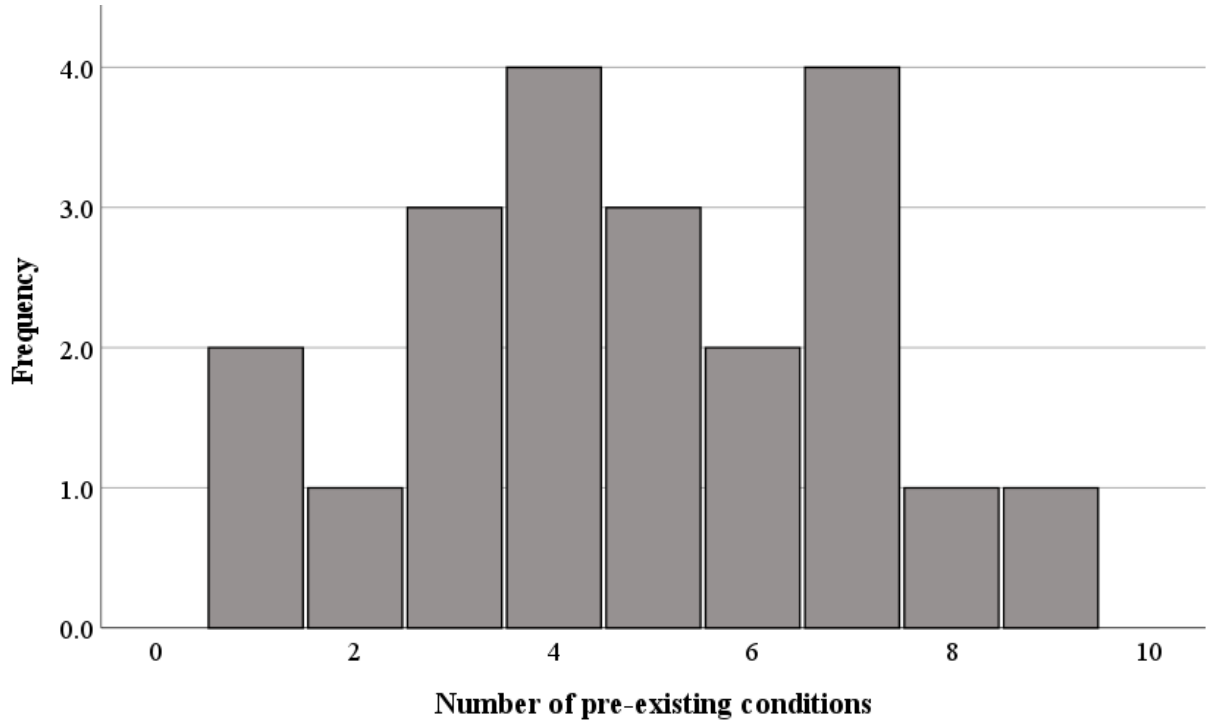
Mobilizations commonly used in both prophylactic management and early mobilization.

Table 19. Descriptions of intensive care physiotherapy part 2.

Patient Positioning	**Description**
Supine in bed	The bed is fully reclined and the patient is supine
Modified bed chair	The bed has been put into a position to allow the patient to sit up with flexion at hip and knee joints. The trunk angle is < 45º
Bed chair	The bed has been put into a position to allow the patient to sit up with flexion at hip and knee joints. The trunk angle is ≥45º
Sitting on the edge of the bed	The patient is sitting on the edge of the bed. They can be doing this assisted or unassisted. The feet may be touching the floor or not touching the floor
Sitting in a chair	The patient is sitting in a chair or wheelchair without support from a bedside clinician.
Standing	The patient is standing with or without the use of a mobility aid or bedside clinician.
Patient Transfers	**Description**
Transfer lie to EOB	The patient is transferred from a supine position to sitting on the edge of the bed without the use of an overhead lift. This can be unassisted, partially assisted with ≥1 bedside clinicians supporting the move or fully assisted with ≥2 bedside clinicians supporting. This transfer also happens in reverse, putting the patient back in bed.
Mobilizations	**Description**
Diaphragm Breathing	The physiotherapist instructs the patient to take deep breaths, activating their diaphragm. This involves their stomach expanding with their breath, usually guided with a hand on the abdominals.
Active assisted exercises	The physiotherapist assists the patient who is actively participating in completing ROM exercises for both the upper and lower extremities. The patient is unable to complete the exercise without assistance from the physiotherapist. The physiotherapist is looking for muscle activation. These can be completed in the first 5 patient positions described.
Active assisted roll right and left	With the help of a physiotherapist the patient rolls onto their right and left. They are actively participating in performing this action, but they are unable to complete it unassisted.
Active exercises	The patient moves their upper and lower extremities without assistance through the ROM exercises as directed by the physiotherapist. These exercises can be completed in all patient positions described.
Sit to stand	The patient moving from sitting on the EOB to standing with or without the support of a physiotherapist or mobility aid
Standing weight transfer	The patient is standing with or without the support of a physiotherapist or mobility aid and transferring their weight between their right and left legs. Their feet are not leaving the floor.
Standing march	The patient is standing with or without the support of a physiotherapist or mobility aid and marching on the spot. This includes lifting one foot fully off the floor, balancing for a moment on one leg and then putting it down and transferring weight to complete this action on the opposite side.
Shuffle from standing to chair or to bed	With or without the support of a physiotherapist or mobility aid, the patient shuffles their feet on the floor to move to their destination chair. The feet do not leave the floor.

