

**Haemodynamic Tolerance of Patients Following Cardiac Surgery  
Receiving Vasoactive Medication in Upright Positioning.**

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**Haemodynamic Tolerance of Patients  
Following Cardiac Surgery Receiving  
Vasoactive Medication in Upright  
Positioning**

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**Bachelor of Physiotherapy**

*A thesis submitted for partial fulfilment for the degree of Master of Medical Research  
at Griffith University in August 2018*

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## Abstract

*Introduction:* Patients undergoing cardiac surgery require post-operative management in the Intensive Care Unit (ICU). Mobilising patients in the ICU has been shown to have many beneficial effects such as increasing muscle strength and increasing health-related quality of life. As a part of routine management, patients following cardiac surgery are mobilised in ICU if they are considered haemodynamically stable.

However, haemodynamic compromise is common after cardiac surgery, often manifesting as hypotension and reduced cardiac output. As a result these patients may require administration of vasoactive medication while they remain in ICU. Therefore, it can be difficult to know when it may be safe to mobilise patients following cardiac surgery who are receiving vasoactive medication. There is no consensus among ICU experts regarding when it is safe to commence exercise with patients who are receiving vasoactive medication. Concerns may exist about haemodynamic instability that could potentially be exacerbated with upright positioning or mobility.

*Objectives:* The primary aim of this study was to measure the effect of exercise in upright positioning on haemodynamic parameters of patients following cardiac surgery receiving vasoactive therapy. The secondary aims were to clarify what level of vasoactive medication may allow safe exercise, and determine the incidence of adverse events. Haemodynamic parameters that were measured included heart rate (HR), respiratory rate (RR), mean arterial pressure (MAP), systolic and diastolic blood pressure (BP), cardiac output (CO), cardiac index (CI), stroke volume (SV), and peripheral oxygen saturation (SpO<sub>2</sub>).

*Methods:* This was a prospective, single-centre, cohort study conducted in an adult ICU of a tertiary, cardiothoracic university-affiliated hospital in Australia. Ethical clearance and site-specific approval from the Prince Charles Hospital was obtained prior to data collection (HREC 17/QPCH/31). Ethical clearance was also obtained from Griffith University (GU Ref No: 2917/186). Eligible participants were recruited from August 2017 to May 2018. The Flotrac-Vigileo™ system was used to obtain haemodynamic measurements. Subjects were positioned from supine, high sitting, sitting on the edge of the bed, standing, marching on the

spot and then returned to supine where they remained for 5 minutes. Subjects remained in these positions for one minute. A between-within repeated measures ANOVA was conducted to compare haemodynamic variables over various positions and interactions with positions\*dose of low versus medium to high levels of vasoactive medication.

*Results:* Twenty participants were recruited; 16 (80%) male; mean age of 65.9 (10.6) years, with 6 (30%) receiving low dose vasoactive medication and 14 (70%) receiving a moderate to high dose. Upright positioning caused statistically significant increases in MAP ( $p=0.018$ ), diastolic BP ( $p=0.008$ ), and RR ( $p=0.049$ ). At an individual level, clinically significant changes in CO, CI, SV, systolic BP, HR and SpO<sub>2</sub> were observed. There was no significant interaction between position and dose of vasoactive medication. One minor adverse event occurred in a participant on low dose Dopamine. This was a transient decrease in MAP, and led to no clinically significant consequences.

*Conclusions:* Upright positioning led to no clinically significant consequences in this study population. The findings suggest that vasoactive medication alone should not be considered a contraindication to upright positioning in patients following cardiac surgery, and should be explored with a larger sample size.

## Statement of Originality

This work has not previously been submitted for a degree or diploma in any university. To the best of my knowledge and belief, the report contains no material previously published or written by another person except where due reference is made in the report itself.

Jemima Boyd

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## Keywords

Intensive care unit, cardiac surgery, inotropes, vasopressors, vasoactive medication, mobility, upright positioning, haemodynamic

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## List of Abbreviations

Blood pressure (BP)  
Body surface area (BSA)  
Cardiac index (CI)  
Cardiac output (CO)  
Cardiopulmonary bypass (CPB)  
Coronary artery bypass graft (CABG)  
Electrocardiogram (ECG)  
Fraction of inspired oxygen (FiO<sub>2</sub>)  
Functional electrical stimulation (FES)  
Glasgow Coma Scale (GCS)  
Heart rate (HR)  
Intensive Care Unit (ICU)  
Intra Aortic Balloon Pump (IABP)  
Intravenous (IV)  
Jugular venous pressure (JVP)  
Marching on the spot (MOS)  
Mean arterial pressure (MAP)  
Non ST Elevation Myocardial Infarction (NSTEMI)  
Partial pressure of carbon dioxide (pCO<sub>2</sub>)  
Partial pressure of oxygen (pO<sub>2</sub>)  
Passive range of motion (PROM)  
Peripheral oxygen saturation (SpO<sub>2</sub>)  
Pulmonary artery catheter (PAC)  
Rating of Perceived Exertion (RPE)  
Respiratory rate (RR)  
Short Physical Performance Battery (SPPB)  
Sitting on the edge of the bed (SOEOB)  
Sit to stand (STS)  
ST Elevation Myocardial Infarction (STEMI)  
Stroke volume (SV)  
Systemic vascular resistance (SVR)  
The Prince Charles Hospital (TPCH)

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## Introduction

The Intensive Care Unit (ICU) provides specialised medical therapy for critically unwell patients with potentially reversible life-threatening conditions such as multiorgan failure, significant exacerbation of respiratory or cardiac disease, trauma, and high-risk surgical patients. Intensive Care Units vary regarding the type of service they deliver; for example, some units may provide care to a broad mix of patients, while other ICUs are centred around a subspecialty of medicine. Examples of ICU subspecialties include neurosurgical, burns, trauma and cardiothoracic medicine.

As technology and knowledge improves, patients are more likely to survive their intensive care stay(1). There are growing concerns regarding the impact of ICU survival on overall quality of life. Cognitive or physical impairments that persist after an ICU admission is known as post-intensive care syndrome(2).

Muscle weakness associated with a prolonged ICU admission can have negative outcomes on activities of daily living after discharge(3-5). Significant long-term cognitive impairments have been observed among ICU survivors (5, 6). In addition, reduced health-related quality of life scores (6) and negative impacts on sleep, energy, and emotional health have been described(7).

Early exercise of ICU patients has been described as the initiation of physical activity at an earlier stage than conventional practice(8). Historically, bed rest has been prescribed for critically unwell patients. Early exercise is gaining interest in ICUs around the globe and there is a growing body of evidence surrounding the benefits. Early exercise can include active in or out of bed exercise. In-bed exercise may include active-assisted upper limb or lower limb exercises or in-bed cycle ergometry. Out-of bed exercise may include tilt table (passively standing via plinth with tilt-in-space function up to 90 degrees), sitting on the edge of the bed (SOEOB), sit to stand (STS), marching on the spot (MOS) or mobilising away from the bedside.

Implementation of early mobility in medical and surgical ICUs leads to reduced ICU and hospital length of stay(9, 10). In addition, the need for ongoing rehabilitation when discharged home is reduced when early mobility in ICU is initiated (10), as well as the rate of

gastrointestinal, cardiac, pulmonary, infective and renal complications in high-risk surgical, trauma and burns ICU populations (9, 11).

Early exercise leads to improvements in quality of life post ICU. A meta-analysis of the available literature found that early mobility leads to increased muscle strength and a higher probability of walking independently at ICU discharge (12). In addition to this, a greater probability of more days alive and out of hospital to day 180 post ICU discharge was associated with early mobility(12). Improvements in patient-centred outcomes, such as quality of life at 6 months post discharge, muscle strength and activity participation, have also been documented(12).

Early exercise of ICU patients has been shown to be safe and feasible(11, 13-18). While there are documented benefits, concerns remain regarding the safety of exercising certain ICU populations. Understandably, it can be difficult for clinicians to identify when it may be safe to commence early exercise with critically unwell patients. There may be apprehension surrounding attachments, medications or patient factors such as pain, anxiety or agitation. Concerns may exist about clinical instability that could potentially be exacerbated by exercise in haemodynamically unstable patients. These patients are monitored closely in the ICU, and may be prescribed vasoactive medication, or administered intravenous (IV) fluids or diuretics to help with their haemodynamic compromise. Vasoactive medications include vasopressors (constrict or dilate vessels), or inotropes (impact cardiac contractility).

A meta analysis and systematic review of safety data regarding mobilisation in ICU was published in 2017 by Nydhal et al (18). Forty-three full-text publications were eligible for this review, which included a total of 22,351 occasions of patient mobilisation. It was found that the risk of a safety event was low, with only 583 potential safety incidences being reported (2.6%). Seventy-eight of the reported potential safety incidences led to subsequent consequences (0.2%), and 43.6% of these included haemodynamic related events such as changes in blood pressure.

International consensus guidelines on exercising critically unwell patients were formed by a panel of multidisciplinary ICU experts in 2014 (19). The panel members were unable to reach consensus about the safety profile of exercising haemodynamically unstable ICU patients who are receiving vasoactive medication. This is reflected in the greater the ICU community,

where it is often thought that exercising a patient who is haemodynamically unstable requiring vasoactive medication may exacerbate their condition. The panel members who formulated the consensus document concluded that the administration of vasoactive medication was not an absolute contraindication to exercise, but that the appropriateness of exercise could be influenced by dose, the trend in dosage (e.g. a rise in the dose would indicate caution), and whether or not the patient was currently haemodynamically stable. They recommended that exercise be considered on a case-by –case basis by the ICU clinician. The panel members agreed that a “grey area” surrounding exercise while receiving vasoactive support remains, and this is a priority area for further research(19). Patients following cardiac surgery are a particular subgroup within the ICU often requiring vasoactive therapy, pose a further dilemma as to assessment of haemodynamic stability.

#### *Management following cardiac surgery – a subspecialty of the ICU*

Post-cardiac surgical management is among the top 5 reasons for admission to an adult ICU in Australia with 5.8% included in this subspecialty(1). The ICU environment is ideal for managing patients following cardiac surgery in the immediate post-operative phase as it allows invasive monitoring from specialised nursing and medical staff.

Cardiac surgery is performed to manage symptoms resulting from a poorly functioning heart. The aim of Coronary Artery Bypass Graft (CABG) surgery is to bypass diseased arteries with a harvested graft to enable delivery of oxygenated blood to areas the blocked artery normally would supply(20). This surgery is recommended for patients with stable angina with coronary vessel disease, unstable angina, coronary artery occlusion, ST or Non-ST segment myocardial infarction (20, 21). Heart valve surgery replaces or repairs a dysfunctioning valve(20). Indications for this surgery include congenital or acquired valvular heart disease such as aortic, mitral or tricuspid valve stenosis or regurgitation, as well as infective valve endocarditis(20, 22, 23).

Over time, advancements in non-surgical interventions for heart disease have occurred, and suitable patients are being recommended for less invasive percutaneous coronary interventions rather than open-heart cardiac surgery. As a result of this evolving technology, cardiac surgery is now being performed on more medically complex individuals. Not only are these complex patients at an increased risk for adverse clinical outcomes (24), there are



specific problems resulting from the open surgical procedures and accompanying techniques that generate increased instability in the post-operative period.

During cardiac surgery, the aorta is cross-clamped and a cardioplegic solution of cold potassium ions is injected into the heart which causes it to cease pumping(20). This reduces myocardial oxygen consumption and allows the surgeons to complete the procedure with a motionless heart (25). The patient is cooled and usually placed on cardiopulmonary bypass (CPB), which provides circulatory support. A CPB circuit includes cannulae, an oxygenator, heat exchanger, a filter and a pump. A cannula is inserted into the right atrium of the heart and drains venous return. The oxygenator removes carbon dioxide and the heat exchanger controls blood temperature. The filter removes air bubbles from the system. The pump works to return oxygenated blood back into the aorta distal to the cross-clamp. It is a complex machine that can monitor parameters such as the patient's temperature, oxygen saturations, blood gases and haemoglobin (25, 26). There are risks associated with CPB and cardiac surgery that may result in adverse changes to a patient's haemodynamic system in the post-operative phase.

#### *Haemodynamic monitoring of patients following cardiac surgery*

Changes in haemodynamic parameters are common after cardiac surgery and the first few hours in ICU are a dynamic period requiring close monitoring by ICU specialists(27). Invasive haemodynamic monitoring can assist in guiding therapy and detecting haemodynamic instability (28), the ultimate goal after cardiac surgery being determining the adequacy of cardiac output and oxygen delivery to vital organs (20, 29). It is important to monitor patients following cardiac surgery who require vasoactive support, as these patients may be more haemodynamically unstable if they are requiring vasoactive support in the first instance. Haemodynamic monitoring of patients following cardiac surgery receiving vasoactive medication is performed using invasive or non-invasive techniques.

Haemodynamic parameters that are commonly monitored and relate to the functioning of the patients cardiovascular system include heart rate (HR) and rhythm, respiratory rate (RR), peripheral capillary oxygen saturation (SpO<sub>2</sub>), mean arterial pressure (MAP), systolic and diastolic blood pressure (BP). More invasive haemodynamic measurements include stroke volume (SV), cardiac output (CO), cardiac index (CI), and systemic vascular resistance

(SVR). Clinical indicators of adequate tissue perfusion are also monitored and give the clinician information regarding the effectiveness of the cardiovascular system in delivering oxygenated blood to vital organs.

#### *Indicators of adequate tissue perfusion*

Patient observation can provide some information about the adequacy of their tissue perfusion and haemodynamic status. Warmth of peripheries and an ability to palpate distal pulses can indicate adequate tissue perfusion whereas poor CO may result in cool peripheries(30). A urine output of at least 0.5ml/kg/hour may indicate acceptable tissue perfusion in patients following cardiac surgery(31). Low urine output post-cardiac surgery may result from hypovolemia or reduced myocardial contractility, indicating potential haemodynamic insufficiency (27). The absence of bowel sounds can indicate poor gut oxygenation in patients following cardiac surgery. Changes in patient mentation can indicate poor cerebral tissue perfusion caused by reduced CO. Transient but higher than normal blood lactate levels are common after cardiac surgery and may be a response to cardioplegia, CPB, tissue hypoxia or hypothermia. However, lactate levels higher than 3mmol/L six hours after admission to ICU are associated with major complications following cardiac surgery and can be a consequence of poor oxygen delivery to tissues(32).

#### *Heart rate and rhythm*

Abnormal rhythms are not uncommon after surgery, such as bradycardia, sinus tachycardia, atrial fibrillation or heart block. These arrhythmias may contribute to hypotension and reduced CO in the post-operative phase (27, 29, 31). These abnormal rhythms can be addressed with medications, pacing, or cardioversion and must be considered in decisions concerning mobility in the post-operative period. (29).

