Diplomarbeit

Effects of Partial Weight Loading on Physiological Responses in Post-Surgical Patients

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Graz, 05.07.2022

Eidesstattliche Erklärung

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Graz, 05.07.2022 *Gregor Lettner eh.*

I. Acknowledgement

I would like to thank all the patients who took part in this study and made this research possible. My special thanks go to my supervisors Assoz. Prof. Priv. Doz. Dr. med. Dr. med. univ. MMedSci PhD. Nandu Goswami and Mag. Dr.rer.nat. Karin Schmid-Zalaudek for their guidance and support and to the teams of the departments of Physiology and Cardiac Surgery. Furthermore, I wish to thank my whole family and my friends Alexander Holzhausen and Vincent Pritzel for their support and friendship.

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II. Glossary & Abbreviations

ACE	Angiotensin Converting Enzyme
ANP	Atrial Natriuretic Peptide
AT-I	Angiotensin I
AT-II	Angiotensin II
BNP	Brain Natriuretic Peptide
BP	Blood Pressure
CO	Cardiac Output
CVP	Central Venous Pressure
ECG	Electrocardiogram
EMG	Electromyogram
GFR	Glomerular Filtration Rate
HR	Heart Rate
LKH	Landeskrankenhaus
MAP	Mean Arterial Pressure
NIRS	Near Infrared Spectroscopy
OH	Orthostatic Hypotension
OI	Orthostatic Intolerance
PWL	Partial Weight Loading
R-A-A-S	Renin-Angiotensin-Aldosterone-System
RRI	RR Interval
SBP	Systolic Blood Pressure
SD	Standard Deviation
STS-Test	Supine to Stand-Test
TPR	Total Peripheral Resistance Index
TPRI	Total Peripheral Resistance Index
VR	Venous Return

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V. Zusammenfassung

Hintergrund

Nach herzchirurgischen Eingriffen sind Patientinnen und Patienten oft über längere Zeit immobil und müssen strenge Bettruhe einhalten. Die horizontale Körperposition und die verminderte Muskelaktivität haben negative Auswirkungen auf den menschlichen Körper. Eintretender Muskelabbau, eine verminderte kardiale Anpassungsfähigkeit und orthostatische Hypotonie führen zu einem erhöhten Sturzrisiko und einer erhöhten Sterblichkeit. Um dem entgegenzuwirken und den Rehabilitationsprozess zu verbessern, untersuchten wir in dieser Studie die Auswirkungen einer täglichen 10-minütigen 15° Kopfhochlagerung auf postoperative Patientinnen und Patienten. Die hämodynamischen Parameter wurden nach einer Herzoperation gemessen.

Methodik

Zur Beantwortung der Forschungsfrage wurde ein prospektives Studiendesign gewählt. Die Patientinnen und Patienten wurden einer Kontrollgruppe (n=8) zugeteilt, in der keine Kopfhochlagerung durchgeführt wurde, und einer Interventionsgruppe (n=8), in der sie sieben Tage lang postoperativ täglich 10 Minuten in eine Kopfhochlagerung von 15° positioniert wurden. Am zweiten und siebten postoperativen Tag wurden der mittlere arterielle Druck, der periphere Gefäßwiderstand und die Herzfrequenz während eines Supine-to-Stand-Tests gemessen.

Ergebnisse

Die statistische Analyse der Ergebnisse zeigte signifikante Haupteffekte im Sinne einer höheren Herzfrequenz in der Interventionsgruppe ($F(1, 7)=6{,}76$, $p<.035$, $\eta 2=.49$) beim Aufstehen, sowie eines niedrigeren peripheren Widerstands am Ende der Erholungsphase in der Interventionsgruppe ($F_{(1,7)}=6.059$, $p=.0043$, $\eta^2=.0464$). Der mittlerer arterieller Druck ($F(1, 7)=4{,}156$, $p=.081$, $\eta 2=.37$) zeigte keine signifikanten Effekte zwischen den beiden Gruppen.

Diskussion

Der höhere Anstieg der Herzfrequenz während des Supine-to-Stand-Tests in der Interventionsgruppe deutet darauf hin, dass die gekippten Patientinnen und Patienten eine ausreichende orthostatische Belastung während der Intervention erhalten hatten. Orthostatische Belastung verbessert bekanntermaßen die Durchblutung der Beinmuskulatur, erhöht den venösen Rückstrom und trägt somit zur Aufrechterhaltung der allgemeinen Gewebedurchblutung bei. Der verminderte Gefäßwiderstand am Ende der Erholungsphase zeigt positive Auswirkungen der Behandlung auf den Barorezeptor Reflex an. Durch die vermehrte orthostatische Belastung konnte seiner Dekonditionierung entgegengewirkt werden. Somit zeigt unsere Studie, dass tägliche zehnminütige 15° Kopfhochlagerung auf der Intensivstation sicher eingesetzt werden können, um die Gesundheit der Patientinnen und Patienten zu sicherzustellen.

VI. Abstract

Background

After cardiac surgery, patients are often immobile for prolonged periods of time and subjected to strict bedrest. The horizontal body position and decreased muscle activity have negative effects on the human body. Incipient muscle loss, decreased cardio postural adaptability, and orthostatic hypotension lead to increased fall risk and mortality. To counteract this and to improve the rehabilitation process, in this study we investigated the effects of 10 minutes per day 15° head up tilt position on post-surgical patients. Hemodynamic parameters where measured after cardiac surgery.

Methodology

A prospective study design was chosen to address the research question. Patients were assigned to a control group (n=8) in which no head-up tilt was carried out and an intervention group (n=8) in which they underwent 10 minutes per day of 15° head up tilt position for seven days post-operation. Mean arterial pressure, total peripheral resistance index and heart rate responses to a supine-to-stand test were recorded on the second and seventh postoperative days.

Results

Statistical analysis of the results showed a significant main effects in terms of a higher heart rate in the intervention group ($F(1, 7)=6.76$, $p<.035$, $\eta 2= .49$) upon standing up and in terms of lower total peripheral resistance index during the end of the recovery phase in the intervention group ($F_{(1,7)}=6.059$, $p=.0043$, $\eta^2=.0464$). The parameter mean arterial pressure ($F(1, 7)=4.156$, $p=.081$, $\eta 2=.37$) showed no significant effects across the two groups.

Discussion

Higher heart rate increase during sit-to-stand test in the intervention group suggests that the tilted patients had received enough orthostatic loading. Orthostatic loading is known to improve blood flow in the leg muscles and maintain general tissue perfusion. Lower peripheral resistance during recovery from orthostatic stress

suggests that higher orthostatic loading also counteracted deconditioning of the baroreceptor reflex in the intervention group. Thereby, our study shows that ten minutes of head-up tilting a day can safely be used in intensive care units to ensure patients health.