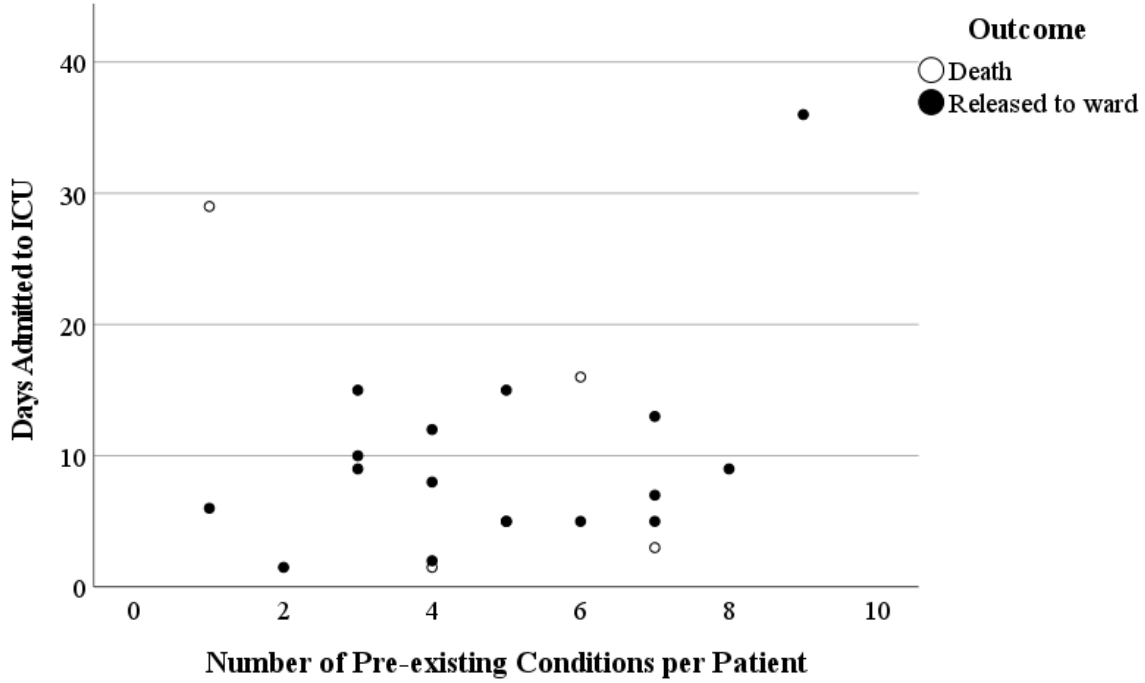
Mobilizations commonly used only during early mobilization physiotherapy sessions. Edge of bed (EOB).

Figure 10. Frequency of the number of pre-existing conditions per patient.