An electrocardiogram (ECG) is used to monitor the patient's HR and identify abnormal rhythms such as premature ventricular contractions, ventricular tachycardia, bradycardia or atrial fibrillation (33).

#### *Peripheral capillary oxygen saturation*

Peripheral capillary oxygen saturation is a measurement of the patient's blood oxygenation. It is recommended that the SpO<sub>2</sub> remains above 90% (33). Peripheral capillary oxygen saturation is measured using pulse oximetry. It provides an indirect, continuous measurement

of the patient's blood oxygenation and is an indication of adequacy of tissue perfusion(30). Peripheral capillary oxygen saturation monitoring allows assessment of the patient's response to exercise and determine whether an increase in supplemental oxygen is required. Measurements using this technique may be inaccurate in the presence of poor peripheral perfusion.

#### *Mean arterial pressure*

Critically ill patients usually require arterial pressure monitoring, which allows for continuous monitoring of systemic arterial BP and provides vascular access for obtaining blood samples. Arterial pressure monitoring is of utmost importance in patients receiving vasoactive infusions or those with fluctuating, unstable BPs. To achieve arterial pressure monitoring, an arterial catheter is inserted into the radial, brachial, femoral, or dorsalis pedis artery. The catheter is attached to a fluid-filled pressure transducer system incorporating a flush device, and an attached transducer senses arterial pressure and converts the pressure signal to a waveform on the bedside monitor. The waveform reflects pressure generated by the left ventricle during systole. The monitor also displays numerical pressure values. Systolic and diastolic are directly measured with MAP calculated as per the equation (33):  $MAP = [(2 \times \text{diastolic}) + \text{systolic}] / 3$ . Mean arterial pressure is the average pressure that is tending to push through the circulatory system. A low or high MAP may indicate poor tissue perfusion (33-35). It is the preferred pressure to be evaluated in unstable patients (31) and is useful clinically as it provides one number relating to CO and the SVR. The acceptable MAP typically ranges from 70 and 110 mm Hg(27, 33).

#### *Stroke volume*

Stroke volume is a value that reflects the amount of blood that is pumped by the heart with each contraction(33). Normal SV ranges from 55 to 130mL(33) and is calculated by the following equation(35):  $SV = CO/HR \times 1000$ .

#### *Cardiac output*

Cardiac output is the amount of blood pumped by the heart in one minute. The normal resting value ranges from 4-8L/min (31, 33, 35) and is calculated by the following equation(35):  $CO = SV \times HR$ .

Cardiac output is the main determinant of MAP, and therefore adequate pressure usually indicates adequate CO. Cardiac output is influenced by many factors including preload, afterload, cardiac contractility, and HR and rhythm(20). Preload is the amount of blood that is left in the right atrium or left ventricle at the end of a diastole or the beginning of systole, and is affected by volume status(20). Afterload is the resistance to a ventricular contraction, that is, how hard the heart must work to eject the blood, and is affected by peripheral vascular tone(20). Increases in afterload after cardiac surgery may be caused by hypothermia, increased sympathetic output, hypervolemia or heart pump failure(20).

#### *Cardiac index*

Cardiac index is a value that reflects CO per square meter of body surface area (BSA). The CI is often reported because a measurement of CI alone does not take into account an individual's specific needs with respect to actual body size(33). Normal CI ranges from 2.5-4.2L/min/m<sup>2</sup> (31). Cardiac index can be variable after heart surgery, however a value greater than 2L/min/m<sup>2</sup> is desirable(27). Cardiac index can be calculated by the following equation(35): $CI = CO/BSA$ .

#### *Systemic vascular resistance*

Systemic vascular resistance refers to the resistance that must be overcome for blood to pass through the vessels in the circulatory system. Vasoconstriction will increase SVR, whereas vasodilation will decrease SVR. Normal SVR ranges from 800-1200dynes/sec/cm<sup>5</sup>. SVR should decrease with exercise as the vessels dilate to allow more blood flow.

Measurements of CO, CI, SV and SVR are more invasive and can be measured by either thermodilution (pulmonary artery catheter), transpulmonary indicator dilution (PiCCO®) and arterial pressure waveform derived devices (Vigileo™) or Doppler (USCOM®, CardioQ™). As the pulmonary artery catheter and the Vigileo are the most commonly utilized in the facility in which this study was conducted they will be discussed in more detail.

#### *Pulmonary artery catheter*

The pulmonary artery catheter (PAC) was developed in 1970 and involves right-heart catheterization using a balloon-tipped catheter(36). It is an invasive instrument, and can

continuously monitor specific haemodynamic variables including mean pulmonary artery pressure, mean right ventricular pressure, CI, CO, SVR, and pulmonary vascular resistance index(20, 31, 33). It is inserted via a central venous access point at the neck, passes into the right atrium, through the tricuspid valve into the right ventricle, through the pulmonary valve and finally into the pulmonary artery(33). As it is able to measure right ventricular and pulmonary artery pressures, it is unique from other methods of cardiac monitoring. The PAC uses a method called thermodilution to calculate CO. Thermodilution involves a bolus of cold fluid being injected into the right atrium. The resulting change in temperature is measured by the PAC. The area under a temperature versus time curve is calculated by the system, and CO is inversely proportional to the area underneath the curve.

Complications that may be encountered using the PAC include damage to structures adjacent to the right heart, air embolism, catheter kinking or perforation of the pulmonary artery(28). The use of PAC is not routine due to the highly invasive nature of the system, as well as the potential complications it poses. Use of the PAC is controversial especially when considering other, less invasive methods of continuous detailed haemodynamic monitoring that are available.

#### *The Flotrac-Vigileo™ system*

The Flotrac-Vigileo™ system (Edwards Lifesciences, Irvine, CA, USA) is a less invasive system that can continuously derive detailed haemodynamic parameters such as CO, CI and SV. The system consists of a Flotrac sensor cuff and a Vigileo monitor. The Flotrac sensor cuff (seen in Figure 1) is a pressure transducer. It's calculations are based on the algorithm where the stroke volume is proportional to the arterial pulsatility (37). The system analyses the arterial waveform with inputted patient data, such as height, body weight, sex, and age taken into consideration. Haemodynamic measurements are continuously derived from these inputs and are displayed on the Vigileo monitor (seen in Figure 1).

Less invasive means of monitoring haemodynamic variables, such as the Flotrac-Vigileo, are gaining interest. The Flotrac-Vigileo system has been shown to reliably measure haemodynamic measurements such as CI (38, 39). Specifically, the Flotrac-Vigileo system has been shown to have significant correlation with haemodynamic measurements derived from the highly invasive thermodilution technique in patients following cardiac surgery (38).



Figure 1 The Vigileo monitor and the FloTrac sensor cuff (40)

*Haemodynamic complications following cardiac surgery: Different types of shock states*

Shock is broadly classified as four main categories, i.e. cardiogenic, hypovolemic, distributive, and obstructive. These types can all occur in the patients following cardiac surgery due to pre-existing disease or intervention required in the surgical procedure. Haemodynamic compromise after cardiac surgery is usually multifactorial. Table 1 lists the four types of shock and examples of incidents during cardiac surgery that impact on perfusion.

Table 1 Examples and vital signs in shock states

Type	Examples in General Patients	Clinical Signs	Reasons for occurrence following cardiac surgery	Management
Cardiogenic	Heart failure, Acute myocardial infarction, Valvular disease, arrhythmia	CO ↓ BP ↓ HR → to ↑ JVP ↑ SVR ↑ Cold peripheries	- Cardiac ischaemia after prolonged CPB or cardioplegia - Post-operative stunning of the myocardium - Peri or post operative myocardial infarction. - Arrhythmia - Reduced pre-operative EF	Inotropes, Diuresis
Hypovolaemic	Haemorrhage, dehydration, Burns	CO ↓ BP ↓ HR ↑ JVP ↓ SVR ↑ Cold peripheries	- Peri or post-operative bleeding - Over-diuresis	IV Fluids, Blood products
Distributive	Septic Shock, Anaphylaxis, Opiates, Inflammation	CO ↑ BP ↓ HR ↑ JVP → SVR ↓ Warm peripheries	- Anaphylactic reaction to anaesthetic medications - Release of inflammatory cytokines in response to CPB	IV Fluids, Vasopressors
Obstructive	Tension Pneumothorax, Pulmonary Embolism, Cardiac Tamponade	CO ↓ BP ↓ HR ↑ JVP ↑ SVR ↑ Cold peripheries	- Blood clot resulting from CPB → pulmonary embolism - Barotrauma, placement of lines or airways during surgery → tension pneumothorax - Myocardial rupture, pericarditis, pericardial effusion → Cardiac tamponade	Manage obstruction (e.g. surgery, drainage of tension pneumothorax)

JVP= Jugular venous pressure

Cardiogenic shock is caused by poor functioning of the heart muscle and can be caused by multiple factors after surgery. For example, heart muscle pump failure caused by myocardial ischaemia after prolonged CPB or cardioplegia, poor myocardial protection during cross-

clamping, post-operative stunning of the myocardium. Post-operative arrhythmias such as bradycardia can also cause cardiogenic shock. A CPB time of greater than 120 minutes and perioperative ischemia are key contributors to reduced contractility(27). The patient's underlying cardiac disease, especially a preoperative ejection fraction (EF) of <35%, may play a role in impaired myocardial contractility in the postoperative phase, therefore contributing to cardiogenic shock (29). Clinically, cardiogenic shock will manifest as reduced CO, HR and BP due to the impaired heart contractility. However, in cardiogenic shock, JVP and SVR is raised as fluid is not being pumped efficiently. In these instances patients may be administered inotropes to assist with myocardial contractility, and/or diuresis to assist with fluid removal.

Bleeding or over-diuresis causing excessive urine output can contribute to hypovolemic shock. This will manifest as hypotension, reduced CO, JVP and SVR due to the overall decreased fluid in the vessels. Vasopressors may also be used in instances of hypotension to improve MAP by vasoconstriction(27).

Distributive shock, also known as vasoplegia, can also occur after cardiac surgery due to the inflammatory response or sepsis. It presents as increased CO, decreased MAP, increased HR and JVP and decreased SVR. Vasoplegia occurs in 25% of patients following cardiac surgery (41), manifesting as hypotension (MAP <60mmHg), a high CI (>3.5L/min) and normal heart filling pressures(41). Vasoplegia may occur in response to the CPB, when inflammatory cytokines are released resulting in systemic vasodilation that can remain for hours after the surgery resulting in decreased SVR (26, 29, 41). Vasopressors are usually administered in this instance(29).

Obstructive shock may be caused by cardiac tamponade, tension pneumothorax or pulmonary embolism post-cardiac surgery. Cardiac tamponade is an emergent condition where blood or fluid occupies the space between the heart and the heart muscle. In patients following cardiac surgery it may be caused by myocardial rupture, pericarditis or pericardial effusion. Cardiac tamponade may be suspected when the MAP fluctuates, there is low CI, acute tachycardia, and decreased urine output(27, 29). Management involves immediately returning the patient back to the operating theatre to find the source of the tamponade and drain the fluid in the sac between the heart muscle and the heart. A tension pneumothorax can also cause obstructive shock. A tension pneumothorax can be described as a closed pneumothorax, in which there is



a progressive build up of air within the pleural space that is unable to escape. It often results from trauma, and in patients following cardiac surgery it could be caused by barotrauma during ventilation, or inaccurate placement of lines or airway during surgery.

It is evident that patients following cardiac surgery may be subject to haemodynamic instability from many potential causes, and as a result may require administration of fluid loading or vasoactive medication. This is why these patients are managed in the ICU in the immediate post-operative phase. In patients following cardiac surgery, extubation normally occurs within 12 hours of returning to the ICU(31), and patients usually leave the unit within 24 hours(27). Mobilisation as early as possible after extubation is prescribed as a part of best evidence management in patients following cardiac surgery (31, 42, 43), however safety has not been ascertained.

It can be difficult to determine when it is safe to begin early mobility with patients following cardiac surgery in the ICU. As previously mentioned, a barrier to early exercise in ICU is the potential for new or exacerbating existing haemodynamic instability, particularly in patients following cardiac surgery who are receiving vasoactive support. Clinicians may consider these patients as having more potential for haemodynamic instability due to their requirement for vasoactive medication in the first instance.

### *Mobilising while receiving vasoactive medication*

It has been outlined that it can be difficult to know when it may be safe to mobilise a patient following cardiac surgery if they are receiving vasoactive medication, as there may be concerns that exercise may potentially exacerbate existing, or lead to, haemodynamic instability. It is known that patients following cardiac surgery may be haemodynamically unstable in the post-operative phase and as a result may be administered vasoactive drugs. Currently, there is little research that has been conducted regarding the safety profile of exercising while receiving vasoactive medication.

A reason why controversy surrounding safe mobility of patients receiving vasoactive medication exists is that the reasons for requirement may differ depending on the clinical presentation. In addition, dosages and particular types of vasoactive medications may vary when considering different ICUs. As discussed, international consensus guidelines formed by

a panel of ICU experts in 2014 concluded that this is a “grey area” and further research is needed to clarify the safety profile of exercising ICU patients receiving vasoactive medication (19).

Boyd and colleagues(44) evaluated the consensus recommendations in a cardiothoracic, tertiary ICU. This was a prospective cohort study that included 91 participants. The consensus recommendations were evaluated against 809 physiotherapy occasions of service, which included in or out of bed exercise. Basic haemodynamic measurements were measured before and during physiotherapy treatment, including HR, RR, MAP and SpO<sub>2</sub>. Two hundred and ninety-nine occasions took place while the patient was receiving vasoactive medication. Exercise rehabilitation occurred with approximately half of these patients. Only one adverse event occurred during exercise with a patient receiving vasoactive medication (0.87%), which was reported to have not led to clinically significant consequences. This was described as cardiovascular instability and occurred during a tilt table session with a patient receiving a low dose of Noradrenaline. This study found that the consensus recommendations were a useful tool to assist in guiding exercise rehabilitation in ICU patients. Their findings indicate that there may be further scope to commence mobility in patients receiving vasoactive medication.


#### *Vasoactive medications: Inotropes and vasopressors*

Inotropes are medications that increase myocardial contractility and therefore CO and BP(20, 34). Inotropes are used in instances of low CO despite optimization of fluid status (preload), vascular tone (afterload), and HR and rhythm(20). Vasopressors primarily cause vasoconstriction on both arterial and venous peripheral vasculature(34).

Inotropes and vasopressors may have effects on both myocardial contractility and peripheral vasculature. Therefore, vasoactive medication is an umbrella term for inotropes and vasopressors to avoid confusion as a result of the overlap of their effects. Combinations of inotropes and vasopressor medications are used when there is evidence of significantly reduced myocardial contractility and severe hypotension(27).

Vasoactive medications are often used in combination. Table 2 summaries commonly used vasoactive medications. The decision as to what medication to use and the specific dosage varies between each institution, and may depend on the treating medical officers' preference or the availability of certain medications, as well as specific patient presentation.