1 Introduction

“The bed is the central focus of hospitals and the standard unit of size for healthcare facilities” (1). Although benefits of early mobilization after surgery are widely accepted nowadays (2), patients, especially elderly ones, experience up to 83% (3) of their in-hospital treatment in beds and under restricted mobility (3). The resulting change in gravitational effects on the body leads to unloading of muscles and bones (5), cardiovascular deconditioning (6) and orthostatic hypotension (6). Loss of lean body mass (8) and postural instability in consequence lead to a higher risk of falls and fall related injuries (9–11). Falls are linked to higher morbidity and mortality in older adults. With demographics shifting to an older average age their shares of total disease incidence and healthcare costs are increasing (12,13).

As early mobilization of patients often proves difficult to implement in everyday hospital workflow, there is a need for easy-to-use and cost-effective ways to counteract cardiovascular deconditioning going along with bedrest (4).

Head down bedrest is used to simulate microgravity in the context of space flight research. Patients undergoing excessive bedrest and astronauts in space experience comparable physiological effects. Therefore, researchers investigated various countermeasures against deconditioning effects of microgravity on the basis of bedrest induced deconditioning. Spaceflight research looked at various measures, including application of hyper gravity (14), lower body negative pressure (15), volume loading (16) and physical exercise (17). Most of these measures have in common that they require personal resources, devices or administration of pharmaceutical products. This impacts their clinical applicability. Reducing the time spent in head-down bedrest by head-up tilt positioning would present a more cost-effective, lower-threshold and less invasive countermeasure against bedrest induced deconditioning. Therefore, this thesis investigated the effects of 10 minutes per day 15° head up tilt position on patients after cardiac valvular surgery.

Patients after cardiac surgery often experience physical deconditioning during their rehabilitation process (18). They undergo intensive cardiovascular examination and monitoring. Therefore, they pose an adequate group to explore new ways to counteract deconditioning effects of bedrest confinement in a clinical setting.

To approach the deconditioning effects of bedrest, it is important to understand the principles of cardiovascular function and blood pressure regulation. These will be explained in the following paragraphs.

1.1 The Cardiovascular System

1.1.1 Fundamentals

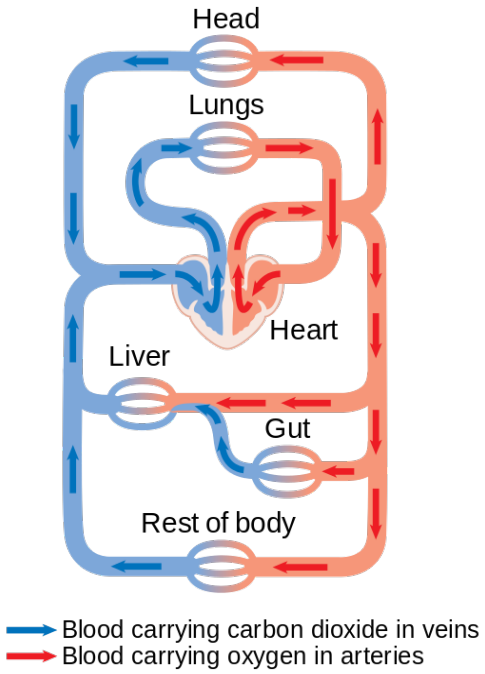

Figure 1: schematic overview of the cardiovascular system; from: https://upload.wikimedia.org/wikipedia/commons/thumb/1/1b/Diagram_showing_the_circulatory_system_of_the_body_CRUK_299.svg/640px-Diagram_showing_the_circulatory_system_of_the_body_CRUK_299.svg.png

The cardiovascular system is a closed circle of blood vessels connected to the heart. Its purpose is to transport oxygen, nutrients, hormones and other important components of the blood to target tissues. The heart functions as a pump to create pressure differences and thereby propel blood through the vessels. The heart does so by contracting its chambers. Vessels transporting blood away from the heart are called arteries, vessels transporting blood to the heart are called veins (19). Starting from the left ventricle blood enters body circulation through the aortic valve. It moves through the aorta into peripheral arteries, arterioles and finally into the capillary system. Here exchange of substances takes place. At the same time, the capillary system represents the border between arterial and venous circulation. After leaving the capillaries, blood flows through venules and veins to the venae cavae and back to the heart. It enters the right atrium, passes the tricuspid valve and is pumped into the pulmonary circulation system through the pulmonary valve. Gas exchange takes place in the pulmonary capillaries and oxygen loaded blood flows through the pulmonary veins

into the left atrium. It goes through the mitral valve into the left ventricle and then re-enters body circulation (20–22).

The pressure that drives this circulation is not continuous. The heart contracts rhythmically, creating higher pressure during the ejection phase (systole) and lower pressure during the filling phase (diastole). To ensure unidirectional blood flow the system is equipped with valves in the heart and veins to stop reversion of flow upon pressure reversal between the systole and diastole or due to gravitational effects (20–22).

The circulatory system can be divided into two sections. The low pressure system, consisting of lung vessels, venules and veins and the high pressure system, consisting of arterioles and arteries in the systemic circulation. The low pressure system contains the major share of the overall blood volume (23). Veins differ from arteries in their wall structure. They are more elastic, less contractible and can therefore contain larger volumes at lower pressure than arteries. These fundamentals are important to approach blood pressure regulation, orthostatic cardiovascular control and cardiac deconditioning (20–22).

1.1.2 Cardiac Function

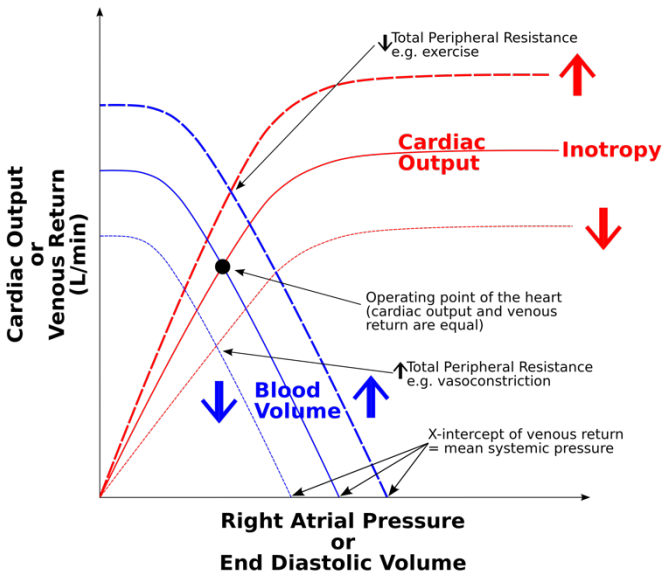

Figure 2: Frank-Starling law; the graph shows the interactions between increasing pre-load and CO. from: https://upload.wikimedia.org/wikipedia/commons/thumb/0/01/Starling_RAP_combined.svg/1920px-Starling_RAP_combined.svg.png