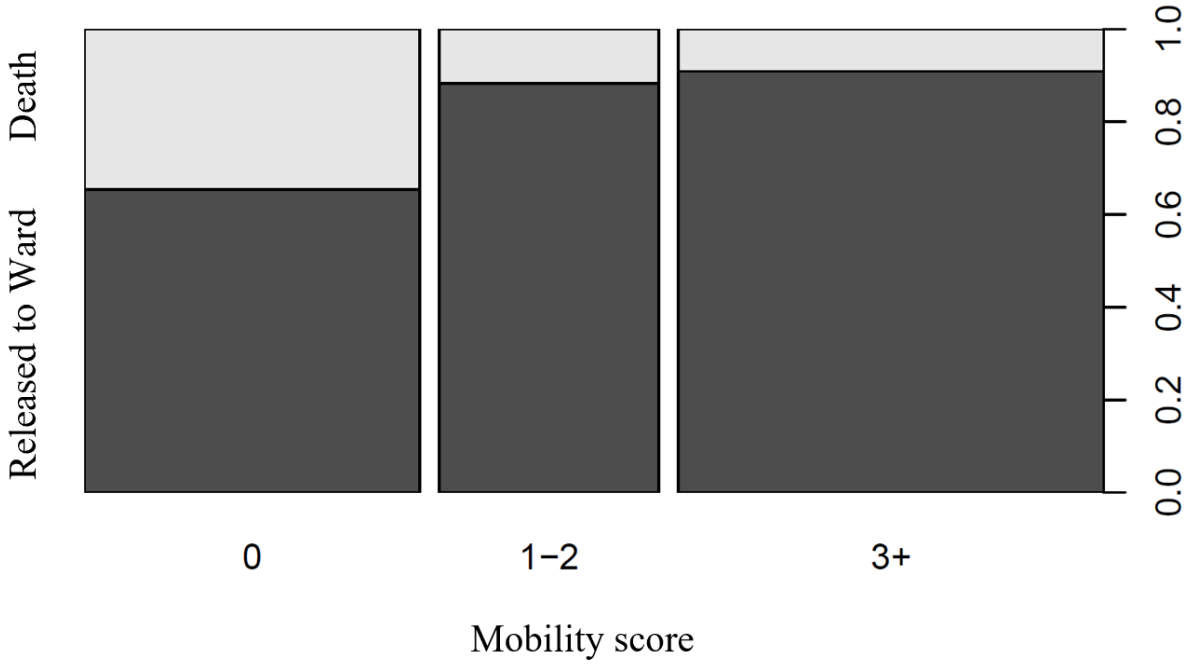
Mean, 4.8; standard deviation, 2.2; number, 21.

Figure 11. Scatterplot of length of ICU stay by total number of pre-existing conditions



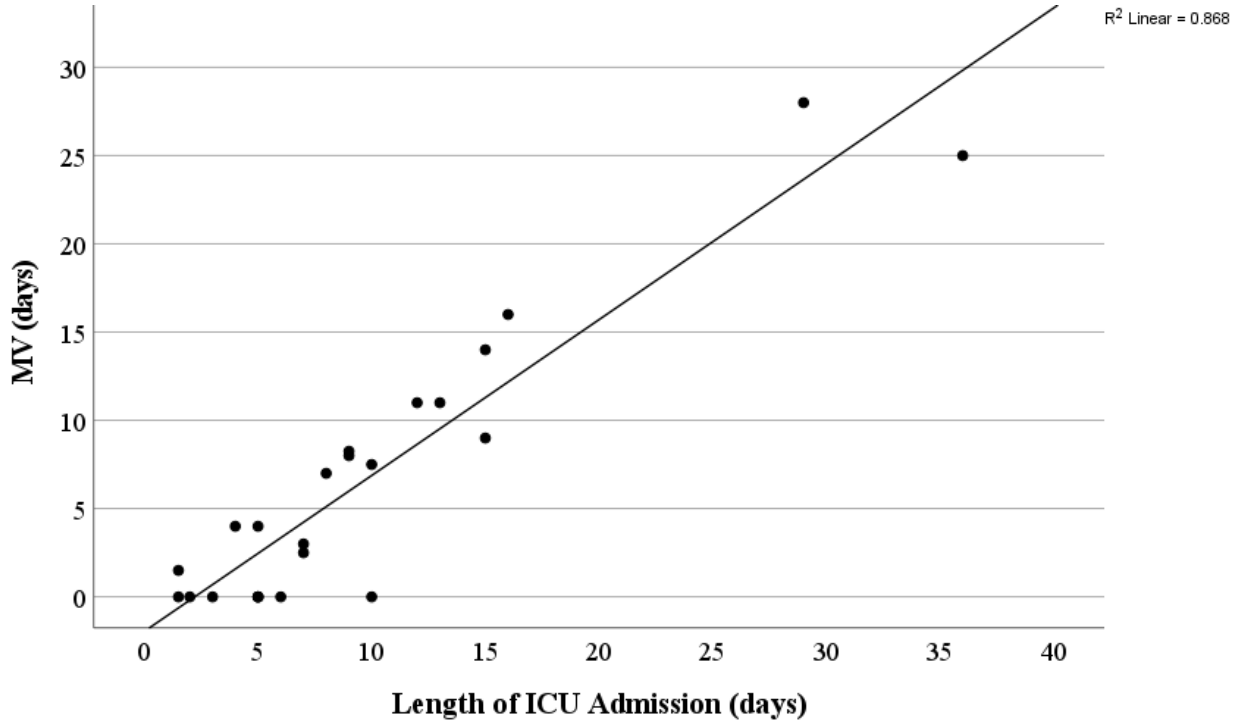
Scatterplot of the number of pre-existing conditions and the days admitted to the intensive care unit (ICU). Open circles (○) signify the ICU stay outcome of death and closed circles (●) signify an ICU stay outcome of being released to ward.