Table 2 Commonly used vasoactive medications in the ICU

	Medication name	Effects	Indications for use in patients following cardiac surgery
<p style="text-align: center;">Inotrope effects</p>  <p style="text-align: center;">Vasopressor effects</p>	Dobutamine	Increases contractility Increases HR Decrease SVR	Cardiogenic shock
	Dopamine	Increase HR Increase SV Increase SVR	Cardiogenic shock Distributive shock
	Levosimendan	Increase contractility Increases HR Increase SV Vasodilation → decreases SVR	Cardiogenic shock
	Milrinone	Vasodilation → decreases SVR	Cardiogenic shock
	Adrenaline	Vasoconstriction → Increase SVR Increase HR Increase MAP	Hypovolemic shock Cardiogenic shock Distributive shock
	Noradrenaline	Vasoconstriction → Increase SVR Increase MAP	Hypovolemic shock Distributive shock

### *Adrenaline*

Adrenaline, also known as Epinephrine, causes venous and arterial vasoconstriction, resulting in increases in systolic BPs. It also causes increases in HR which, combined with the vasoconstriction, can lead to increased venous return and CO(45). At high doses, Adrenaline increases SVR and consequently MAP and diastolic pressure.

### *Noradrenaline*

Noradrenaline has both inotropic and vasopressor effects(45). Also known as norepinephrine, this medication primarily causes significant vasoconstriction which increases SVR. This leads to increases in diastolic BP, left ventricular afterload, cardiac filling pressures and venous return. As a result of the vasoconstriction, stimulation of baroreceptors occurs, which sense the changes in pressure and counteract these effects. Consequently CO and HR can be reduced or unchanged(46).

### *Dopamine*

Dopamine is a primarily inotropic medication used in ICU. The action of the drug is dose-dependent. At low levels (less than 5 mcg/kg/min), Dopamine causes vasodilation in renal, mesenteric, cerebral and coronary vessels giving a mild increase in CO without affecting arterial BP (45). At more moderate levels of administration (5-10mcg/kg/min) it works to increase stroke volume by elevating HR and enhancing contractility of the myocardium. Additionally, higher levels stimulate alpha-adrenergic receptors which leads to vasoconstriction and increased SVR. This leads to elevated BP and CO (34, 45).

### *Dobutamine*

Dobutamine, is an inotrope that can improve CO by increasing cardiac contractility and HR (20, 45). It decreases SVR. Dobutamine may have adverse effects such as arrhythmias or hypertension, and exacerbate myocardial ischaemia.

### *Milrinone*

Milrinone is a potent pulmonary vasodilator and can improve CO by reducing arterial pressure and left ventricular end-diastolic pressure (28). This vasoactive drug can cause increases in ventricular contractility and HR. The significant vasodilatory effect of Milrinone causes decreased SVR and therefore, Milrinone is often used in combination with Noradrenaline to counteract the vasodilatory response (20, 45).

### *Levosimendan*

Levosimendan has effects similar to Milrinone. It increases myocardial contractility, stroke volume and HR, thereby increasing CO. It also causes vasodilation, which leads to reductions in preload, afterload and SVR. This medication is often used as a rescue therapy in post-surgical heart failure(47). It has been shown to increase CI in patients with reduced left ventricular function post-cardiac surgery, difficulty weaning from cardiopulmonary bypass or during high risk elective cardiac surgery patients peri-operatively(47).

### *The role of vasoactive medications in the patients following cardiac surgery*

Vasoactive medications may be administered in patients following cardiac surgery to prevent or manage haemodynamic issues resulting from the surgery. Many patients following cardiac surgery require temporary administration of vasoactive medications to assist with weaning from the CPB and improving or maintaining CO(48). Gillies and colleagues define low CO as a CI less than 2.4L/min with evidence of organ dysfunction(48). Examples of evidence of organ dysfunction include decreased urine output, elevated lactate levels, the absence of bowel sounds or compromised mentation. There is no consensus regarding the ideal medication to treat low CO following cardiopulmonary bypass(48).

Adrenaline, Noradrenaline, and in some institutions Dopamine, are considered first-line medications post-cardiac surgery to assist with weaning from cardiopulmonary bypass(34).

Noradrenaline and Adrenaline, while effective at increasing myocardial contractility, are commonly used in cases of severe hypotension due to their potent vasoconstrictive abilities which cause immediate effects (46). Gunnicker et al found that in patients with low CO following CABG surgery for coronary artery disease, adrenaline at a dose of 0.03 mcg/kg/min was associated with a significant increase in CI and HR(49).

A systematic review (48) of vasoactive medications after cardiac surgery found that Dopamine at a dose of 2.5 to 5 mcg/kg/min was associated with significant increases in CI and HR. A prospective randomized study conducted by Salomon and colleagues(50) found that at doses of 5 mcg/kg/min, Dopamine and Dobutamine both increased CI without changing HR, MAP or peripheral vascular resistance in patients following CABG. Interestingly, they found that by increasing the dose of Dopamine from 5.0 to 7.5 mcg/kg/min caused significant increases in MAP and peripheral vascular resistance without increasing

CO, whereas by increasing Dobutamine to 7.5 mcg/kg/min caused a further increase in CI with no changes in the other variables.

A prospective observational study conducted by Christakis et al (51) investigated the predictors of a prolonged ICU stay in patients undergoing CABG surgery. Over 100 potential risk factors were collected prospectively in 889 patients who were undergoing CABG surgery. This study was well conducted as it investigated a large number of potential risk variables and involved a large sample size of a specific cohort of patients. They found that an inotrope requirement and low CO were predictors of prolonged intensive care stay, indicating that they were more critical patients.

Ryan and colleagues also conducted an observational study investigating the predictors of outcomes in patients following cardiac surgery with prolonged ICU stay(52). Three-hundred and twenty four patients following cardiac surgery who had been in the ICU for at least 14 days were included. The investigators found that after a 28-day stay in ICU, a requirement for Dopamine or Adrenaline were independent predictors of prolonged hospital stay(52). These studies highlight the implications that vasoactive therapy may have on the patient and the healthcare system.

A systematic review by Gillies et al(48) looked at 26 studies that investigated the effects of Dobutamine in patients following cardiac surgery. The most consistent finding amongst the studies was that Dobutamine caused a dose-related increase in CI. The same systematic review also looked at the effects of Milrinone in this patient population. The main findings were that Milrinone is as effective as Dobutamine, and causes significant increases in CI without tachycardia, and decreases SVR (48).

#### *Available literature surrounding effect of mobilisation and positioning in patients receiving vasoactive medication*

There is emerging data regarding the effect of mobilisation and upright positioning in patients who are receiving vasoactive medication(10, 44, 53-56). Databases searched for the purpose of this literature review include CINAHL, MEDLINE, Ovid, and PEDro.

In an observational study conducted in a general mixed ICU, mobilisation was found to be safe with patients receiving vasoactive medication within the first 24 hours of ICU admission (53). In this study early mobilisation was defined as a series of progressive physical activities able to induce acute physiological responses that commences within 24 hours of ICU admission. This study included 171 patients, 81% of which participated in early mobilisation. Noradrenaline was being administered during 361 occasions of mobilisation at an average dose of 0.10 mcg/kg/min. This study did not clarify what low, moderate or high levels of vasoactive medication were. The investigators found that there were no clinically significant changes in HR, RR or arterial pressure readings after mobilisation, with readings returning to baseline after 15 minutes of ceasing the activity. Eleven (0.8%) adverse events occurred during mobilisation. Two of these were transient hypotension with patients who were receiving Noradrenaline, and this led to no clinically significant consequences. There were no measurements of more invasive haemodynamic readings such as CO, CI or SV, and measurements were only taken at the beginning, end and 15 minutes after mobilisation. This study adds to the growing literature that supports mobility in patients receiving vasoactive medication and highlights the need for further research in this area.

A recent study conducted in 2017 by Corcoran et al (10) looked at the benefits of early mobility in a medical and surgical ICU compared to a historical control group that received usual care. As opposed to the previously discussed study (53), early mobility was defined as during the first 3 days of an ICU admission. The sample sizes were 160 patients in the early mobility group and 123 in the historical control group. There was no statistically significant difference in the presence of vasoactive medication administration between the two groups. This study did not clarify what level of vasoactive medications were being administered.

It was found that the hospital and ICU length of stay was reduced in the early mobility group. In addition, 25.3% of the early mobility group were mobilising independently at ICU discharge compared with 8.1% of the control group. As there were no statistically significant differences in vasoactive medication administration, this study adds to the literature by suggesting that mobilising while receiving vasoactive therapy may be safe and feasible. The incidence of adverse events was not reported in this study.

A retrospective cohort study conducted in a 31 bed Australian tertiary ICU of 119 patients receiving vasoactive therapy was published in early 2018, and looked at factors associated

with mobility and adverse events(54). It was a medical, trauma and surgical ICU. Basic haemodynamic parameters including HR, MAP, RR and SpO<sub>2</sub> were observed. The investigators documented details about the dosage of vasoactive medication, type of exercise, and any adverse events that occurred as a result of mobility. Vasoactive medication dosage was classified in this study and was classified as follows (54):

Medication	Low	Moderate	High
Noradrenaline	<15 mcg/kg/min	15-30 mcg/kg/min	>30 mcg/kg/min
Metaraminol	0.5 mcg/kg/min	1-5 mcg/kg/min	> 5 mcg/kg/min
Vasopressin	<0.03 units/min	0.03 units/min	>0.03 units/min
Adrenaline	<15 mcg/kg/min	15-30 mcg/kg/min	>30 mcg/kg/min
Dobutamine	5 mcg/kg/min	5-10 mcg/kg/min	> 10 mcg/kg/min
Milrinone	0.5 mcg/kg/min	2.5 mcg/kg/min	5 mcg/kg/min
Levosimendan	0.05 mcg/kg/min	0.1 mcg/kg/min	0.2 mcg/kg/min

Dopamine was not administered to the study participants or classified into dosage levels by the investigators. Seventy-seven per cent of patients were classified as being on a low dose of vasoactive medication, 14% medium and 9% high. Patients receiving low dose medication were mobilised 44% of the time, while patients on a moderate dose were mobilised 22% of the time. Only 6% of patients receiving a high dose of vasoactive therapy were mobilised. The rate of an adverse event occurring was 7.8%. Similar to the study conducted by Hickman et al (53), the majority of adverse events involved transient hypotension that led to no clinically significant consequences. An interesting finding was that adverse events were more likely to occur in participants with a lower baseline MAP reading. There was no statistically significant relationship between adverse events and dosage of vasoactive medication. This study suggests that there is scope to safely mobilise patients receiving vasoactive medication. Similar to the previously discussed studies, only indirect parameters such as BP were observed. However, this study adds to the literature by classifying patients according to dosage of vasoactive medication.

Another recent study (56) analysed retrospective data on the effects of passive limb movements on the haemodynamics of sedated, ventilated patients who were receiving vasoactive medication (68%), compared to those receiving no vasoactive medication (32%).



Pre and post passive limb movement HR, MAP, central venous pressure and SpO<sub>2</sub> measurements was analysed. These basic measurements of haemodynamic parameters are similar to what has been measured in the previously discussed studies. In this study, low dose of vasoactive medications were defined as Dopamine <10 mcg/kg/min, Noradrenaline or Adrenaline <0.1 mcg/kg/min. This classification of low Adrenaline and Noradrenaline doses is different to that described by Rebel et al (54).

In the patients who were receiving vasoactive medication, HR and MAP did not change significantly during passive limb exercises, however central venous pressure increased after passive limb exercises, indicating an increase in preload. None of the changes were found to be clinically significant. Adverse events were defined as a change in MAP or HR < or > 20% of baselines values. There was no significant difference in adverse events between groups on inotropes (7.3%) or not receiving inotropes (7.9%). This is an interesting finding that adds to the literature regarding the safety profile surrounding limb movements in patients receiving vasoactive support. It indicates that passive limb movements in these patients is safe and leads to no clinically significant consequences. However passive limb movements would potentially increase preload whilst mobilization can cause a drop in preload and requires adequate compensation available.

Medrinal and colleagues (55) conducted a randomised, single-blind placebo-controlled crossover trial evaluating the haemodynamic and metabolic effects of four rehabilitation techniques in ICU patients. The four techniques that were evaluated were passive range of motion (PROM), passive cycle-ergometry, quadriceps electrical stimulation, and functional electrical stimulation (FES) with cycling. The patients were in supine for the techniques. Each technique was performed for 10 minutes. Cardiac output, RR and MAP was recorded using ultrasound at baseline and every 3 minutes during the exercises. By including CO measurements this study adds to the available literature as the previously described studies only measured basic haemodynamic parameters such as blood pressure and HR.

Thirteen (68%) of the patients were receiving Adrenaline or Noradrenaline at the time of the exercises, however specific dosages were not classified in this study. The investigators found that CO increased significantly after 9 minutes of FES with cycling. This was clinically significant, as the other techniques did not cause a cardiac response to exercise. Furthermore, there were significant increases in HR and MAP with FES cycling. This suggests an

appropriate response to exercise in this patient cohort. No adverse events occurred with exercise, which adds to the literature supporting that active exercise of patients receiving vasoactive medication is safe and feasible. Another interesting finding of this study was that FES cycling caused an increase in HHb (deoxyhaemoglobin and deoxymyoglobin). While this was not found to be statistically significant, it suggests that an increase in muscle metabolism may have occurred due to exercise-induced muscle consumption of oxygen. This was not observed in the other techniques.

A randomised controlled trial conducted by Soeding et al (57) looked at the haemodynamic effects of phenylephrine (chemically related to the vasopressor Adrenaline) in patients being placed in upright positioning during surgery. The control group received saline. Upright positioning (also known as the “beachchair” position, head elevation >75 degrees) is used in patients undergoing shoulder surgery, and is commonly associated with hypotension(57). The investigators continuously measured MAP and HR during upright positioning. Cardiac output and CI were measured before upright positioning, and then 3-5 minutes after adopting this posture. Thirty-four patients were randomised to either the control or intervention group and all were included in the analysis. No patients in the phenylephrine group required intervention, as opposed to 11 patients in the control group. A significant decrease in MAP was observed in the control group with upright positioning, compared to a small reduction in MAP in the phenylephrine group. Cardiac index decreased in both control and intervention groups with upright positioning. Systemic vascular resistance index decreased on upright positioning in the control group however significantly increased with the group who received phenylephrine. The phenylephrine was found to be effective in counteracting hypotension by preventing a decrease in SVR. This paper provides useful insight into the haemodynamic tolerance of patients receiving phenylephrine, a medication that is chemically similar to the vasopressor Adrenaline. It provides an idea of how patients following cardiac surgery who are receiving vasopressors may respond to upright positioning.