Different filling and pressure levels of cardiac chambers and blood vessels are important for the hearts mechanical output performance and autoregulation of stroke volume (SV). Pressure inside the vessels entering the right atrium determines pre-load. Pressure inside the vessels connected to the left ventricle determines after-load. Pre-load influences how much volume is supplied to the heart to build up pressure during contraction. After-load has to be overcome by the heart to transport blood into the periphery. Changes in pre- and after-load induce altered wall tensions in the hearts´ ventricles, which in

turn affect contractability, ejection fraction (EF, proportion of the volume ejected by the heart in systole to its total volume after diastole) and cardiac output (CO). Increasing after-load means higher pressure in the aorta directed against the pressure built up by the left ventricle upon contraction. Consequently, opening time of the aortic valve is shortened, less blood can pass through before the end of the systole and EF is reduced. Higher pre-load parallels higher central venous pressure (CVP) and venous return (VR). More blood enters the heart, ventricle filling increases and subsequently contractability and CO increase. The effect of increasing pre-load can be described by the **Frank-Starling Law of the Heart** (see Figure 2). This law states that the contractive force of heart musculature grows with increasing wall stretch. This effect is mediated by optimized overlapping of actin- and myosin-filaments and changes in calcium sensitivity, meaning that less calcium is necessary to induce stronger contraction triggering action potential (22). These correlations show the importance of VR for cardiac performance. If too much blood is trapped in the low-pressure system, VR and ventricle filling decrease. Consequently, drops in EF, CO and SV occur and the heart can no longer maintain sufficient mean arterial Pressure (MAP) (21,22).

1.1.3 Blood Distribution and Mean Arterial Pressure (MAP)

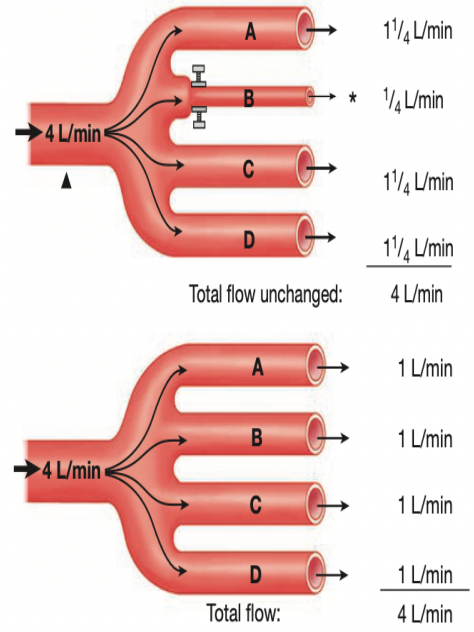

Figure 3: modulating blood distribution via changing vessel diameter & increasing resistance (21)

The underlying goal of cardiovascular control mechanisms is to maintain sufficient MAP and blood supply to target tissues. Different tissues have different perfusion requirements (see Figure 4). To meet these requirements the cardiovascular system needs to direct different volumes to different body areas. It does so by reducing the diameter of afferent blood vessels and increasing vascular resistance. With increasing resistance, blood flow decreases, and more blood is directed through vessels with bigger diameters and less resistance (see Figure 3) (21). These processes are

mediated, among others, by autonomous vegetative control and local paracrine or metabolic signals.

MAP describes arterial BP, without pressure peaks during the sys- or diastole. It is the “driving force for blood flow” (21) and drops in MAP can lead to insufficient organ perfusion, orthostatic intolerance, syncope (24) or even shock. MAP can be described with different formulas. The most useful one in our context reads:

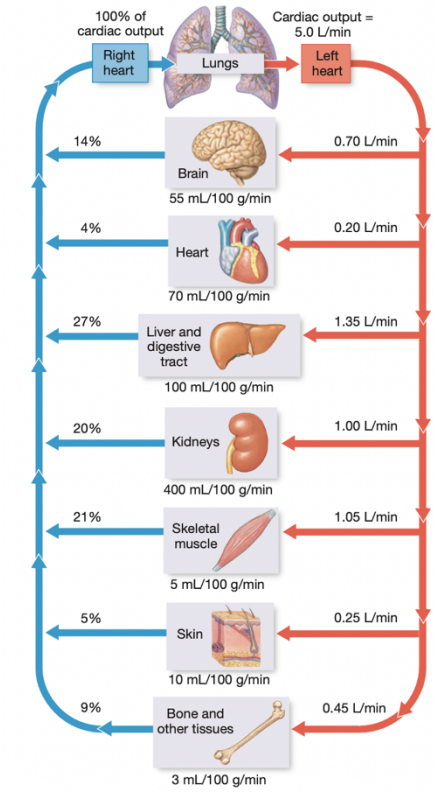

Figure 4: needs adjusted distribution of blood flow to target organs (21)

MAP = HR x SV x TPR. This formula shows that the body can maintain adequate MAP by adjusting either the HR, SV or TPR. Higher HR and SV increase MAP by pumping additional volume into the high-pressure system (HR x SV = CO). TPR does not directly affect CO, it increases MAP via vasoconstriction. Less space in the arterial system upon constriction, for the same amount of blood, also leads to higher pressure on the vessel wall. Also, upon arterial vasoconstriction more volume is shifted to the low-pressure system. Higher CVP and pre-load then increase CO via the Frank-Starling law of the heart, described in the previous paragraph (21). These mechanisms are important to react on changes in posture, fluid balance or increased oxygen consumption.

1.1.4 Cerebral Blood Flow Autoregulation

Some tissues are more sensitive to under perfusion than others and therefore have special autoregulation mechanisms. This plays a big role in the regulation of brain perfusion.

Brain tissue is highly depended on stable perfusion conditions. Periods of insufficient blood flow are known to cause loss of consciousness and syncope. Ischemic brain damage occurs after minutes of oxygen deprivation and can lead to irreparable impairments (22). Figure 5 shows that cerebral blood flow stays constant in a wide range of systemic MAP. This is achieved via myogenic, neurogenic, metabolic, and endothelial mechanisms. Myogenic refers to vessels´ smooth musculature contraction or relaxation upon transmural pressure changes. Reactively brain vessels contract or dilate to regulate blood flow. Neurogenic modulation describes vascular reactions to in- or decreased neural stimulation. Metabolic vessel stimulation is triggered by changing levels of oxygen or carbon dioxide in the blood. Lower oxygen concentration leads to vasodilatation to improve perfusion and oxygen inflow. Metabolic mechanisms include vasoactive substances, like nitric oxide, mediating vasodilatation.