Figure 12: Segmented bar graph of patient outcomes.



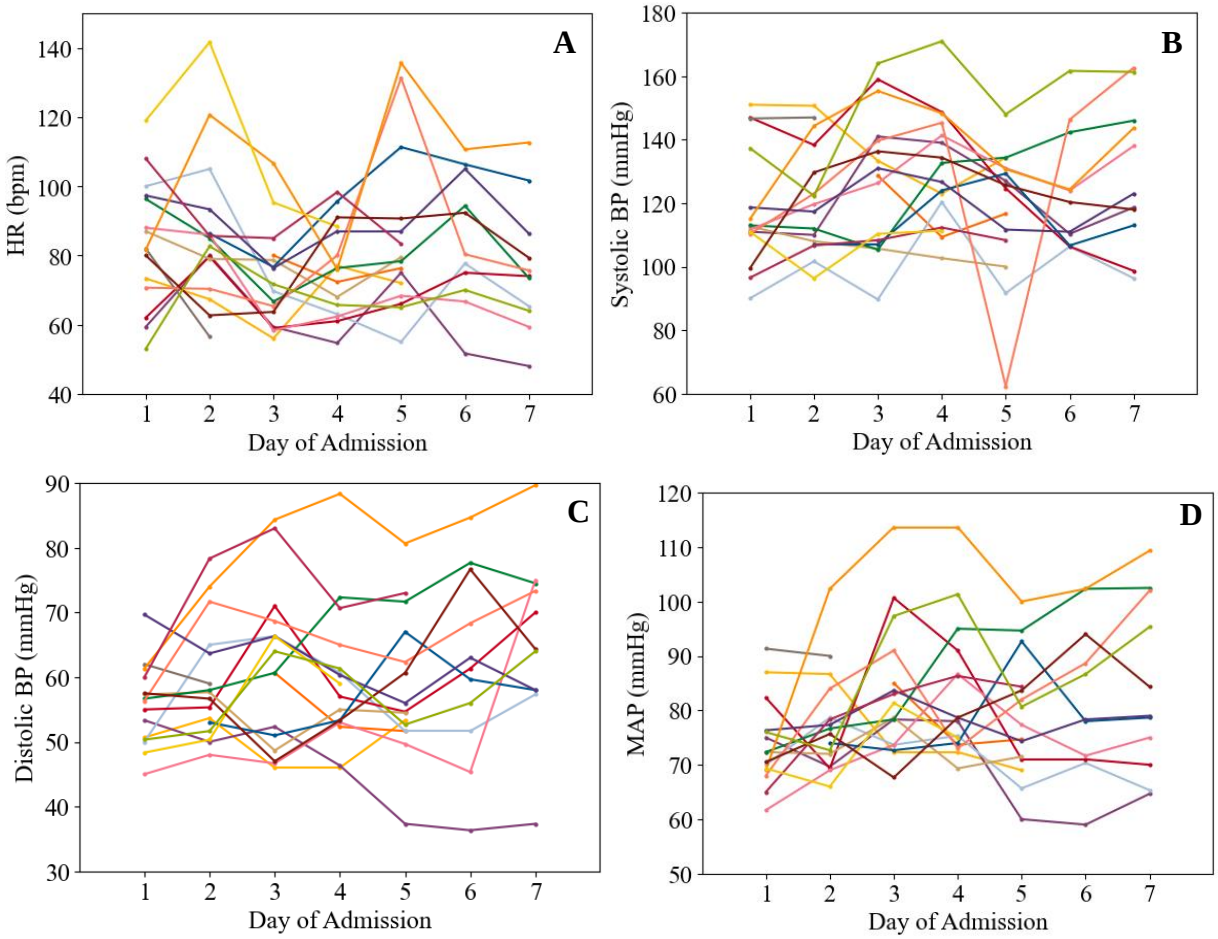
Every physiotherapy session was grouped to consider the patients final outcome, released to ward (dark grey) and death (light grey) and the highest mobility score achieved during individual physiotherapy sessions. The 11-pt mobility scale was used.

Figure 13. Scatterplot of the number of days MV by length of ICU stay.