## *Available literature surrounding mobilising without vasoactive medication*

### *Haemodynamic responses in healthy individuals*

Van Empel et al looked at the haemodynamic effects of exercise on healthy patients(58). They examined 55 healthy patients with a mean age of 49.6 years. Thirty six per cent of participants were older than 55 years. Right sided heart catheterization was used, a very reliable instrument to measure haemodynamic parameters. Exercise was defined as lower limb cycling ergometry in a supine position. They found that an increased age was associated with decreased CO during exercise. This was thought to be due to age-related diastolic dysfunction(58). Age was negatively associated with CI response to exercise(58). These findings are relevant to the present study, as cardiac surgery tends to occur in older patients.

Jin et al (59) looked at the effect of supine, seated and standing exercise on haemodynamics on normal subjects. The methodology of this study was not clearly explained. Exercise intensity and cessation was not clearly defined. It does, however, describe physiological mechanisms and compensatory action by the body in response to exercise in normal circumstances. They found that BP response varied significantly in different exercise positions, which may be associated with the effect of gravity in conjunction with muscle pump action when transitioning from sitting to standing. Their results indicated that when in standing, the HR increased to maintain sufficient CO. This study additionally calculated SV and CO of their subjects whilst in each position. They explained that the SV in standing decreased about 25% compared to that in the supine. It was suggested that to compensate for the decrease in blood supply, the HR in standing was increased. Consequently, despite the decreased SV in standing, the CO was maintained at a relatively stable level and adequate compensation was achieved. This paper provides an idea of how normal subjects respond to postural challenges in terms of haemodynamics, and this can be compared to the observations and measurements that result from the planned study.

### *Haemodynamic responses in ICU patients*

While research has been outlined that looks at the haemodynamic changes that occur with positioning and mobility in patients receiving vasoactive medication, there is also data available regarding haemodynamic changes in ICU patients who are not dependent on vasoactive medication.

Stiller and colleagues looked at the effects of 69 mobility sessions on the haemodynamic status of 31 critically unwell patients (16). Similar to this study, exercise was defined as moving from supine to sitting on the edge of the bed, standing and marching on the spot. Patients undergoing passive forms of exercise such as a tilt table or hoist transfers were not included. Surgical patients made up 38.7% of the study cohort. Exercise consisted of mainly sitting on the edge of the bed and standing. Only one participant marched on the spot. Basic measurements of haemodynamic parameters were recorded, including absolute HR and HR as a percentage of age-predicted maximum HR, rhythm, SpO<sub>2</sub>, and invasive BP. In addition, clinical observations were made regarding patient appearance that related to tissue perfusion. This included level of consciousness, RR, pallor, cyanosis, clamminess, or signs of pain, discomfort or fatigue. In this study, Stiller and colleagues found that exercise was associated with significant increases in HR, as well as systolic and diastolic BP. A decrease in SpO<sub>2</sub> was observed with exercise in upright positioning however this was not statistically significant. It was postulated that the decrease in SpO<sub>2</sub> was a result of the cardiovascular system being unable to meet the increased oxygen demand resulting from exercise. The authors make mention of the fact that the BP readings may have been overestimated due to potential inaccuracies in calibration. This is important to note and needs to be taken into consideration when interpreting the findings of the study. Three (4.3%) adverse events occurred during sitting or standing involving decreases in SpO<sub>2</sub> that led to no clinically significant consequences. This is a small number and mirrors what has been found in previously outlined studies that report on adverse events resulting from mobility.

An observational study by Zafiropolous et al(60) investigated the effect of postural challenges on haemodynamics of intubated patients after abdominal surgery. While no invasive measurements of haemodynamics were recorded, the subjects' basic haemodynamic measurements of BP and HR during these postural challenges were measured. Subjects were recruited via convenience sampling, and the sample size was seventeen patients. Postural challenges were defined as progressing from supine, sitting over the edge of the bed, standing and then marching on the spot for one minute, as able. BP measurements were obtained in each of these positions. Subjects were stabilized in each of the positions for thirty seconds, after which one minute of data collection began. In each position, arterial lines were re-zeroed before recording the haemodynamic data. Positional challenges were ceased if the following was observed:

- Mean arterial pressure less than 60mmHg or MAP greater than 120mmHg.
- ST segment depression on electrocardiogram with anginal chest pain.
- Respiratory rate greater than 35 breaths per minute.
- SpO<sub>2</sub> less than 90%.

Changes in haemodynamics were observed with upright positioning in these patients, including significant increases in systolic BP, diastolic BP, and MAP when the subjects sat on the edge of the bed, as well as significant increases in HR when the subjects were standing. This paper did not include patients who were inotrope dependent. In addition, the study only included those post-abdominal surgery that were intubated. Patients were included if they were haemodynamically stable (this was not clearly defined) and were not receiving inotropes. This indicates that a gap in the literature may be evident regarding the effects of exercise on inotrope dependent patients. This initial research regarding the effects of upright positioning and exercise on haemodynamics can be progressed by including patients following cardiac surgery requiring inotropes, and additionally, obtaining more haemodynamic measurements.

#### *Summary of findings from previous studies*

Emerging evidence suggests that mobilising patients who are dependent on vasoactive medication is safe(10, 53-55). Mobilising patients receiving vasoactive support has been shown to cause no significant changes in HR, RR or MAP(53). The available literature surrounding the effect of mobilisation and upright positioning in patients who are receiving vasoactive medication does not include more invasive measures of haemodynamics such as CO, SI or SV. In addition, there is no consistent classification of vasoactive medication doses into low, moderate or high amongst the studies, with most studies not classifying the doses at all.

Studies(10, 44, 54-56) have described nil or very small percentages of adverse events that have resulted from mobility or upright positioning in patients receiving vasoactive medication, which have not led to clinically significant consequences. Adverse events when mobilising patients on vasoactive medication have been described as transient hypotension(53, 54) that has not led to clinically detrimental outcomes.

The available literature highlights the need for further research to be conducted regarding haemodynamic changes that occur specifically with upright positioning in patients following cardiac surgery. Data collection should include more comprehensive measurements of haemodynamic stability, such as CO, CI and SV. This is because most previous studies involving vasoactive-dependent ICU patients have only included measurements of HR, RR, MAP and SpO<sub>2</sub>, and it would be useful to gather more information. Furthermore, there is no consistent classification of vasoactive medication doses in the available literature.

## Rationale

Cardiac surgery, such as CABG surgery and heart valve replacement/repairs, are common surgeries that are managed post-operatively in the ICU(61). Mobilisation is prescribed as a part of routine management in patients following cardiac surgery (31, 42, 43). Early mobility of patients following cardiac surgery can reduce length of hospital stay, prevent post-operative complications and functional capacity(42).

It can be difficult to know if it can be safe to begin mobility with patients following cardiac surgery who require vasoactive medication for haemodynamic instability. This includes sitting on the edge of the bed, standing, marching on the spot, or mobilising. Patients who have had cardiac surgery and are receiving vasoactive medication are routinely mobilised post-surgery(43), despite a lack of supporting literature regarding of the effect of exercise on their haemodynamic status.

While some research has looked into the effect of upright positioning and also mobility on the haemodynamics of patients receiving vasoactive medications(53, 54, 62), a lack of consensus remains regarding the safety profile of mobilising patients following cardiac surgery receiving vasoactive medication in ICU(19, 44). A recent evaluation of consensus guidelines found that there is further scope to safely exercise patients receiving vasoactive support and that further research needs to be conducted in this field(44).

## Significance

This study is significant to the ICU community. It is important as it is relevant to the safe delivery of patient care in ICU. Patients who are receiving vasoactive medication following cardiac surgery are routinely mobilised in ICU. As outlined, there is a lack of consensus amongst ICU clinicians (including nursing staff, physiotherapists and medical staff) regarding the safety profile of exercising patients receiving vasoactive medication in the ICU(19). There is minimal previous research into the effect of exercise on haemodynamic parameters of ICU patients receiving vasoactive support(19). There is no available literature regarding the haemodynamic tolerance of exercise in patients following cardiac surgery receiving vasoactive support. This will be the first study to observe haemodynamic parameters of patients following cardiac surgery receiving vasoactive support in the ICU. It will be the first study to measure and describe changes in haemodynamic parameters such as CO, CI and SV that occur with exercise in upright positioning in ICU patients receiving vasoactive medication. As a small prospective cohort study, the results from this research will be used to power future studies in this field.

## Aims and objectives

### *Aims*

This study aimed to determine the effect of upright positioning on the haemodynamic parameters of adult patients following cardiac surgery receiving vasoactive medication in the ICU. In addition, a further aim was to clarify what level of vasoactive medication may indicate safe mobility in patients following cardiac surgery, and to describe whether any defined adverse effects occur as a result of mobility.

### *Objectives*

1. To measure the effect of upright positioning on haemodynamic parameters of post-cardiac surgical patients receiving vasoactive support using the FloTrac-Vigileo system.  
Haemodynamic measurements:

- Cardiac output
- Stroke volume



- Cardiac index
- Heart rate, rhythm and (if applicable) pacing details
- Non-invasive blood pressure
- Mean arterial pressure
- Respiratory rate
- SpO<sub>2</sub>

2. Determine the incidence of adverse events with upright positioning in patients following cardiac surgery receiving vasoactive support

3. To clarify what level of vasoactive medication may indicate safe exercise in upright positioning in patients following cardiac surgery receiving vasoactive support.

## Null Hypotheses

### *Haemodynamic changes with upright positioning*

- Upright positioning will not cause a significant change in CO, CI, SV, MAP, HR, or RR in patients following cardiac surgery receiving vasoactive support.

### *Dose of vasoactive medication*

- There will be no differences in response to upright positioning in patients following cardiac surgery receiving either low or moderate to high doses of vasoactive medication.

### *Adverse events*

- There is no risk of an adverse event occurring due to upright positioning in patients following cardiac surgery receiving vasoactive support.

# Methodology

## *Study design*

This was a prospective, single centre, observational cohort study.

## *Setting*

Data collection occurred at the Prince Charles Hospital (TPCH) cardiac surgical ICU. The Prince Charles Hospital is a specialist cardiothoracic, tertiary institution. Ethical clearance was obtained from TPCH prior to data collection (HREC 17/QPCH/31) (Appendix 1). Ethical clearance was also obtained from Griffith University (GU Ref No: 2017/186) (Appendix 2).

## *Participants*

Informed consent was obtained from participants before elective CABG or valve replacement/repairs, during their in-hospital pre-operative physiotherapy assessment. Consent was gained pre-operatively as it is not possible to predict all patients who will require vasoactive support after cardiac surgery. Patients were subsequently screened post-operatively to determine whether they satisfied the inclusion criteria for the study. If a patient was deemed eligible for the study post-operatively however was not consented pre-operatively, informed consent was gained from the next of kin. Reasons why a patient might not have been consented pre-operatively include:

- Emergency surgery.
- Late arrival to hospital on the day preceding their surgery.

## *Inclusion criteria*

- Over eighteen years of age.
- Undergoing elective CABG surgery or valve repair/replacement at TPCH.
- Receiving low, moderate or high levels of vasoactive support, as defined in following Table 3. The classification of low, moderate and high doses of vasoactive support was developed in consultation with the Medical Director of ICU at TPCH.

Table 3 Classification of vasoactive medication dosage

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

*Exclusion criteria*

- Has undergone major heart surgery in the last 6 months preceding this operation (including CABG, valve replacement/repair).

*Withdrawal criteria*

- Remains mechanically ventilated.
- Exercise in upright positioning is contraindicated due to attachments. This includes the following:
  - Femoral Intra-Aortic Balloon Pump (IABP).
  - Femoral sheath.
- Exercise in upright positioning is contraindicated for reasons such as:
  - Intravenous antihypertensive therapy for a hypertensive emergency.
  - Awaiting emergency pacemaker insertion.
  - Cardiac ischemia as shown by new ECG changes, a rise in troponin levels or chest pain.
  - Known active uncontrolled bleeding.
  - Patient is combative or highly agitated (e.g. Richmond Agitation Sedation Scale >+2).
  - Active management of intracranial hypertension, with intracranial pressure not in desired range.
  - Spinal precautions.
  - Uncontrolled seizures.

### *Sample size*

A small equipment grant to the value of \$4994.00 was obtained by the principal investigator to purchase equipment for this study. The Flotrac sensor cuffs cost \$227 each and are single patient use only. Therefore, only twenty-two Flotrac sensor cuffs were able to be purchased for this study. As a result it was anticipated that 22 subjects would be recruited to this study.

### *Pre-operative data collection process*

Once written informed consent was obtained, participant details were recorded on a password protected Excel spreadsheet. Basic assessment of the participant's pre-surgical physical function then occurred. This included completion of the Short Physical Performance Battery and a self-reported measure of mobility status.

#### *Short Physical Performance Battery*

The Short Physical Performance Battery (SPPB) was used to assess physical function pre surgery. The SPPB is a reliable and valid tool that is used to measure physical performance and functional status in aging population studies. It was first described in 1994 by Guralnik and colleagues(63). It consists of tests of balance, mobility and lower-limb strength(63, 64). It consists of three tasks. This includes a 4m walk test at usual speed, five repetitive chair stands and a balance task of increasingly difficult levels(64). The SPPB takes approximately 10 to 15 minutes to administer and is easy to conduct. No specific training is required to administer the test. It is scored out of 12, where a higher score indicates better balance and mobility. Using this tool allowed the investigators to obtain a measurement and greater understanding of the participant's pre-operative function. The SPPB can be found in Appendix 3(63).

#### *Self-reported mobility status*

Participants were asked about their mobility status. Specifically, they were asked whether or not they could mobilise 100m, and asked whether they could walk with or without a gait aid. This was recorded on the pre-operative data collection sheet, which can be found in Appendix 4.

## *Post-operative data collection process*

### *Screening*

Participants were screened for suitability in ICU on a daily basis by the principal research investigator. This was done by using the database of patients who had consented to the study and screening them for suitability once their surgery had taken place. Screening occurred every morning on weekdays before any mobilisation had taken place. Screening did not occur on weekends or public holidays due to staffing limitations.

### *Timing*

In most cases, data collection occurred in the morning to reduce the influence of potential confounding factors such as fatigue. Occasionally data collection occurred in the afternoon due to unavoidable procedures such as routine nursing and medical procedures and investigations.

### *Equipment*

The following equipment was required to complete data collection:

- Personnel – Three personnel were required to deliver the intervention and record measurements i.e. physiotherapist, physiotherapy assistant, research investigator. The research investigator timed each of the upright positions and ensured consistency of positions between participants. They ensured that the arterial line was at the level of the participant's phlebostatic axis with each change in position to increase accuracy of readings. The research investigator recorded all data pre, during, and post intervention.
- The Flotrac-Vigileo™ system.
- Post-operative data collection form (see Appendix 5).
- Stopwatch that provided readings to 2 decimal points.