These autoregulatory mechanisms (see Figure 5) manage to keep brain perfusion on a constant level in a MAP window between 50 mmHg and 150 mmHg (22). This is achieved by reacting to increasing MAP with higher cerebrovascular resistance and to decreasing MAP with lower resistance in brain vessels. When MAP drops below the autoregulatory threshold the consequence is cerebral hypoperfusion and ischemia (25). Initial symptoms can include feelings of dizziness and nausea, followed by orthostatic hypotension (OH), syncope and loss of consciousness up to ischemic brain damage (26). Consequences of hyperperfusion include headache, cerebral edema, or even hypertensive cerebral hemorrhage.

1.1.5 Short-Term and Long-Term Regulation of BP

BP regulation can be divided in long-term and short-term adaptation mechanism. Long-term regulation mainly affects effective intravascular volume via hormonal effects. Short-term regulation takes place in matters of seconds and is mostly mediated by autonomous neurogenic activation. Both play a role in deconditioning going along with bedrest or microgravity environments and orthostatic cardiovascular control.

Short-term BP regulation is, among others, controlled by the **baroreflex**.

The baroreflex is a negative feedback cycle affecting vascular tone and heartrate (HR) via sympathetic and parasympathetic innervation (27). Baroreceptors in the aorta and carotid sinus are sensitive to changes in stretch conditions of the vessel wall (28). They therefore react to in- or decreasing BP via sympathetic or parasympathetic stimulation of the cardiovascular system (29). When blood pressure goes up, stimulation of baroreceptors increases as they detect more strain to the vessel wall (29). Higher receptor activity leads to higher parasympathetic activation via stimulation of the medullary cardiovascular control center (30). The resulting dominant parasympathetic influence on the cardiovascular system leads to lower CO, lower total peripheral resistance (TPR) and eventually to lower BP (31). When blood pressure goes down, stimulation of baroreceptors decreases because they detect less strain to the vessel wall. Lower receptor activity leads to higher sympathetic activation via stimulation of the medullary cardiovascular control center.

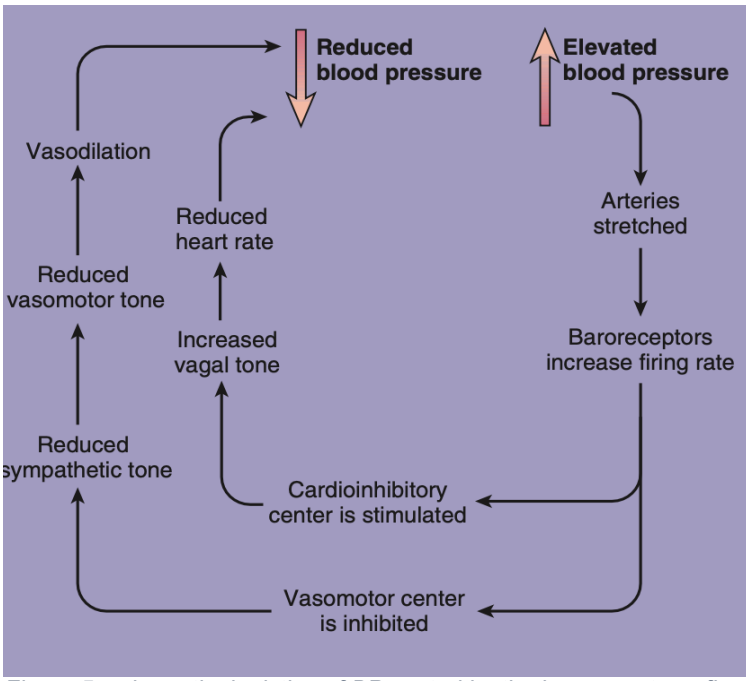

Figure 5: schematic depiction of BP control by the baroreceptor reflex (20)

The consequently dominating sympathetic influence on the cardiovascular system increases BP by raising cardiac output and TPR (21). In addition to the baroreflex, central nervous and local chemoreceptor responses to changes in levels of oxygen and carbon dioxide play a role in short-term BP regulation (27).

Long-term regulation of BP is mostly mediated by hormones of the Renin-Angiotensin-Aldosterone-System (R-A-A-S) and Natriuretic Peptides Atrial Natriuretic Peptide (ANP) and Brain Natriuretic Peptide (BNP). These hormones modulate effective intravascular fluid volume via renal fluid excretion and vascular tone. Cardiovascular deconditioning, resulting from bedrest, is accompanied by changes in hormone levels. These alterations can be measured as soon as after 4

hours of head down bedrest (32). Elevating effects on BP are mediated by the R-A-A-S. It´s initial component is renin, which is secreted by granular cells in the afferent arteriole of the juxtaglomerular apparatus (33). Secretion is triggered by low arterial blood pressure, sympathetic innervation level, changing sodium level and negative feedback from the system itself via Angiotensin II (AT II) (34). Renin enzymatically converts Angiotensinogen into Angiotensin I (AT I) (35). AT I is turned into the main effector AT II via Angiotensin Converting Enzyme (ACE) (36). AT II is a strong vasoconstrictor mediating higher total peripheral resistance (TPR) and thereby increasing MAP (21). Further, Angiotensin promotes secretion of Aldosterone from the adrenal cortex and Antidiuretic Hormone (ADH) from the pituitary gland (21) and leads to increased thirst and oral fluid and salt intake (37). Aldosterone is a steroid hormone and increases sodium and water resorption in the kidney, while ADH reduces renal fluid excretion (21). These processes lead to higher effective intravascular volume and elevated BP (see Figure 6).