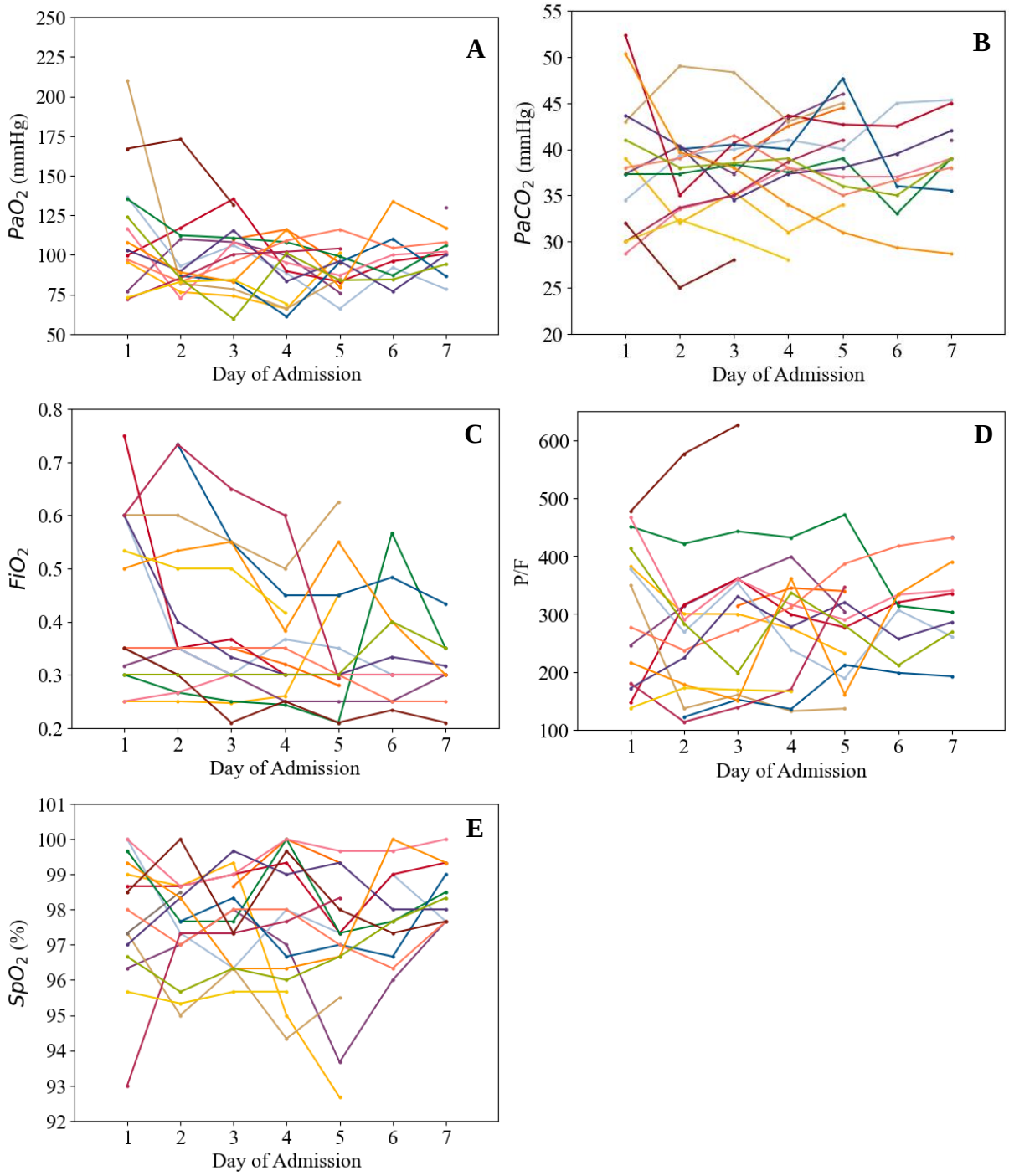
Number of days mechanically ventilated (MV) compared to length of intensive care unit (ICU) stay in days.

Figure 14. Average vital signs for the first 7 days.