### *Pre intervention*

Demographic information was collected prior to data collection. This included age, sex, type of surgery, length of surgery, length of time on bypass, number of grafts, reasons for and dosage of vasoactive medications, and pre-surgical level of function. It was also noted whether the vasoactive medication was being weaned, or if a vasoactive medication had been ceased prior to data collection.

The researcher investigator documented clinical indicators of adequate tissue perfusion prior to commencing upright positioning with the participant. These indicators included:

- Level of consciousness.
- Warmth of peripherals. This was assessed by palpating the temperature of the participant's hands and feet and was documented as being either "warm" or "cool".
- Lactate level, pH, partial pressure of oxygen (pO<sub>2</sub>), partial pressure of carbon dioxide (pCO<sub>2</sub>), and bicarbonate level was obtained from the most recent arterial blood gas reading.
- Supplemental oxygen requirements.
- Average urine output was determined by liaising with the treating nursing staff.
- Presence or absence of bowel sounds. This information was obtained by liaising with the treating medical officer.

In this study, the participant's level of consciousness was a clinical factor that affected whether or not upright positioning and mobilisation occurred. For example, if a patient was combative, agitated, and drowsy or had difficulty following commands, mobilisation did not occur due to safety concerns for the participant and staff. In addition, the decision that mobilisation was suitable was influenced by arterial blood gas results and their supplemental oxygen requirement at rest. For example, if the patient's arterial blood gas results showed signs of poor respiratory reserve (such as a low pO<sub>2</sub>) or if they had a high oxygen requirement (such as an FiO<sub>2</sub> of greater than 0.5) i.e. a low pO<sub>2</sub>/FiO<sub>2</sub> ratio. The other clinical indicators- warmth of peripheries, urine output, bowel sounds and lactate level did not influence whether or not mobilisation occurred in this study.

### *Upright positioning*

Data collection occurred during various upright positions, beginning with the participant in supine. The upright positions were completed in the following order:

1. Supine.
2. High sitting (60 degrees).
3. Sit on the edge of the bed (SOEOB).
4. Standing.

5. Marching on the spot (MOS).
6. SOEOB.
7. High sitting (60 degrees).
8. Supine.

### *Borg Rating of Perceived Exertion*

The participant's perceived level of exertion was measured before beginning the upright positions, during the data collection and 5 minutes after data collection had finished. This was done using the Borg Rating of Perceived Exertion (RPE) Scale(65). It is a scale that ranges from 6-20, and was designed to correlate with healthy subjects HR (60-200bpm). It is based on the equation that  $HR = RPE \times 10$ (65).

For the purpose of this study the modified Borg RPE scale (Appendix 6) was used. It was thought that a scale from 0-10 it might be easier for the post-surgical subjects to read and understand given that the participant's may have been influenced by fatigue, pain, anxiety or confusion in the immediate post-operative phase.

### *Haemodynamic Measurements*

#### *Flotrac-Vigileo™ system*

Specific haemodynamic measurements were obtained using the Flotrac-Vigileo system (4<sup>th</sup> generation). Specific haemodynamic parameters were measured before the upright positions when they were in supine, after one minute of adopting each upright position and 5 minutes after finishing the positions when the participant had returned to supine. The research investigator recorded the CO, CI and SV from the Vigileo 1 minute after each postural challenge.

#### *Bedside monitoring*

HR, rhythm +/- pacing details, systolic and diastolic BP, MAP, RR, and SpO<sub>2</sub> were obtained from the participant's bedside monitor (Phillips™). These measurements were also recorded after one minute of the participant adopting each posture. A stopwatch was used to record the

time. After the participant had adopted the posture for one minute, they were guided into the next position by the physiotherapist and the physiotherapy assistant. If a participant could not adopt one of the positions due to reasons such as pain, anxiety, nausea, discomfort or shortness of breath, then they were moved to the next position in the sequence that was tolerated by the participant. Participants were unable to mobilise away from the bedside as the Flotrac-Vigileo system is not portable, therefore participants were marched on the spot instead.

The level of physical assistance that the participant required to complete the various upright positions was documented as 1 or 2-person assist. It was also documented whether a walking aid was utilized for standing or MOS. Reasons for ceasing a position were documented.

#### *Adverse events*

Adverse cardiovascular or haemodynamic effects were defined as follows (66):

- Alteration in BP  $>$  or  $<20\%$  of resting values which necessitated stopping intervention or required remedial intervention (e.g. inotropes).
- Alteration in HR  $>$  or  $<20\%$  of resting values which necessitated stopping intervention or required remedial intervention.
- New arrhythmia (e.g. atrial fibrillation, increased number of ectopic beats per minute, ST depression or elevation, increased magnitude of ST depression, bigeminy, trigeminy, ventricular tachycardia, ventricular fibrillation, asystole).
- Desaturation of SpO<sub>2</sub>  $>10\%$  of baseline levels or a figure that necessitated stopping intervention or required remedial intervention.
- Agitation resulting in detachment of equipment or lines or requiring increase sedation.

Other adverse events, complications, or issues with the upright positioning that were not listed were documented in the comments sections of the data collection form.



### *Statistical analysis*

Statistical analyses were performed using SPSS 25 (IBM Corporation, Somers, NY, USA). Participants were categorised into either low or moderate/high level of vasoactive medication dose (see Table 3).

Tests for normality were conducted and appropriate statistical tests were used based on the outcome of these tests. On initial normality tests, the diastolic BP variable was not normally distributed. Kurtosis values in the positions of sitting on the edge of the bed and standing were greater than three. The data set was scrutinised and two outlier measurements in these two positions was evident. Participant 18 had an outlier diastolic BP measurement when sitting on the edge of the bed (112mmHg). Participant 12 had an outlier value in the standing position (115mmHg). When these two outlier values were removed, normality was assumed for this variable. Therefore, for the purpose of the statistical analyses, diastolic BP was treated as a normally distributed variable. Non-normally distributed variables included SV, systolic BP and SpO<sub>2</sub>.

#### *Normally distributed variables- statistical tests*

A one-way repeated measures ANOVA was used to identify and compare any significant changes in normally distributed haemodynamic variables that occurred with upright positioning. The SPSS analysis did not include subjects with missing data and as a result not all twenty subjects were included in the one-way repeated measures ANOVA outputs.

Initially it was planned to include all 9 upright positions in the analyses. During the data collection phase, it was evident that certain positions were difficult for some participants to adopt and/or tolerate, and as such there was missing data from these positions. One position that was difficult for patients to adopt included returning to high sitting after sitting on the edge of the bed. This was due to participants sitting too close to the end of the bed after marching on the spot, and when being guided back into high sitting they were too low down the bed to achieve the desired 60 degrees of head up. Lying supine for 5 minutes after upright positioning was a position that was also not tolerated well by some participants. They reported discomfort, shortness of breath, and pain at their sternal wound. Therefore, only 5 positions were included in the one-way repeated measures ANOVA. The positions were:

supine, SOEOB, standing, MOS and one minute after return to supine. These positions were chosen as they had the least amount of missing data and included a range of upright positions.

A repeated measures between-within ANOVA was used to identify if there was any significant difference in changes in haemodynamic variable measurements between subjects receiving low or mod/high vasoactive doses.

*Non-normally distributed variables- statistical tests*

The Friedman test was used to identify and compare any significant changes in non-normally distributed haemodynamic variables that occurred with upright positioning. The same 5 upright positions used for the normally distributed variables statistical analyses were included in these analyses, these being supine, SOEOB, standing, MOS and one minute after return to supine.

## Results

### *Participant characteristics*

Twenty participants were studied, 16 (80%) male. The mean age was 66.0 (SD 10.6) years. The mean height of participants was 173.25cm (SD 8.27), and the mean weight was 84.7kg (SD 24.7).

It was originally planned to study twenty-two participants, as this was how many Flotrac sensor cuffs were available at the start of data collection. Two Flotrac sensor cuffs had to be discarded. This was due to one patient withdrawing their consent and another participant having their Noradrenaline ceased, in both cases after the Flotrac sensor cuff had been opened and attached to their arterial line.

### *Pre-surgical details*

#### *Mobility status*

The majority of participants (85%) self-reported that they were able to mobilise greater than 100 metres prior to surgery. Additionally, 90% of participants were able to mobilise independently without a gait aid; the remaining 10% reporting that they needed a gait aid (4 wheeled-walker or single point stick) to mobilise independently. None of the participants required assistance to mobilise prior to surgery.

#### *Short Physical Performance Battery Score*

Sixteen of the 20 (60%) participants had their SPPB score measured during the pre-operative consent process. Of these participants, 2 (12.5%) scored 8/12, 2 (12.5%) scored 10/12, 1 (6.25%) scored 11/12 and the remaining 11 (68.75%) scored 12/12. It was not documented why some participants did not have their SPPB measured, however reasons could potentially include that they were too medically unwell during the pre-operative assessment to complete the physical assessment, therapist time constraints, or the participant was attending another pre-operative procedure or assessment (for example, chest x-ray or pre-operative discussion with the anaesthetics or surgical team).

### *Ejection fraction*

Sixteen of the 20 participants had pre-operative echocardiogram results available. The mean pre-operative ejection fraction was 47.3% (SD 18.7).

### *Surgery details and indications*

Eleven participants underwent CABG (55%), seven had valve replacement or repairs (35%), one participant had a CABG with two valve replacements (5%), and one participant had an aortic root replacements (5%). The average mechanical ventilation time in ICU was 619.3 minutes (SD 342.08), average CPB time 83.89 minutes (SD 41.95), and mean cross-clamp time was 57.68 minutes (SD 30.71). The majority of participants (75%) were Day 1 post surgery. Two participants (10%) were Day 2 post surgery, another two participants (10%) Day 3 post surgery and one participant (5%) was Day 4 post surgery.

### *Type of surgery*

#### *Coronary Artery Bypass Graft Surgery*

Eleven participants (55%) had CABG surgery. The majority of participants who had undergone CABG surgery had two or three grafts harvested. The most common grafts used were the internal mammary artery and the saphenous vein. The radial artery was used on two occasions.

#### *Valve replacement*

Five participants (25%) solely underwent valve replacement surgery. Three participants had aortic valve replacements, and two participants had a mitral valve replacement.

#### *Valve repair*

Two participants (10%) had valve repairs. One participant (5%) had a mitral valve repair, the other participant (5%) had a mitral and tricuspid valve repair.

### *Coronary artery bypass graft surgery with valve replacements*

One participant (5%) had CABG surgery in combination with aortic and mitral valve replacements.

### *Aortic root replacement*

One participant (5%) underwent aortic root replacement surgery.

### *Indications for surgery*

As can be seen in the graph below, the four most common reasons for cardiac surgery were STEMI, NSTEMI, aortic stenosis and mitral valve regurgitation.

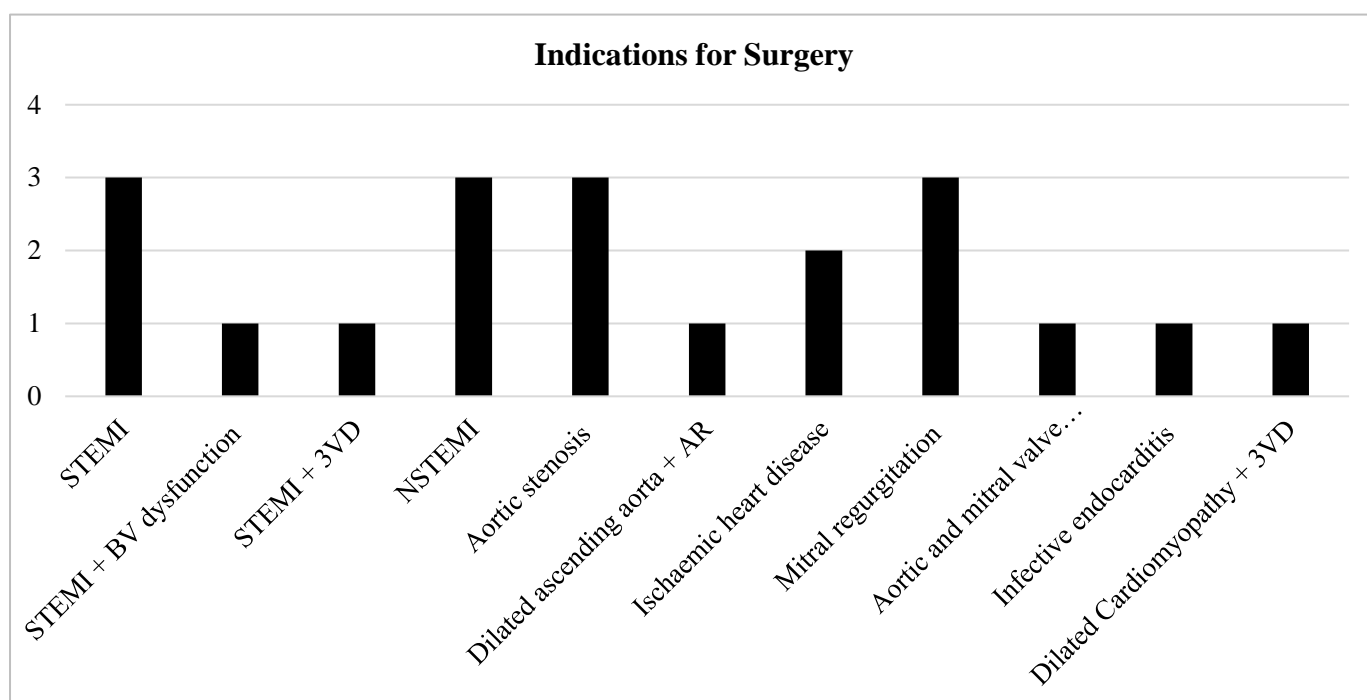


Figure 2 Indications for cardiac surgery amongst the study subjects

(STEMI= ST-Elevation Myocardial Infarction, NSTEMI= Non ST-Elevation Myocardial Infarction, 3VD= Three Vessel Disease, AR= Aortic Regurgitation)

### *Peri operative surgical complications*

The occurrence of perioperative surgical complications was small. One (5%) participant went into cardiac arrest when being weaned from the CPB machine. This was successfully managed by the surgical team in theatre.

### *Post operative surgical complications*

Two (10%) of participants experienced post-operative surgical complications as defined by the medical team. One complication was the discovery of a small apical pneumothorax. The other complication was a surgical reopen of the sternotomy to investigate the cause of a high mediastinal drain output. Both participants were managed successfully by the treating medical team prior to data collection occurring.

### *Vasoactive medication details*

Details of participants and their requirement for and dosage of vasoactive medication are summarised in Appendix 7.

Further details regarding administration of vasoactive medication among the participants is summarised below in Table 4. Among the participants, sixteen (80%) were receiving one medication at the time of data collection. Three (15%) participants were receiving two medications and one (5%) participant was receiving four medications.