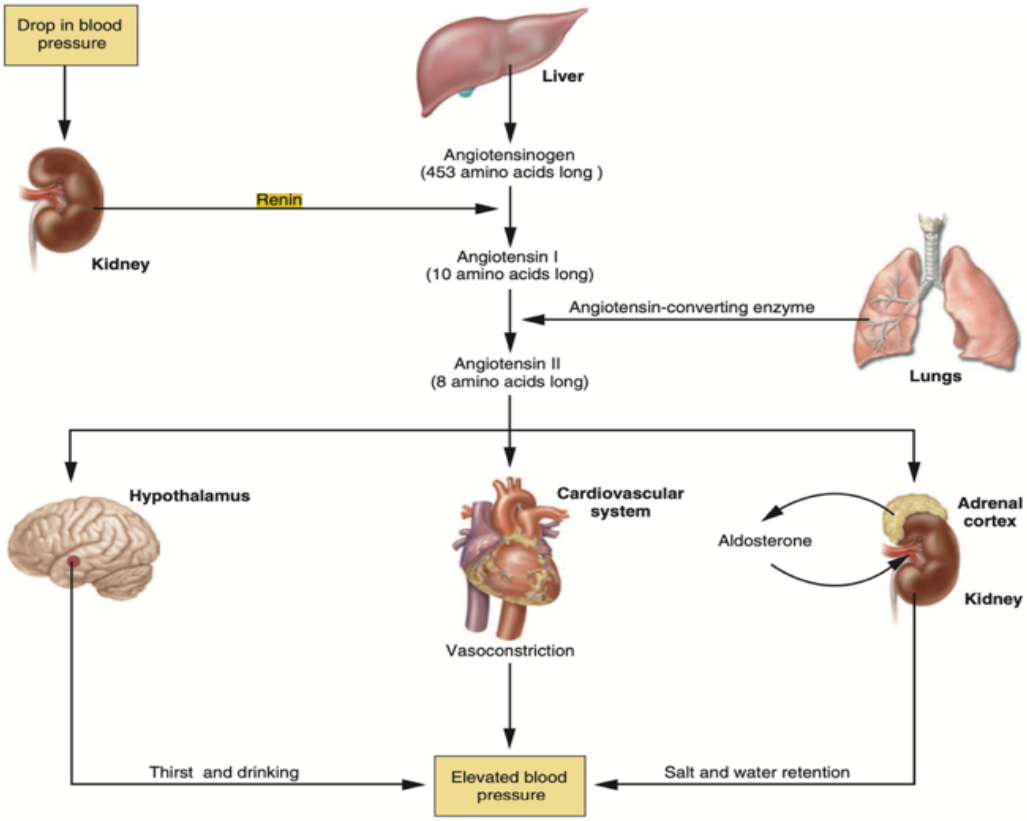

Figure 6: Schematic Visualization of the R-A-A-S (19)

Natriuretic peptides are hormones with opposite effects to those of the R-A-A-S. They increase Na+ and fluid excretion (21) and thereby have decreasing effects on effective intravascular volume. Released from the cardiac atria and ventricles upon increasing BP, sensed by strain receptors, natriuretic peptides counteract the triggering stimulus and decrease BP (38). Antihypertensive effects are achieved via several pathways. In the kidneys, they increase the glomerular filtration rate (GFR) (39) and decrease tubular reabsorption (40). Thereby overall urine output is increased, and intravascular fluid reduced. Natriuretic peptides inhibit renin release (41) and thereby counteract the blood pressure increasing mechanisms described in the preceding paragraph (see 1.5.2.1). They also have an inhibiting effect on catecholamine release via the hypothalamic - pituitary -adrenal - axis (42). The resulting vasorelaxation and reduced TPR (43) contribute to a decrease in BP. For better understanding Figure 7 shows a schematic visualization of the above-described effects.

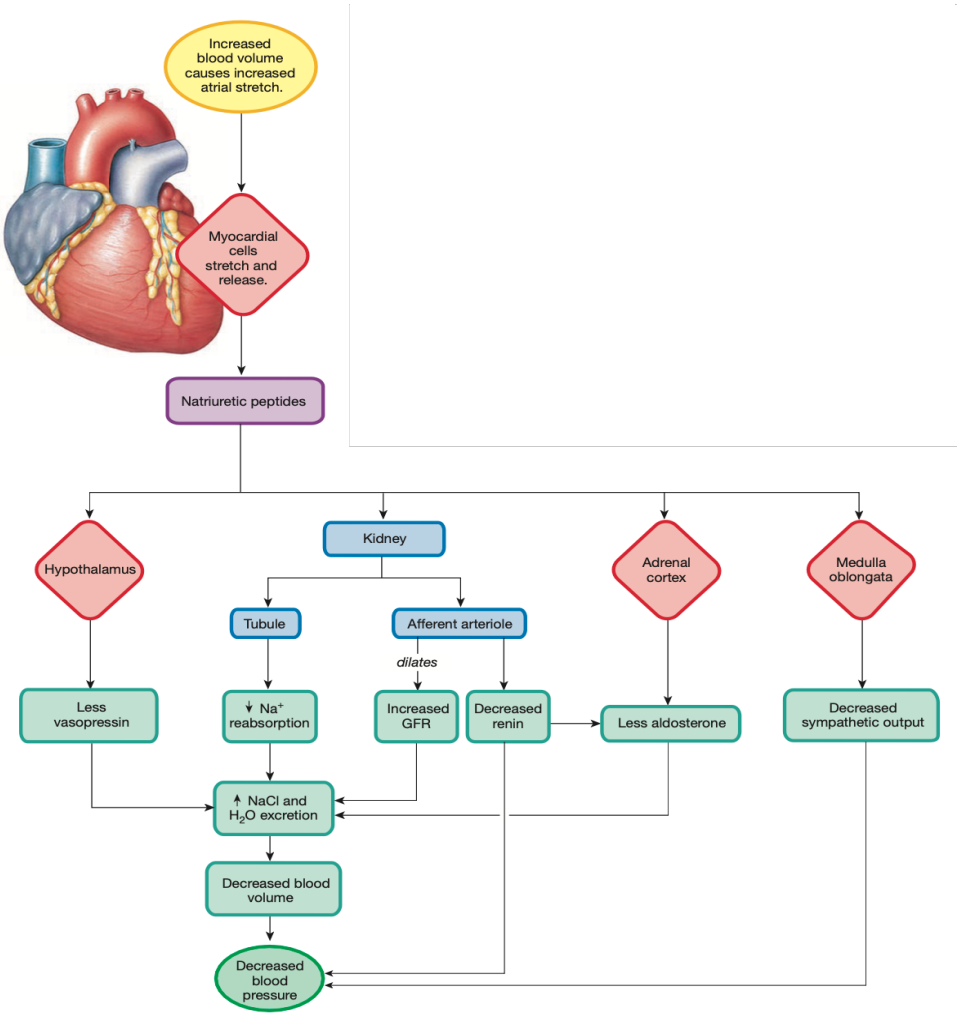

Figure 7: Schematic Visualization of ANP & BNP effect (21)