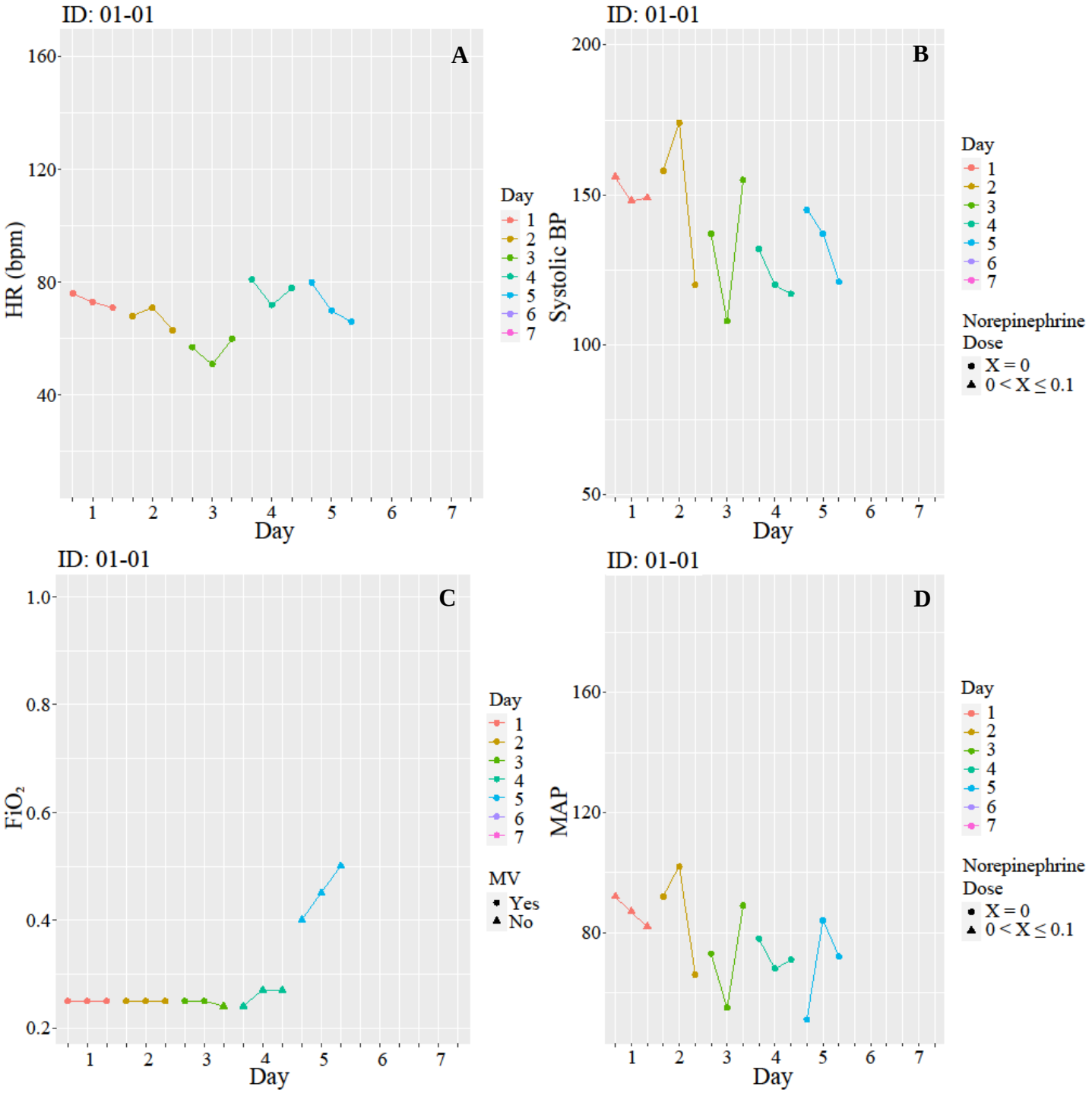
Daily vital signs for the first 7 days of ICU admission. The daily average is reported. (A) heart rate (HR), (B) systolic blood pressure (BP), (C) diastolic blood pressure (BP), (D) mean arterial pressure (MAP). Patient random identification colour code; 01-01, 02-01, 03-01, 04-01, 06-04, 07-04, 08-08, 09-10, 10-12, 11-15, 12-16, 13-16, 15-17, 16-18, 17-19, 18-22, 19-23, 20-24, 21-24, 23-26.

Figure 15. Blood gas analysis results and related values for first 7 days of admission.