Every participant was receiving Dopamine at the time of data collection. As can be seen in Table 4, the average dosage of Dopamine administered among the subjects was 3.89 mcg/kg/min (SD 1.12). Four of these participants were receiving one or more other vasoactive medication in combination with Dopamine. Two participants were receiving Adrenaline, one was receiving Noradrenaline, and one participant was receiving Adrenaline, Noradrenaline as well as Vasopressin.

Table 4 Average doses of vasoactive medications delivered to participants

Vasoactive medication	Number of subjects receiving medication	Mean dose (mcg/kg/min)
Dopamine	20	3.89 (SD 1.12)
Noradrenaline	2	1.03 (SD 1.38)
Adrenaline	3	0.06 (SD.05)
Vasopressin	1	0.02

Six (30%) of participants were classified as receiving low dose of vasoactive medication at the time of data collection, with the remaining 14 (70%) being classified as receiving a moderate to high dose.

*Indications for vasoactive medication*

Seventy-five per cent were receiving vasoactive medication for “BP support” and hypotension. Two participants were receiving vasoactive therapy as a result of both hypotension and left ventricular dysfunction, one participant had existing left ventricular dysfunction. One participant experienced cardiogenic and vasodilatory shock. Finally, one participant was receiving vasoactive medication as a result of right ventricular dysfunction after their surgery.

*Weaning of vasoactive medications at the time of data collection*

Among the participants, just over half (55%) were not being weaned from their vasoactive medication at the time of data collection. The remaining 45% were being weaned in ranges varying from 0.5ml-4ml every 1-6 hours. In six participants, Noradrenaline had been weaned off less than 4 hours prior to data collection.

*Clinical observations prior to data collection*

Clinical indicators of tissue perfusion were documented prior to data collection. This included their level of consciousness, lactate level, fraction of inspired oxygen (FiO<sub>2</sub>)

requirement, average urine output, temperature of peripheries and the presence/absence of bowel sounds. The findings are summarised in Table 5.

Table 5 Observed clinical indicators prior to data collection

Clinical Indicator	N (%)
Lactate level	N=20
<1.0	6 (30%)
1.0-2.0	9 (45%)
>2.0	5 (25%)
Oxygen requirement (FiO <sub>2</sub> )	N=20
0.28	7 (35%)
0.30	1 (5%)
0.32	4 (20%)
0.34	6 (30%)
0.40	1 (5%)
0.50	1 (5%)
Average urine output (ml/hour)	N=19
<60	6 (31.58%)
60-80	4 (21.05%)
80-100	5 (26.32%)
100-150	1 (5.26%)
>200	3 (15.79%)
Peripheries	N=20
Warm	16 (80%)
Cool	4 (20%)
Bowel sounds	N=20
Present	19 (95%)
Absent	1 (5%)

All participants had a Glasgow Coma Scale (GCS) of 15 indicating that they were appropriate and able to follow commands. The majority of participants had a lactate level ranging between 1.0-2.0 mmol/hour and an oxygen requirement ranging from a FiO<sub>2</sub> of 0.28 to 0.34.



Bowel sounds were present in 95% of participants prior to the intervention and 80% had warm peripherals. Average urine output per hour varied amongst the participants, however the majority had an average urine output of less than 100mls/hour.

#### *Data collection*

Data collection occurred in the morning in 95% of cases. Data collection corresponded with the participant's first mobility in 16 (80%) instances. The majority (60%) of participants required the assistance of two people to perform the upright positioning. No participants required the use of a walking aid to perform standing or marching on the spot. The average duration of intervention was 18.1 (5.36) minutes. Rate of perceived exertion was recorded pre mobility, during mobility, and 5 minutes post mobility. The median RPE pre mobility was 0.5 (3.0), during mobility was 4.5 (2.5), and 5 minutes post mobility was 3.0 (3.25).

#### *Haemodynamic observations in upright positioning using the Flotrac-Vigileo system*

Haemodynamic measurements of key importance to this study are reported in this results section, including CO, MAP, and diastolic BP. Additional haemodynamic measurements of CI, SV, SpO<sub>2</sub>, HR and RR can be found in the Appendix (8-11) section of this document.

#### *Cardiac output in upright positioning*

A one- way between-within repeated measures ANOVA was conducted to compare CO measurements of participants receiving low and moderate to high doses of vasoactive medication, in each of the 5 positions. The means and standard deviation are presented in Table 6. There was no statistically significant changes in CO measures with upright positioning, Wilks' Lambda=0.748, F (4,8)=0.675, p=0.628, multivariate partial eta squared=0.252.

It was observed that CO tended to decrease with upright positioning in participants receiving low dose vasoactive medications. The mean CO in these participants was lower than baseline levels after completing upright positioning. However, only 3 participants were classified as receiving low dose vasoactive medication and therefore this is clinically insignificant. While there were no statistically significant changes observed, changes in CO was observed at an

individual level in some cases. These cases are detailed in Table 7 and are further highlighted in Figure 3. It can be seen that Subject 5 (red) had increase in CO from standing to marching on the spot. Subject 11 (green) had a decrease in CO from supine to high sitting, and an increase when transitioned to standing. Finally, Subject 17 (blue) had a decrease when transitioning from sitting on the edge of the bed to standing, and again when transitioning from marching on the spot to sitting on the edge of the bed again. All of these individual changes that were observed were transient and recovered when transitioned to the following position. These changes did not necessitate stopping data collection.

Table 6 Descriptive statistics for CO measurements in 5 upright positions

Position	Vasoactive medication dose	N	Mean	Standard deviation
Supine	Low	3	7.7	1.1
	Mod/High	10	6.2	1.7
SOEOB	Low	3	7.3	0.7
	Mod/High	10	6.5	1.9
Standing	Low	3	6.6	1.8
	Mod/High	10	6.4	1.7
MOS	Low	3	6.4	0.9
	Mod/High	10	6.9	2.3
Supine	Low	3	5.9	2.5
	Mod/High	10	6.5	1.4

Table 7 Examples of CO changes at an individual level

Subject number	Cardiac output (L/min)						
	Baseline (supine)	High sitting	SOEOB	Standing	MOS	SOEOB	Supine 1min
5	6.4	6.9	8.2	7.3	11.6	9.6	9.2
11	8.7	4.9	6.5	8.4	7.3	7.2	-
17	6.5	6.4	7.5	4.9	5.4	3.3	-

*Between subjects effects*

There was no significant difference in CO measurements over time in each of the 5 positions in participants receiving low or moderate/high vasoactive medication dosage ( $p= 0.797$ ).

*Interaction effects*

There was no statistically significant interaction effect for time\*dose (low and mod/high vasoactive medication), Wilks' Lambda=0.662,  $p=0.453$ .

Figure 3 illustrates the changes observed in CO measurements seen with each upright position. Examples of changes at an individual level that have been described and are detailed in Table 7 are highlighted in Figure 3.

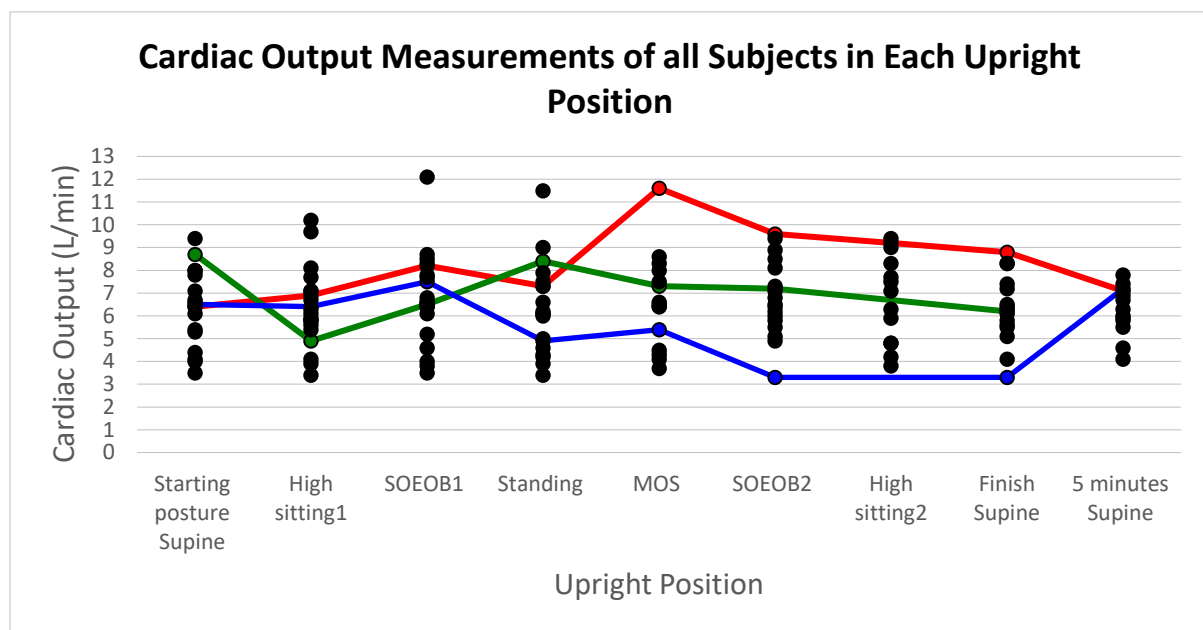


Figure 3 Cardiac output measurements of all subjects in each upright position

*Mean arterial pressure in upright positioning*

A one- way between-within repeated measures ANOVA was conducted to compare MAP measurements of participants receiving low and moderate to high doses of vasoactive medication, in each of the 5 positions. The means and standard deviation are presented in Table 8. There was a statistically significant increase in MAP with upright positioning, Wilks' Lambda=0.216,  $F(4,7)=6.355$ ,  $p=0.018$ , multivariate partial eta squared=0.784. The

mean MAP measurements when participants had returned to supine were greater than baseline levels.

Table 8 Descriptive statistics for MAP measurements in 5 upright positions

Position	Vasoactive medication dose	N	Mean	Standard deviation
Supine	Low	3	65.3	6.0
	Mod/High	9	69.3	9.1
SOEOB	Low	3	68.3	6.0
	Mod/High	9	74.7	12.9
Standing	Low	3	71.7	20.0
	Mod/High	9	69.7	9.1
MOS	Low	3	75.7	16.8
	Mod/High	9	70.3	11.8
Supine	Low	3	73.7	3.2
	Mod/High	9	76.8	8.2

*Between subjects effects*

There was no significant difference in MAP measurements in each of the 5 positions between participants receiving low or moderate/high vasoactive medication dosage ( $p=0.831$ ).

*Interaction effects*

There was no statistically significant interaction effect of MAP between the two groups of low and mod/high vasoactive medication doses, Wilks' Lambda=0.642,  $p=0.477$ . There was no difference in change in MAP measurements between the two groups over time in upright positions.

*Diastolic blood pressure in upright positioning*

A one- way between-within repeated measures ANOVA was conducted to compare diastolic BP measurements of participants receiving low and moderate to high doses of vasoactive medication, in each of the 5 positions. The means and standard deviation are presented in Table 9. There was a statistically significant increase in diastolic BP with upright positioning, Wilks' Lambda=0.170,  $F(4,7)=8.522$   $p=0.008$ , multivariate partial eta squared=0.830.

Table 9 Descriptive statistics for diastolic BP measurements in 5 upright positions

Position	Vasoactive medication dose	N	Mean	Standard deviation
Supine	Low	3	45.3	7.6
	Mod/High	9	52.3	8.5
SOEOB	Low	3	50.3	7.2
	Mod/High	9	56.4	11.0
Standing	Low	3	56.7	13.7
	Mod/High	9	54.3	9.9
MOS	Low	3	58.0	4.4
	Mod/High	9	52.3	11.7
Supine	Low	3	58.7	3.1
	Mod/High	9	57.7	8.9

*Between subjects effects*

There was no significant difference in diastolic BP measurements in each of the 5 positions between participants receiving low or moderate/high vasoactive medication dosage ( $p=0.883$ ).

*Interaction effects*

There was no statistically significant interaction effect of diastolic BP between the two groups of low and mod/high vasoactive medication doses, Wilks' Lambda=0.363,  $p=0.093$ .

There was no difference in change of diastolic BP measurements between the two groups over time in upright positions.

### *Adverse events*

It was originally planned to investigate any associations between dose of vasoactive medication and risk of adverse event, however due to the low number of adverse events the results are descriptive.

One adverse event occurred with a participant in upright positioning. This event was categorised(67) as an alteration in BP less than 20% of resting values which necessitated stopping intervention. The participant was a 57 year old female Day 1 post CABG x 3 for STEMI and three vessel disease. It was their first attempt at upright positioning. The pre-operative EF was 67%, SPPB score was 10/12 and the participant was independently mobile. They underwent a CPB time of 47 minutes and a cross-clamp time of 38 minutes. The participant had no peri or post-operative complications. They were mechanically ventilated for 685 minutes. Time from extubation until data collection was 340 minutes.

With regards to vasoactive medication details, this participant was receiving a low dose of Dopamine and this was weaning 4mls every hour at the time of data collection. The indication for Dopamine administration was for hypotension.

This participant's indicators of tissue perfusion before commencing upright positioning were as follows:

FiO <sub>2</sub>	0.28
Peripheries	Cool
Lactate	1.5 mmol/hour
GCS	15
Urine output	50ml/hour
Bowel sounds	Yes

The only clinical indicator that may have indicated impaired haemodynamic parameters was that the participant's peripheries were cool. The participant was in sinus rhythm (95bpm),

was not being paced. The participant's RPE was 9/10 pre-upright positioning however the participant did not show signs of physical exertion, excessive pain or fatigue pre-intervention. This high reporting of RPE is abnormal, may be attributed to the participant's misinterpretation of the RPE scale.

The participant was unable to march on the report due to dizziness. A 50ml bleed from the wound drain was observed with standing. From the starting position to standing, the participant's systolic and diastolic BP readings decreased, as did measurements of SV, CI and MAP. Heart rate and RR increased. Cardiac output measurements were stable. There was no change to the participant's rhythm or SpO<sub>2</sub> during upright positioning.

As the participant was unable to complete marching on the spot, they therefore skipped this position and was moved to the next position in the sequence, which was sitting on the edge of the bed. From this point on there were no further significant decreases in CI, MAP or systolic and diastolic BP measurements and the participant's dizziness resolved. The participant was able to complete the remaining positions without any symptoms. This was the only adverse event that occurred amongst the participants in upright positioning. The changes in haemodynamic parameters were transient, and led to no clinically significant consequences.

## Discussion

This study aimed to determine the effect of upright positioning on the haemodynamic parameters of adult patients following cardiac surgery receiving vasoactive medication. Upright positioning caused statistically significant increases in MAP and diastolic BP, which rejects the null hypothesis of this study in relation to these two variables. This mirrors findings from Medrinal and colleagues(55), who found that MAP increased significantly during supine cycling in patients receiving vasoactive medication. While their subjects were supine, the results also complement the finding from our study and may serve to highlight the impact the muscle pump from leg activity may have in maintaining and increasing MAP. Hickman et al (53) found that upright positioning caused no significant changes in arterial pressure readings in patients receiving vasoactive medication. However, their study cohort consisted of patients who were receiving Noradrenaline, as opposed to this study where the majority were receiving Dopamine. Previous studies that have looked at the effect of upright positioning in ICU patients who were not receiving vasoactive medication (16, 60) have also found significant increases in arterial pressure readings, which reflects the results of this study.