1.1.6 Skeletal Muscle Pump and Cardio-Postural Interactions

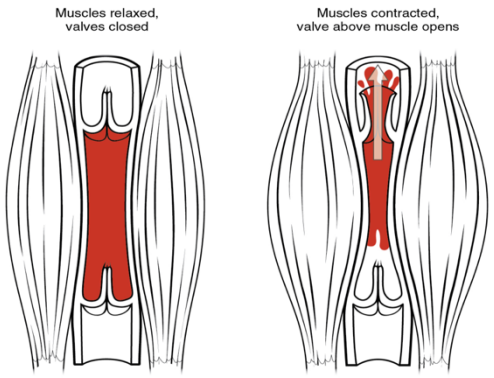

Figure 8: Muscle Pump

Picture from: https://openstax.org/apps/archive/20220118.185250/resources/bb4f1be2e1e74ba296dbd0935cdabf78195a3d3c

To counteract fluid shift into the lower extremities upon standing up the body can use its skeletal muscle pump to contract leg veins. It thereby prevents venous pooling and improves venous return (44). Due to their anatomical structure with thinner walls and less intramural musculature (45) veins have a higher compliance than arteries and contain up to 70 % of the total intravascular blood volume (23). Compared to arteries veins are less capable of autonomous contraction upon sympathetic stimulation and have a lower vascular tone. Therefore they are more susceptible to fluid pooling upon standing up (46) and by smooth muscle contraction alone, veins are not capable of generating sufficient VR to keep CO and MAP upright. Contracting effects though can be achieved by activation of the muscular tissue surrounding the veins (44,47). Muscular contractions compress the adjacent veins. The lumen of veins is equipped with venous valves (48) which create a one-way outlet effect directed to the center of the body (49). Thereby, fluid is moved upwards against the effect of gravity (see Figure 8), VR increases and the in paragraph 1.1.2. described mechanism lead to increased CO and MAP.

Investigating the connections between calf-muscle activation, postural sway, VR and BP has led to the concept of the cardio-postural model. It “describes interactions between cardiovascular control and postural changes” (3) and showed interactions between calf-muscle activation during passive standing and increasing BP. This observation led to the integration of postural control mechanisms and cardiovascular control mechanisms (see Figure 9). Postural control takes place through the utilization of impressions from the sensory organs and their implementation by the musculoskeletal system. Cardiovascular control is achieved via baroreceptor activity and the short-term regulation processes described in 1.1.4.1. The connection between these two concepts shows, for example, that postural sway

upon standing up is not only to be interpreted as a sign of postural instability, it also engages calf musculature and thereby activates the muscle pump to increase venous return and prevent fainting (50).

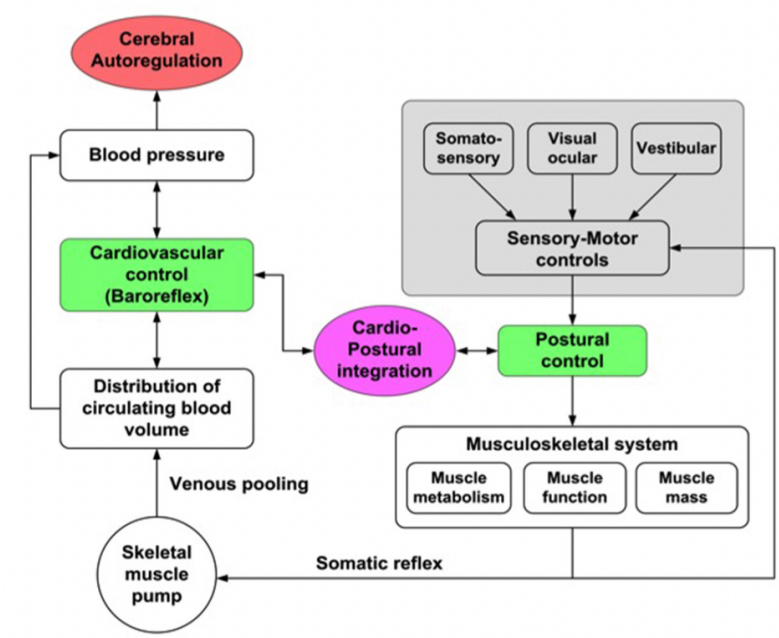

Figure 9: depiction of the cardio postural model (81)

1.2 Orthostatic Hypotension

Lack of gravity, excessive bedrest and advanced age can lead to insufficient adaptation to postural changes. This phenomenon is called orthostatic hypotension (OH) and leads to orthostatic intolerance and impaired postural control. The final terminus of dysregulated orthostatic adaptation is the orthostatic syncope i.e. temporary unconsciousness due to dropped mean arterial pressure (MAP) (51) and cerebral hypoperfusion. Prodromal symptoms are feelings of dizziness, vertigo or nausea experienced by patients upon standing up. Explained in numbers, orthostatic hypotension is defined as a drop of systolic blood pressure over 20% within 3 minutes of standing up (9). Orthostatic hypotension can be diagnosed with the Schellong-Test (52) or a Tilt-Table-Test (53).

Under orthostatic stress various changes occur in the cardiovascular system (see Figure 10) and blood is redistributed to lower body regions. 10-15 % of blood are pooled in the lower extremities upon standing up (54). Consequently, VR and pre-load are reduced. As shown in paragraph 1.1.2 this also leads to decreases in CO and MAP. Normally this decrease can be cushioned by sufficient activation of the baroreceptor reflex. Baroreceptors sense the MAP drop and reactively increase CO and TPRI, which leads to compensatory BP increase. When compensation is insufficient, the unfavorable fluid distribution leads to uncompensated decrease of MAP. If this decrease exceeds the brain´s autoregulatory capacity, brain perfusion is reduced, and patients experience the symptoms of OH. There are various