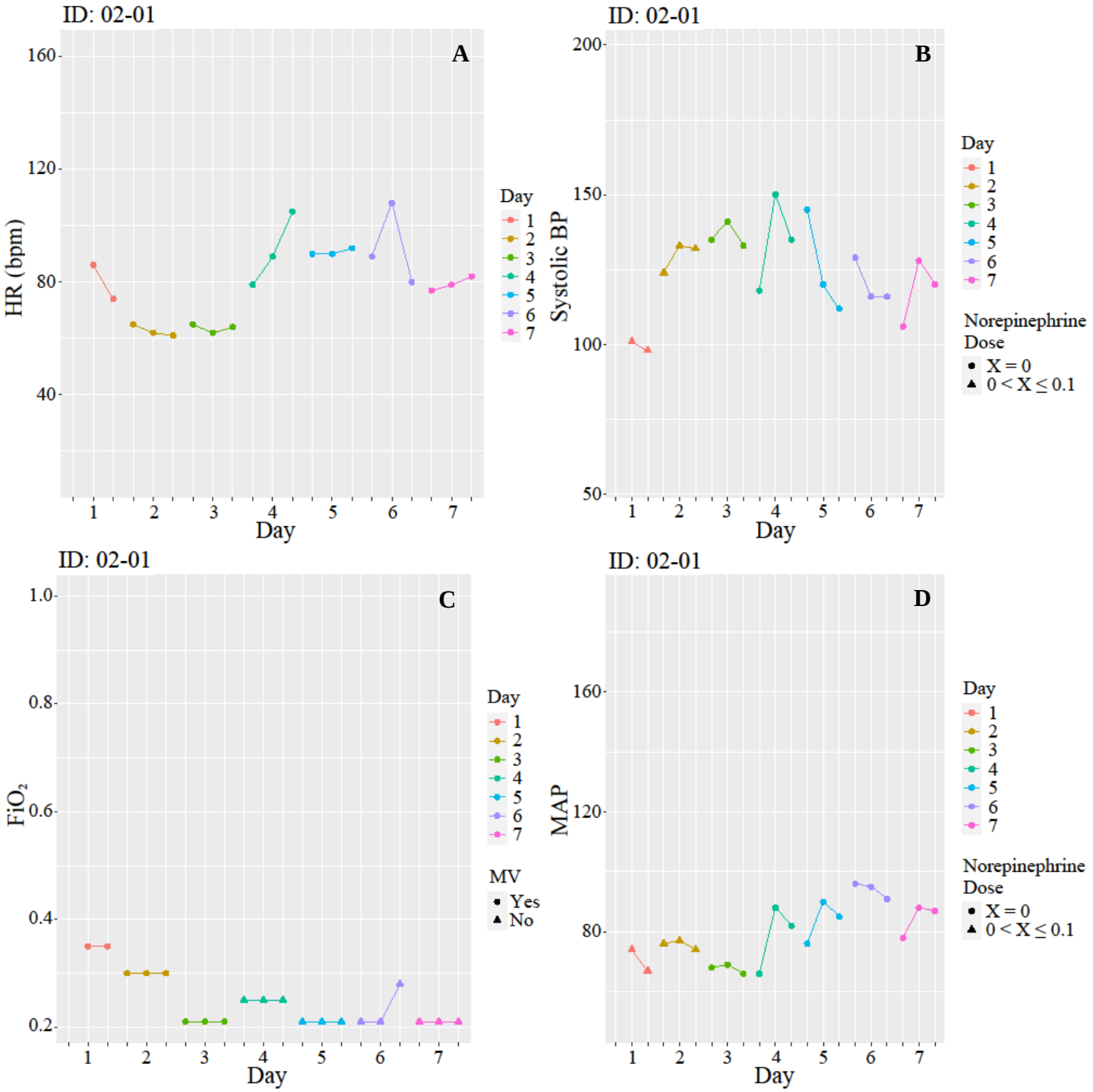
Daily blood gas analysis results and related measurements for the first 7 days of admission. The daily average is reported. (A) partial pressure of arterial oxygen (PaO_2), (B) partial pressure of arterial carbon dioxide ($PaCO_2$), (C) fraction of inspired oxygen (FiO_2), (D) Calculated PaO_2/FiO_2 (P/F) ratio. (E) Percent saturation of peripheral oxygen (SpO_2). Patient random identification colour code; 01-01, 02-01, 03-01, 04-01, 06-04, 07-04, 08-08, 09-10, 10-12, 11-15, 12-16, 13-16, 15-17, 16-18, 17-19, 18-22, 19-23, 20-24, 21-24, 23-26.

Figure 16. Recorded HR, Systolic BP, MAP and FiO_2 for patient 01-01.