In this study, there were no statistically significant changes observed with CO in upright positioning, and therefore the null hypothesis has been accepted when considering this variable. Changes were observed in some subjects at an individual level; however, these changes were transient and therefore not clinically significant. Previous studies involving upright positioning in patients who are receiving vasoactive medication have not reported on the effect on CO. Therefore this study adds preliminary information to the limited literature available on this subject. Due to the heterogeneous nature of this study cohort, it would be interesting to investigate the effect of upright positioning on cardiac output in a larger cohort.

A normal response to exercise is an increase in CO that is achieved by increasing HR and SV (68). As seen in Appendix 9, an increase in HR was observed with upright positioning. In addition, patients classified as receiving low doses of vasoactive medication, a downward trend of CO and CI (see Appendix 8) with upright positioning was measured. Mean CO and CI measurements were in fact lower after upright positioning had occurred and the participant had returned to supine. This suggests an inadequacy of cardiac contractility during upright



positioning. This may be due to many reasons. Poor contractility of the heart can occur after surgery due to myocardial ischaemia during cross-clamping or cardioplegia induced myocardial dysfunction(27). There is a possibility that some participants had sustained myocardial injury as a result of surgery. This may have affected the heart's ability to pump to achieve adequate SV and maintain CO when placed under stress. Diastolic dysfunction may also be responsible for the lack of increase in CO, SV and CI measurements observed. The average age of the participants was 65.9 (SD 10.6) years. Age-related diastolic dysfunction has been observed in healthy individuals during exercise(58). Only 3 participants were classified as being in the low dose group and this should be taken into consideration when interpreting these results. Furthermore, it is likely that the one participant who experienced transient hypotension during upright positioning and was receiving low dose Dopamine contributed to the observed downward trend amongst the low dose participants. Therefore this downward trend of CO and CI is clinically insignificant.

The fact that there was a statistically significant increase in MAP and diastolic BP with upright positioning however no increase CO and SV may indicate that the patients were receiving the vasoconstrictive effects of the vasoactive medications however contractility of the heart remained suboptimal. Another explanation for this could be sympathetic vasoconstriction secondary to a transient drop in preload and BP that occurred too quickly to be picked up by the FloTrac-Vigileo system.

It is important to note that haemodynamic responses are complex and may vary between patients. This is evident when considering at an individual level the differing pathophysiology and responses in haemodynamic parameters with upright positioning in this heterogenous population. It must be considered that an increase or decrease in one haemodynamic parameter at one point in time does not necessarily reflect exact haemodynamic responses that a patient may be having to upright positioning. Overall trends and patterns of changes must be observed to more readily understand the haemodynamic responses of the patient. It would be useful to perform this study in a larger population with more extensive monitoring.

A further aim of this study was to clarify what level of vasoactive medication may indicate safe mobility in patients following cardiac surgery. Previous studies have not looked into differences in response to upright positioning depending on dose of vasoactive medication. In

this study, between-subject and interaction effects derived from the ANOVA that were conducted found that there was no difference in magnitude of change with MAP, CO and diastolic BP over time and in different upright positions depending on whether the subjects were receiving low or moderate to high doses of vasoactive medication, accepting the null hypothesis.

This study also aimed to describe whether any defined adverse effects occurred as a result of upright positioning. Only one adverse event occurred in this study. This low rate of adverse events associated with upright positioning mirrors findings from previous studies (16, 53, 54), and adds to the available literature that upright positioning of ICU patients who are receiving vasoactive medication is safe. Rebel et al(54) reported a low rate of adverse events associated with mobility in their patient cohort who were receiving vasoactive medication. The majority of these adverse events were described as transient hypotension that led to no clinically significant consequences, which reflects the adverse event observed in this study. Transient hypotension was also an adverse event observed in the study conducted by Hickman et al(53), whose patients were receiving Noradrenaline. This led to no clinically significant consequences. In this study, the risk of an adverse event occurring when mobilising a patient receiving vasoactive medication was low, rejecting the null hypothesis.

The findings of this study are pertinent to clinicians who mobilise patients following cardiac surgery who are receiving vasoactive support. The safety of mobilising patients receiving vasoactive medication remains a point of contention among the ICU community(19). As outlined in the literature review, classification of vasoactive medication dosages amongst study participants rarely occurs, and is inconsistent and varied due to differing institutions and type of patient cohort. Genc et al (56) included participants they classified as all receiving a low dose of vasoactive medication, whereas Rebel et al (54) had a study cohort consisting of 77% low dose, 14% moderate dose, and 9% high dose. In these studies, Dopamine was not classified into dosages, and therefore it may be unlikely that the classification systems used are pertinent to patients following cardiac surgery. All of the participants in this study were receiving Dopamine. This study classified patients according to vasoactive medication dosage in consultation with the medical director of TPCU ICU and due to the varied nature of previous studies classifications these were not utilised. In addition, it is important to consider that each institution has varied patient cohorts and therefore their requirements for vasoactive medication may be different to patients following cardiac

surgery. This study's participants were classified into low dose, or moderate to high dose of vasoactive medication. The study group consisted of 30% receiving a low dose of vasoactive medication, with the remaining 70% receiving a moderate to high dose. This is different to the previously mentioned studies (54, 56), where the majority of their study participants were classified (by their criteria) as receiving low doses.

## Strengths and Limitations

A major strength of this study is that it occurred in a cardiothoracic, tertiary ICU and therefore it has occurred in a clinical setting. Early mobility is encouraged in the unit and it is well staffed and equipped, which enabled ease of data collection. However, the fact that this study occurred in a single ICU with a specific cohort of patients limits the generalisation of the findings to other ICUs. Extrapolation of the findings of this study should be limited to similar ICUs with similar patients and mobility practices. While not intentional, this study primarily investigated the effects of Dopamine due to the practices and patient cohort in the unit. Therefore, generalisations of findings should be limited to patients receiving Dopamine in the cardiac surgical setting.

A limitation of the study is the small sample size. However, the results could be used to power future studies in this field. Additionally, not all participants could tolerate each of the positions, which reduced the amount of data collected in each position. Data collection corresponded with the participant's first mobility in 16 (80%) instances. This may have influenced patient performance with upright positioning. Patients may have experienced less anxiety, pain and/or fatigue with upright positioning if they had already mobilised previously that day or the day before. It should be noted that human error and/or inaccurate readings from the Flotrac-Vigileo system may have occurred and this may have contributed to some of the outlier data points.

It would have been worthwhile to measure changes in SVR, as this appears to be a key measure of haemodynamic stability. Obtaining SVR measurements throughout upright positioning in these patients would have provide information about whether vasoconstriction had occurred. This would have provided more insight about the haemodynamic response to upright positioning in this patient cohort. Furthermore, stroke volume variation could not be measured in these patients as they were not ventilated. Stroke volume variation is the

difference in minimal and maximal SV. It is a naturally occurring phenomenon, however measurements of SV variation are not accurate unless a patient is receiving full mechanical ventilation at least 8mls/kg/minute. Additionally detailed pathophysiology as to why patients required vasoactive support was not available in the patient notes and it was unknown as to whether the hypotension was due to cardiogenic, hypovolemic or distributive shock. Knowledge of this detail would have enabled a more detailed explanation as to individual changes.

## Future directions

Given the wide variety of uses of vasoactive medication and the interest that early mobility is gaining, future studies should include a range of patient presentations. It would be worthwhile including septic patients, or non-surgical cardiac patients such as those with chronic heart failure. Future studies of this nature should aim to include a much larger sample size, and investigate the effects of upright positioning as well as marching on the spot for longer duration and/or different intensities over multiple days. It would also be interesting to observe the effects of standing or mobilising for longer periods of time. In this study, participants only stood and marched on the spot for approximately 2-3 minutes. Perhaps different changes in haemodynamics could be observed if haemodynamic measurements, such as SVR, were made after 5 minutes of standing or marching on the spot. Finally, it would be informative to examine the effects of other commonly used vasoactive medications on haemodynamic parameters during exercise, such as Noradrenaline or Adrenaline. Given that early exercise is being performed with more critically unwell patients, future research should also investigate the effects of novel in-bed exercise such as lower-limb cycle ergometry or upper limb exercises on haemodynamics.

## Conclusion

This study aimed to determine the effect of upright positioning on the haemodynamic parameters of adult patients following cardiac surgery receiving vasoactive medication in the ICU. A further aim was to clarify what level of vasoactive medication may indicate safe mobility in patients following cardiac surgery, and to describe whether any defined adverse effects occur as a result of mobility.

Significant increases in MAP and diastolic BP were observed. There were no statistically significant changes to CO, CI, SV, systolic BP, HR or SpO<sub>2</sub>. However, changes in CO were observed at an individual level. There was no difference in magnitude of change with MAP, CO and diastolic BP over time and in different upright positions depending on the dose of vasoactive medication. The risk of an adverse event was low, which mirrors findings from previous studies in the field.

The findings from this study adds to the small body of literature regarding haemodynamic responses to upright positioning in patients receiving vasoactive medication, and will be of interest to the ICU community. Further research into this area is needed to continue building on understanding the safety profile of exercising ICU patients receiving vasoactive support.

## Appendix 1: Ethical approval TPCCH

Enquiries to: [ResearchTPCH@health.qld.gov.au](mailto:ResearchTPCH@health.qld.gov.au)  
Office Ph: (07) 3139 4198  
(07) 3139 4500  
Our Ref: HREC Final Approval



9 March 2017

**The Prince Charles Hospital  
Human Research Ethics Committee**  
The Prince Charles Hospital  
Building 14  
Rode Road, Chermide QLD 4032

Ms Jemima Boyd  
Department of Physiotherapist  
The Prince Charles Hospital

Dear Ms Boyd

**Re: HREC/17/QPCH/31: Haemodynamic tolerance of cardiac surgical patients with inotropic dependence in upright positioning.**

Thank you for submitting the requested documents for the above project for further review which was received on 8 March 2017. This project was considered by The Prince Charles Hospital Human Research Ethics Committee (HREC) (EC00168).

This HREC is constituted and operates in accordance with the National Health and Medical Research Council's (NHMRC) *National Statement on Ethical Conduct in Human Research (2007)*, *NHMRC and Universities Australia Australian Code for the Responsible Conduct of Research (2007)* and the *CPMP/ICH Note for Guidance on Good Clinical Practice*.

I am pleased to advise that this proposal meets the requirements of the National Statement (NS 5.1.30) and that The Prince Charles Hospital Human Research Ethics Committee has granted final approval of this research project. The documents reviewed and approved for the above mentioned project include:

Document	Version	Date
Application	AU/1/731B211	
Protocol	1	7 December 2017
Participant Information Sheet and Consent Form	4	8 March 2017
Participant Information Sheet and Consent Form: Person Responsible	4	8 March 2017
Response to Request for further information		7 March 2017

This information will be tabled at the next meeting on 23 March 2017 for noting.

Please note the following conditions of approval:

1. The Principal Investigator will immediately report anything which might warrant review of ethical approval of the project in the specified format, including:
  - a. Unforeseen events that might affect continued ethical acceptability of the project.

<b>Office</b> Research, Ethics & Governance Office The Prince Charles Hospital	<b>Postal</b> Building 14 Rode Road, Chermide Q 4032	<b>Phone</b> (07) 3139 4500 (07) 3139 4198
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**Your Human Ethics Protocol 2017/186 has been Fully approved**

**rims@griffith.edu.au**

3/23/17

to me, james.walsh, j.paratz, research-ethics, k.madison

**GRIFFITH UNIVERSITY HUMAN RESEARCH ETHICS COMMITTEE**

I write in relation to your application for ethical clearance for your project "Haemodynamic tolerance of cardiac surgical patients with inotropic dependence in upright positioning." (GU Ref No: 2017/186). The research ethics reviewers resolved to grant your application a clearance status of "Fully Approved".

This is to confirm receipt of the remaining required information, assurances or amendments to this protocol.

Consequently, I reconfirm my earlier advice that you are authorised to immediately commence this research on this basis.

The standard conditions of approval attached to our previous correspondence about this protocol continue to apply.

Regards

Kim Madison | Human Research Ethics

Office for Research

Griffith University | Nathan | QLD 4111 | Level 0, Bray Centre (N54)

T +61 7 373 58043 | email [k.madison@griffith.edu.au](mailto:k.madison@griffith.edu.au)

### Appendix 3: The Short Physical Performance Battery

**Name:**

**DOB:**

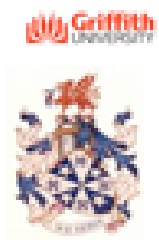
**UR:**

**Short Physical Performance Battery**

<b>Balance</b>  <b>Total Balance Score:</b> <u>          </u> / 4 <b>points</b>	<b>Side by Side Stand</b> (Feet together side by side for 10 seconds)	<b>&lt;10 seconds (0 points)</b> <i>Go to 4 metre Gait Speed Test</i>
	<b>10 seconds (=1 point)</b>	
	<b>Semi-Tandem Stand</b> (Heel of one foot against side of big toe of the other for 10 seconds)	<b>&lt;10 seconds (+0 points)</b> <i>Go to 4 metre Gait Speed Test</i>
	<b>10 seconds (+1 point)</b>	
	<b>Tandem Stand</b> Feet aligned heel to toe for 10 seconds	
	<b>10 seconds (+2 points); 3-9.99 seconds (+1 point); &lt; 3 seconds (+0 points)</b>	
<b>Gait</b>  <b>Total Gait Speed Score:</b> <u>          </u> / 4 <b>points</b>	<b>Gait Speed Test</b> (Measures the time required to walk 4 metres at a normal pace - use best of 2 times)  Best time: _____ seconds	<b>&lt;4.82 seconds (4 points)</b> <b>4.82-6.21 seconds (3 points)</b> <b>6.21-8.70 seconds (2 points)</b> <b>&gt;8.70 seconds (1 point)</b> <b>Unable (0 points)</b>
<b>Chair Stand</b>  <b>Total Chair Stand Score:</b> <u>          </u> / 4 <b>points</b>	<b>Chair Stand Test (50cm)</b> Pre-test: Participants fold their arms across their chest and try to stand up once from a chair  ↓ Able  <b>5 repeats</b> Measures the time required to perform five rises from a chair to an upright position as fast as possible without the use of the arms Best time: _____ seconds	<b>Unable</b> <b>→ Stop (0 points)</b>
		<b>≤11.19 sec (4 points)</b> <b>11.20-13.69 sec (3 points)</b> <b>13.70-16.69 sec (2 points)</b> <b>&gt;16.7 sec (1 point)</b> <b>≥60 sec or unable (0 points)</b>
<b>Total score: _____ /12</b> (≤9 has been defined as low physical function)		