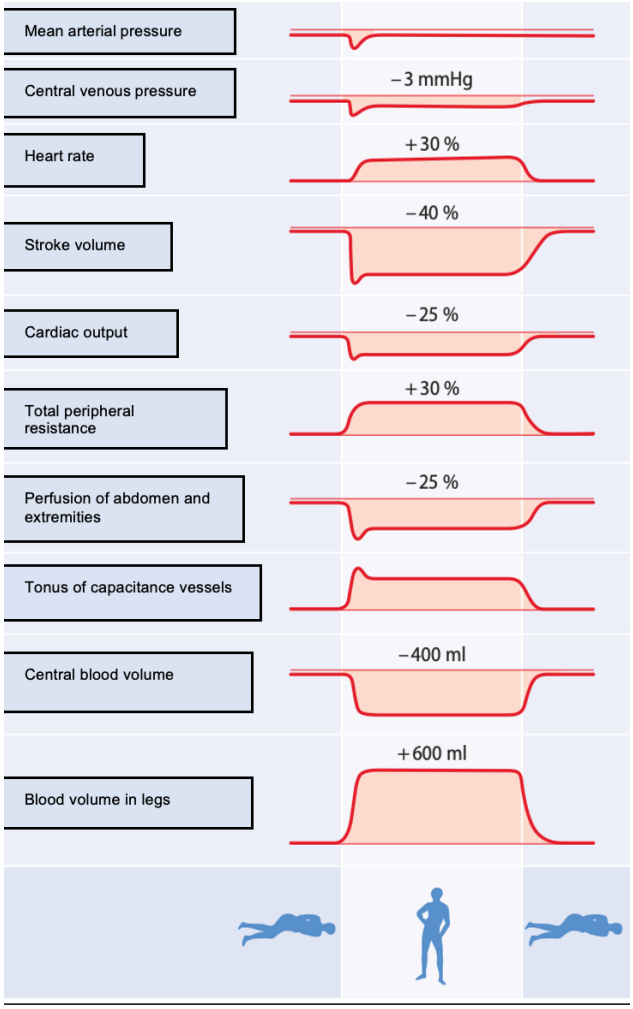

Figure 10: cardiovascular changes going along with orthostatic challenge (22), edited by the author

reasons for the occurrence of OH. With progressing age baroreflex sensitivity is reduced (55) and the prevalence of orthostatic hypotension in the elderly rises up to 30 % (9,56). Other causes are drug side effects and various neurogenic (e.g. Parkinson's disease) and non-neurogenic factors (e.g. hypovolemia) (57). Studies have shown correlations between orthostatic hypotension and increased risk for falls and fall related injuries as well as increased morbidity and mortality (57,58). Also, the occurrence of OH is linked to prolonged bedrest confinement (57).

1.3 Bedrest

The therapeutic value of bedrest has been regarded differently in the course of history. Rarely used before the 19th century (59), bedrest as a treatment became more commonly used until the mid of the 20th century. During World War II physicians in field hospitals observed quicker recovery in patients who had to mobilize faster due to limited bed capacities (10). Findings from the emerging field of spaceflight research, where bedrest was used as surrogate for zero gravity conditions, showed that prolonged recumbent positioning had negative effects on various physiological regulatory systems (60). Early mobilization and physiotherapy are widely recognized as modern clinical practice nowadays (2). Nonetheless, inpatients still experience long periods of reduced physical activity and bedrest (4). Hospital associated deconditioning as well as low physical activity levels of patients (61) are subjects of research (62).

1.3.1 Physiological Implications of Bedrest

Under normal conditions, the human body is constantly exposed to the effects of gravity and has "evolved to function optimally in the upright position for around 16 hours per day" (10). Prolonged periods without the effects of gravity were not part of the natural evolutionary process that determined the structure and function of the human body since the process took place under the influence of gravity. Therefore, excessive bedrest as well as spaceflight pose challenges to a variety of physiological systems, such as the cardiovascular-, musculoskeletal-, respiratory-, hematological-, gastrointestinal-, endocrine-, nervous-, renal-, reproductive- and the immune-system (10,63–66).

Bedrest induces **cardiac deconditioning** (68). When placed in a horizontal position the cardiovascular system works under different premises than in an upright position. Cardiovascular adaptation mechanisms are dependent on gravity due to the influence of hydrostatic pressure on the cardiovascular system. In absence of gravitational effects, fluids are redistributed to upper body regions (69) and BP relatively increases in the aortic arch and carotid glomus, where baroreceptors are located. Consequently, mechanisms for blood pressure downregulation are triggered (see paragraph 1.1.4). This leads to increased fluid excretion (70). The reduced total amount of intravascular volume leads to reduced CO (68) and diastolic BP (71) and thus, reduced workload for the heart (72). Following the basic principle of “use it or lose it” (1) left ventricular muscle mass decreases (73), resulting in diminishing cardiovascular power (74). Another aspect of the deconditioning process is reduced baroreceptor sensitivity. In an upright position the pressure difference between the heart and the location of the baroreceptors (usually above heart level) is higher than in a horizontal position. When placing the bodies´ longitudinal axis in a horizontal position, both locations are on the same level and exposed to the same hydrostatic pressure. This leads to decreased effectiveness of the baroreceptor reflex (71) and to decreased inotropic and chronotropic effects upon activation. Both, animal studies and studies with human subjects have shown that measurable physiological changes indicating cardiac deconditioning already occur after several hours of head-down tilt positioning (75,76).

Also the phenomenon of **OH** and **orthostatic intolerance** (dizziness and nausea upon standing up, possibly accompanied by postural instability) (see 1.2) is etiologically linked to bedrest (77). Bedrest and bedrest related issues have been stated as high-risk factors for OH and orthostatic intolerance in numerous studies (78–80). Many of the causes given in the literature for OH (57) are caused or promoted by excessive bedrest and lack of gravitational influences by contributing to cerebral hypoperfusion. As stated above bedrest leads to increased fluid excretion and hypovolemia. It does so by redistributing fluid to the upper body half. Activation of baroreceptors and increasing levels of BP lowering hormones are the result. The following lack of intravascular fluid leads to decreased VR upon standing up. Pre-load and ventricular filling are therefore also reduced. According to the Frank-Starling-Law, CO decreases and the heart is incapable of producing sufficient MAP to maintain sufficient cerebral perfusion. The problem of decreasing VR

additionally is persevered by decreasing muscle mass in the lower extremities upon excessive bedrest. As shown in the cardio-postural model (81), the skeletal muscle pump plays an important role in the maintenance of sufficient VR and cardio-postural control (see Figure 11). Reduced mass of muscular tissue surrounding lower extremity veins decreases the amount of fluid that is propelled back to the heart upon standing up. Bedrest has also shown to reduce the sensitivity of the baroreceptor reflex. As explained earlier, the altered effect of hydrostatic pressure on the cardiovascular system results in an attenuation of the baroreceptor response to orthostatic challenge. This not only has direct effects on the heart, but it also leads to a diminished orthostatic vascular response. Upon standing up, lower baroreflex activation leads to less distinct sympathetic stimulation of peripheral blood vessels, less vasoconstriction, and less increase in TPR. This, on the one hand, directly decreases MAP (MAP = CO x TPR), it also leads to decreased fluid shift into the low-pressure system and thereby also reduces VR. Consequently, MAP decreases and cerebral perfusion is reduced.

Ultimately the described cascade of deconditioning effects of bedrest lead to increased **risk of falls** and fall related injuries. Several sources in the context of fall prevention and geriatrics have pointed to increased incidence of falls and related injury in the elderly and upon bedrest (58,81–83). OH is a strong contributor to the occurrence of falls (84) and can, as shown above, be facilitated by bedrest (85). Reasons for higher risk of injury upon falling include decreases in bone density (86) and increased overall frailty upon bedrest (87).