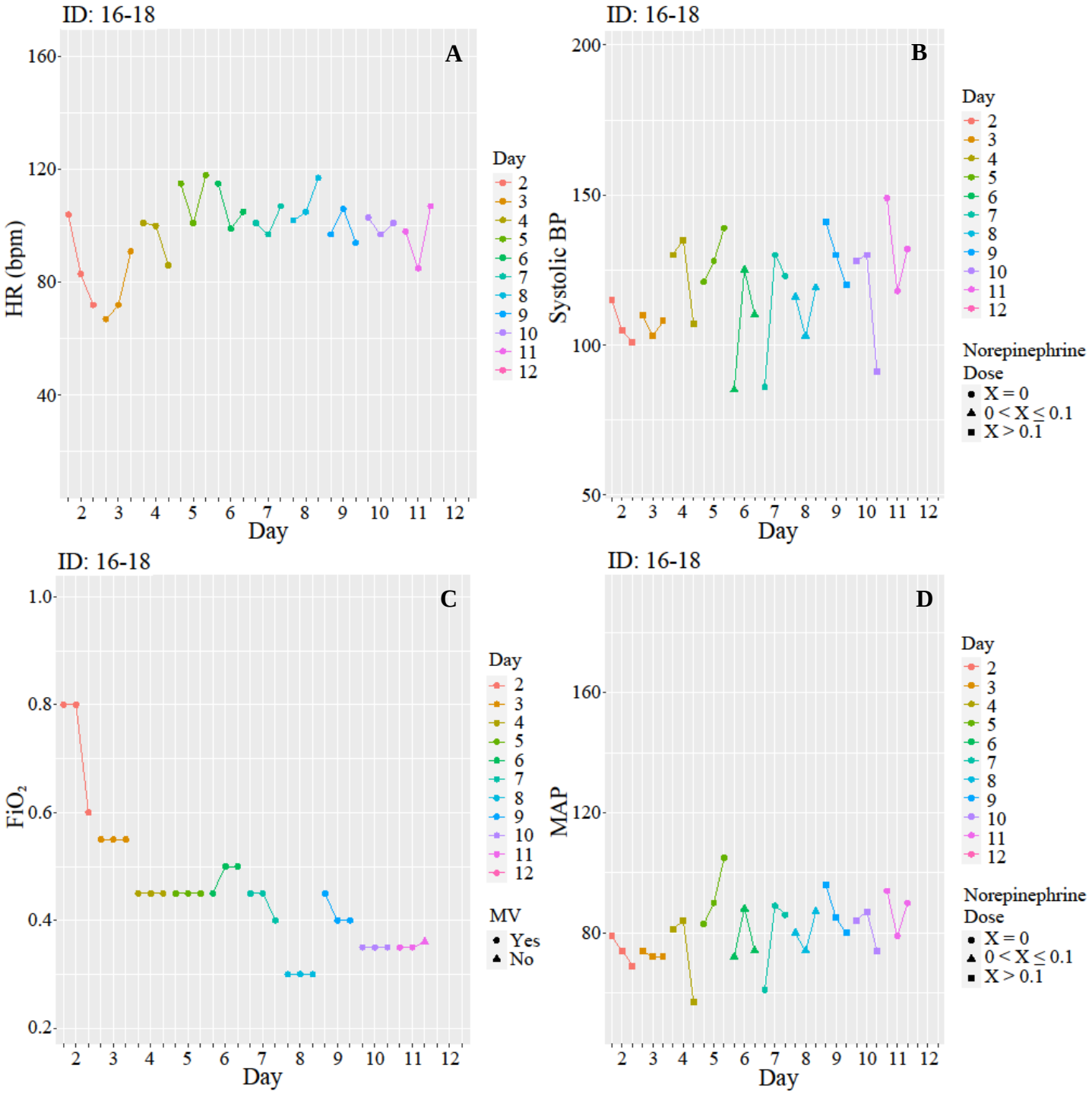
Measurements taken at three time points for patient identified (ID) as 01-01. (A) heart rate (HR), (B) systolic blood pressure (BP), (C) fraction of inspired oxygen (FiO2) and (D) mean arterial pressure (MAP). Norepinephrine dose in mcg/kg/min, mechanical ventilation (MV).

Figure 17. Recorded HR, Systolic BP, MAP and FiO_2 for patient 02-01.



Measurements taken at three time points for patient identified (ID) as 02-01. (A) heart rate (HR), (B) systolic blood pressure (BP), (C) fraction of inspired oxygen (FiO2) and (D) mean arterial pressure (MAP). Norepinephrine dose in mcg/kg/min, mechanical ventilation (MV).

Figure 18. Recorded HR, Systolic BP, MAP and FiO_2 for patient 16-18.



Measurements taken at three time points for patient identified (ID) as 16-18. (A) heart rate (HR), (B) systolic blood pressure (BP), (C) fraction of inspired oxygen (FiO_2) and (D) mean arterial pressure (MAP). Norepinephrine dose in mcg/kg/min, mechanical ventilation (MV).