## Appendix 4: Pre-operative Data Collection Form



The Prince Charles Hospital  
Metro North Hospital and Health Service



Haemodynamic tolerance of cardiac  
surgical patients with inotropic  
dependence in upright positioning  
**HREC/17/QPCH/31**

**PATIENT IDENTIFICATION**  
**STICKER**

Assessment date:

Surgery: CABG/ valve replacement or repair (circle)

Expected DOS:

Patient details:	
Sex:	Height:
Weight:	Current medications:
Social history:	PMHx:
Physical function:	
Mobility status:	Exercise tolerance
Able to walk >100m / <100m	Limiting factor(s) if applicable:
Able to climb one flight of stairs?	Short Physical Performance Battery score:

## Appendix 5: Post-operative Data Collection Form

(Affix patient identification label here)

URN: \_\_\_\_\_

Family Name: \_\_\_\_\_

Given Name: \_\_\_\_\_

Address: \_\_\_\_\_

Date of Birth: \_\_\_\_\_ Sex: M F

### Haemodynamic Tolerance of Cardiac Surgical Patients with Inotropic Dependence in Upright Positioning (HREC/17/QPCH/31)

Consent gained from NOK/patient preoperatively:

Patient is appropriate for recruitment post-operatively:

Subject number: \_\_\_\_\_

DOS: \_\_\_\_\_

<b>Subject details:</b> Sex: M <input type="checkbox"/> F <input type="checkbox"/>  Height: _____ cm  Weight: _____ kg  PMHx: _____ _____ _____ _____ _____	<b>Pre-operative:</b> SPPB: _____ Comments: _____ _____  Mobility status: <input type="checkbox"/> IND <input type="checkbox"/> S/V <input type="checkbox"/> 1XA <input type="checkbox"/> 2XA <input type="checkbox"/> Unable Aid Required?: <input type="checkbox"/> N <input type="checkbox"/> Y _____ Distance: _____ m  Exercise tolerance: _____	<b>Surgery Details:</b> Type of surgery: _____  Graft used (if applicable): _____  Bypass time: _____ hrs / mins  Cross clamp time: _____ mins  Comments: _____ _____ _____
<b>Mechanical ventilation time in ICU:</b>  _____ mins  Comments: _____ _____ _____	<b>Time from extubation to first attempt at exercise:</b>  _____ mins  Comments: _____ _____ _____	<b>Peri-operative surgical complications (if applicable):</b>  _____ _____ _____ _____

(Affix patient identification label here)

URN:

Family Name:

Given Name:

Address:

Date of Birth:                      Sex:    M    F

Date: \_\_\_\_\_ Day \_\_\_\_\_ post surgery

Subjective information pre-intervention:

BORG (Modified 1-10): \_\_\_\_\_

Inotrope/Vasopressor	Dose (micrograms/kg/min)	Reason for administration

Clinical observations pre-intervention	Details:
Peripherals (warm/cool)	
Lactate level	
Heart rate and rhythm	
Bowel sounds present	
Urine output	
Neurological state	
Respiratory (ventilation and gas exchange)	

(Affix patient identification label here)

URN: \_\_\_\_\_

Family Name: \_\_\_\_\_

Given Name: \_\_\_\_\_

Address: \_\_\_\_\_

Date of Birth: \_\_\_\_\_ Sex: M F

	Supine	High sitting (60 degrees) >1 min	SOEOB >1min	Standing >1 min	MOS > 1min	SOEOB >1min	High sitting (60 degrees) >1 min	Supine >1min	5 minutes post: Supine
Cardiac Output	L/min								
Stroke Volume	mL/b								
Cardiac Index	L/min/m <sup>2</sup>								
Stroke volume variation	%								
HR and rhythm	bpm								
BP	mmHg								
RR	Breaths/min								
SpO <sub>2</sub>	%								
Comments									

(Affix patient identification label here)

URN: \_\_\_\_\_

Family Name: \_\_\_\_\_

Given Name: \_\_\_\_\_

Address: \_\_\_\_\_

Date of Birth:      Sex:    M    F

**Intervention Details:**

<p><b>Level of assistance/aid required for standing/MOS:</b></p> <p><input type="checkbox"/> IND   <input type="checkbox"/> S/V   <input type="checkbox"/> 1XA   <input type="checkbox"/> 2XA</p> <p><input type="checkbox"/> Unable</p> <p>Aid Required?:   <input type="checkbox"/> N   <input type="checkbox"/> Y _____</p>	<p><b>Oxygen requirement:</b></p> <p>NP <input type="checkbox"/> _____ L    Mask <input type="checkbox"/> _____ L</p> <p>Humidified <input type="checkbox"/> _____</p> <p><b>Total duration of intervention (mins):</b> _____</p>
<p>RPE during intervention (0-10): _____    Comments : _____</p>	
<p>RPE post intervention (0-10): _____    Comments : _____</p>	
<p><b>Adverse event (circle):</b></p> <ol style="list-style-type: none"> <li>1. No adverse event</li> <li>2. Alteration in blood pressure <u>greater</u> than 20% of resting values which necessitates stopping intervention or requiring remedial intervention (e.g. inotropes).</li> <li>3. Alteration in blood pressure <u>less</u> than 20% of resting values which necessitates stopping intervention or requiring remedial intervention (e.g. inotropes).</li> <li>4. Alteration in heart rate <u>greater</u> than 20% of resting values which necessitates stopping intervention or requires remedial intervention.</li> <li>5. Alteration in heart rate <u>less</u> than 20% of resting values which necessitates stopping intervention or requires remedial intervention</li> <li>6. New arrhythmia (e.g. atrial fibrillation, increased number of ectopic beats per minute, ST depression or elevation, increased magnitude of ST depression, bigeminy, trigeminy, ventricular tachycardia, ventricular fibrillation, asystole).</li> <li>7. Desaturation of SpO2 <u>less</u> than 10% of baseline levels or a figure that necessitates stopping intervention or requires remedial intervention.</li> <li>8. Agitation resulting in detachment of equipment or lines or requiring increased sedation.</li> <li>9. Fall</li> </ol> <p><small>Adapted from: Zeppos, L., et al., <i>Physiotherapy intervention in intensive care is safe: an observational study. Australian Journal of Physiotherapy</i>, 2007. 53(4): p. 279-283.</small></p>	

## Appendix 6: Modified Borg Rating of Perceived Exertion Scale

### **Modified Borg Dyspnoea Scale**

0	Nothing at all	
0.5	Very, very slight (just noticeable)	
1	Very slight	
2	Slight	
3	Moderate	Exercise Training Zone
4	Somewhat severe	
5	Severe	
6		
7	Very severe	
8		
9	Very, very severe (almost maximal)	
10	Maximal	

#### **Patient Instructions for Borg Dyspnoea Scale**

"This is a scale that asks you to rate the difficulty of your breathing. It starts at number 0 where your breathing is causing you no difficulty at all and progresses through to number 10 where your breathing difficulty is maximal. How much difficulty is your breathing causing you right now?"

Appendix 7 Summary of participants detailing their dosage of and requirement for vasoactive medication

Subject	Type of surgery	Indication for vasoactive medication administration	Name of medication/s	Dosage/s (mcg/kg/min)	Comments
1	CABG x 3	BP support	Dopamine	4.91	Weaning 1ml/4hr. Weaned off Noradrenaline 2 hour prior to data collection
2	CABG x 5	Hypotension	Dopamine	5.00	Not weaning
			Adrenaline	0.09	
			Noradrenaline	0.05	
			Vasopressin	0.02	
3	Aortic valve replacement	Cardiogenic and vasodilatory shock	Dopamine	5.00	Weaning 1ml/4hr
4	CABG x 3	Hypotension	Dopamine	2.50	Weaning 4mls/hr
5	Mitral valve replacement	Hypotension	Dopamine	5.00	Weaning 1ml/hr
6	Mitral valve repair	Hypotension and LV dysfunction	Dopamine	5.00	Not weaning
			Adrenaline	0.02	
7	Aortic root replacement	Existing LV dysfunction	Dopamine	4.88	Weaning 1ml/6hr
8	CABG x 2	Hypotension	Dopamine	5.00	Not weaning
9	CABG x 2	Hypotension	Dopamine	2.50	Not weaning
10	Aortic valve replacement	Hypotension	Dopamine	5.00	Not weaning
			Noradrenaline	0.02	

11	Aortic valve replacement	Hypotension	Dopamine	2.99	Weaning 1ml/2hr
12	CABG x 2 and aortic valve and mitral valve replacement	BP support	Dopamine	2.86	Weaning .5mg/2hr
13	CABG x 3	Hypotension	Dopamine	3.00	Not weaning
14	CABG x 4	Hypotension	Dopamine	2.5	Not weaning
15	Mitral valve and tricuspid valve repair	Hypotension	Dopamine	5.00	Not weaning. 0.02 Noradrenaline weaned off 1 hour prior to data collection
16	CABG x 3	Hypotension and LV dysfunction	Dopamine	3.00	Not weaning
17	CABG x 2	Hypotension	Dopamine	2.00	Not weaning. 0.04 Noradrenaline ceased immediately prior to data collection
18	CABG x 1	BP support	Dopamine	3.50	Weaning 1ml/4hr
19	Tricuspid ring and mitral valve replacement	RV dysfunction	Dopamine	3.70	Weaning 1ml/4hr
20	CABG x 2	Hypotension	Dopamine	4.50	Not weaning
			Adrenaline	0.02	



## Appendix 8: Cardiac index in upright positioning

A one- way between-within repeated measures ANOVA was conducted to compare CI measurements of participants receiving low and moderate to high doses of vasoactive medication, in each of the 5 positions. The means and standard deviation are presented in Table 10. There was no statistically significant changes in CI measures over time with upright positioning, Wilks' Lambda=0.629, F (4,8)=1.177, p=0.390, multivariate partial eta squared=0.371.

While not statistically significant, it was observed that CI measurements tended to decrease with upright positioning in participants receiving low dose vasoactive medications. The mean CI in these participants was lower than baseline after completing upright positioning. However, only three participants were classified as receiving low dose vasoactive medication and therefore this finding is not clinically significant.

Table 10 Descriptive statistics for CI measurements in 5 upright positions

Position	Vasoactive medication dose	N	Mean	Standard deviation
Supine	Low	3	3.6	0.3
	Mod/High	10	3.2	0.9
SOEOB	Low	3	3.4	0.9
	Mod/High	10	3.4	0.9
Standing	Low	3	3.0	0.3
	Mod/High	10	3.3	0.7
MOS	Low	3	2.9	0.1
	Mod/High	10	3.6	1.1
Supine	Low	3	2.6	0.9
	Mod/High	10	3.4	0.8

### *Between subjects effects*

There was no significant difference in CI measurements for time\*dose in each of the 5 positions between participants receiving low or moderate/high vasoactive medication dosage (p= 0.589).

### *Interaction effects*

There was no statistically significant interaction effect between the two groups of low and mod/high vasoactive medication doses, Wilks' Lambda=0.662, p=0.453. There was no difference in change in CI measurements between the two groups over time in upright positions.

## Appendix 9: Heart rate in upright positioning

A one- way between-within repeated measures ANOVA was conducted to compare HR measurements of participants receiving low and moderate to high doses of vasoactive medication, in each of the 5 positions. The means and standard deviation are presented in Table 11. There was not a stastically significant increase in HR with upright positioning, Wilks' Lambda=0.343,  $F(4,8)=3.839$ ,  $p=0.050$ , multivariate partial eta squared=0.657.

Table 11 Descriptive statistics for HR measurements in 5 upright positions

Position	Vasoactive medication dose	N	Mean	Standard deviation
Supine	Low	3	96.7	10.8
	Mod/High	10	96.6	11.1
SOEOB	Low	3	95.3	5.7
	Mod/High	10	101.6	15.2
Standing	Low	3	123.3	33.5
	Mod/High	10	104.6	18.5
MOS	Low	3	125.7	34.5
	Mod/High	10	112.1	17.9
Supine	Low	3	95.3	10.5
	Mod/High	10	99.4	11.1

### *Between subjects effects*

There was no significant difference in HR measurements over time in each of the 5 positions between participants receiving low or moderate/high vasoactive medication dosage ( $p=0.663$ ).

### *Interaction effects*

There was no statistically significant interaction effect of HR for time\*dose between the two groups of low and moderate/high vasoactive medication doses, Wilks' Lambda=0.421,  $p=0.105$ .

## Appendix 10: Respiratory rate in upright positioning

A one- way between-within repeated measures ANOVA was conducted to compare RR measurements of participants receiving low and moderate to high doses of vasoactive medication, in each of the 5 positions. The means and standard deviation are presented in Table 12. There was a statistically significant increase in RR with upright positioning, Wilks' Lambda=0.341,  $F(4,8)=3.857$ ,  $p=0.049$ , multivariate partial eta squared=0.659.

Table 12 Descriptive statistics for RR measurements in 5 upright positions

Position	Vasoactive medication dose	N	Mean	Standard deviation
Supine	Low	3	22.0	2.0
	Mod/High	10	20.4	5.5
SOEOB	Low	3	25.0	3.6
	Mod/High	10	24.4	4.6
Standing	Low	3	21.7	5.0
	Mod/High	10	24.7	4.2
MOS	Low	3	30.3	5.5
	Mod/High	10	31.1	7.0
Supine	Low	3	24.7	3.5
	Mod/High	10	20.6	4.3

### *Between subjects effects*

There was no significant difference in RR measurements in each of the 5 positions between participants receiving low or moderate/high vasoactive medication dosage ( $p=0.777$ ).

### *Interaction effects*

There was no statistically significant interaction effect of RR between the two groups of low and mod/high vasoactive medication doses, Wilks' Lambda=0.614,  $p=0.362$ . There was no

difference in change of RR measurements between the two groups over time in upright positions.

## Appendix 11: Non-normally distributed variables- stroke volume, systolic blood pressure and peripheral oxygen saturation in upright positioning

### *Stroke volume in upright positioning*

As a non-normally distributed variable, a non-parametric Friedman Test of differences among repeated measures of SV in the 5 upright positions was conducted and rendered a Chi- square value of 6.819 which was not significant ( $p=0.146$ )

### *Systolic blood pressure in upright positioning*

As a non-normally distributed variable, a non-parametric Friedman Test of differences among repeated measures of Systolic BP in the 5 upright positions was conducted and rendered a Chi- square value of 5.198, which was not significant ( $p=0.268$ ).

### *Peripheral oxygen saturation in upright positioning*

As a non-normally distributed variable, a non-parametric Friedman Test of differences among repeated measures of SpO<sub>2</sub> in the 5 upright positions was conducted and rendered a Chi-square value of 3.406, which was not significant ( $p=0.492$ ).

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