The deconditioning effects of bedrest are analogous to general signs of aging. Reduced muscle mass, decreased CO and brain perfusion, loss of bone mass and postural instability as well as cognitive impairment can be observed under both circumstances (88). From this, it becomes clear that the two conditions mutually reinforce each other and thus older persons are especially affected. Global demographics are shifting towards an older average age (89). As a result, the importance of fall prevention is increasing and the costs resulting from falls represent a considerable share of total healthcare costs (13). Upon injury, elderly patients can enter a downward spiral of bed rest and further injury from falls. Patients enter the hospital because of their initial injury, experience bedrest confinement during their treatment and are consequently more susceptible to again falling because of the deconditioning effects of bedrest confinement (81). Also, research

has shown that falls is associated with increased mortality in elderly people (90) and decreases in life quality (91).

1.3.2 Clinical Context

Patients spent most of their time in hospital lying in bed (81). Although it might not explicitly be prescribed by the doctor, confinement in bed prevails and possibilities to stay physically active are limited during hospitalization (83). In most settings, patients are supplied with in-bed-entertainment as nursing care of stationary and resting patients is more resource-effective compared to physically active and moving patients (92). Along with limited personal resources in e.g., physical therapy and nursing staff, also impairments due to illness restrict mobilization. Especially patients after cardiac surgery are highly limited in mobility (93). They are under surveillance at the Intensive Care Unit (ICU) and suffer from pain as well as cardiovascular stress due to traumatizing surgery. As a result of bedrest confinement, patients not only have to recover from surgery and fundamental disease, but they are also exposed to the deconditioning effects as described above (93,94).

In summary, the obstacles to sufficient mobilization of hospitalized patients and the negative consequences for patient health show, that there is a clear need for simple, effective, and implementable measures to address the problem of excessive bed rest.

2 Aims and Objectives

2.1 Aims

The main aim of this thesis was to examine the effects of head up tilt positioning on patients´ postural cardiovascular control after cardiac surgery.

2.2 Objectives

Positioning the body in 15° head-up-tilt could impact several cardiovascular parameters. As described above, negative effects of bedrest result from reduction of gravitational effects on the human body and the cardiovascular system. The idea is, to counter this by exposing the body to more orthostatic loading with the intervention. Bedrest confinement leads to cardiac deconditioning, loss of muscle and bone mass, reduced SV, CO and brain perfusion and desensitization of the baroreceptor reflex and consequently to impaired cardio-postural control and increased fall risk. Increasing hydrostatic pressure on lower body regions by head-up tilting, could help train postural cardiovascular control and keep adaptation mechanisms more engaged compared to flat recumbency. Higher leg perfusion and muscle-pump activation should lead to higher VR and consequently have positive influences on SV, CO, brain perfusion and MAP during orthostatic challenge. Engaging the baroreceptor reflex should adverse it´s deconditioning during post-surgical rehabilitation and could lead to higher HR, and TPR upon standing up, resulting in improved brain perfusion and less orthostatic intolerance. Also, the intervention could have positive effects on the recovery from orthostatic challenge and lead to quicker return to initial values after performing the STS-Test. HR and TPR could normalize quicker after reassuming the initial body position, due to positive effects of the intervention on baroreceptor reflex activity.

2.3 Hypothesis

Applying 15 ° head up tilt positioning for 10 minutes per day over the duration of one week in patients after cardiac surgery has measurable effects on cardiovascular parameters during the STS-Test.

3 Methods

A prospective design was chosen to conduct this study. Interventions and measurements were performed at the Department of Cardiac Surgery of the Landeskrankenhaus (LKH) Graz. Measurements were carried out by researchers of the Department of Physiology, Medical University of Graz and medical doctors of the Department of Cardiac Surgery (LKH) and assisting students.

3.1 Ethical Approval

Ethical approval was obtained beforehand by the ethics committee of the Medical University of Graz (EK: 31-343 ex 18/19). The declaration of Helsinki was implemented in the design and realization of this research project. All participants were informed accordingly and gave their written consent for their role in the study.

3.2 Study Protocol

3.2.1 Subject Selection

Potential participants for the study were approached by involved members of the Department of Cardiac Surgery upon beginning their course of treatment.

3.2.1.1 Inclusion Criteria

Eligible to participate in the study were patients between the ages of 65 and 85 years after conventional aortic valve replacement or elective coronary bypass surgery who were not affected by the following exclusion criteria and gave their written consent beforehand.

3.2.1.2 Exclusion Criteria

Not eligible to participate in the study were patients fulfilling one or more of the following criteria:

- Euro Score II > 8 (95)
- Patients in a state of delirium on the second postoperative day
- Patients depending on artificial ventilation on the second postoperative day
- Patients in need for higher doses of catecholamines on the second postoperative day, i.e., Noradrenalin > 0.05-0.1 µg/kg bodyweight, Suprarenin > 0.05-0.1 µg/kg bodyweight, Dobutrex > 5 µg/kg bodyweight.
- Patients with preexisting thromboses detected via ultrasound screening before surgery

3.2.2 Group Allocation and Randomization

The participants were randomized and allocated to one of the groups listed below. Randomization was executed with the Medical University of Graz online service randomizer.at.

3.2.2.1 Intervention Group

This study group consisted of eight randomly assigned patients (n=8). Interventions in this group consisted of 10 minutes of 15° head up tilt bed positioning additionally to standard physiotherapy. Interventions were performed daily for one week, starting on the second day post-surgery. Purpose of this group was to compare the head up tilt positioning to standard physiotherapy. Data from this group after completion of the intervention cycle, compared to data from the control group, are the focus of this diploma thesis.

3.2.2.2 Control Group

The eight individuals (n=8) assigned to study group C served as control group and received standard physiotherapy (including sitting upright in bed and standing up) only. Measurements were conducted at the same times and in the same manner as in the intervention group. Besides standard physiotherapeutic treatment no additional interventions were carried out on the patients in this group.

3.2.3 Dropouts

Not all patients who entered the study generated useable data during their whole course of treatment. Due to poor data quality, missing data or artefacts not all measurements where statistically evaluable. The following table shows the development of group numbers and drop-outs during the study. The pre-intervention measurement was performed along with first mobilization 24-48 hours post-surgical. The post-intervention measurement was conducted 7 days post-surgical.

	Pre-Intervention Measurement	Post-Intervention Measurement
Intervention Group (n=8, 1 female)	7	5
Control Group (n=8, 2 female)	7	6
Total	14	11

Table 1: numbers of patients by group and measurement date

3.2.4 Data Acquisition

Data were collected at the Department of Cardiac Surgery of the Medical University of Graz. Measurements took place at defined times in the morning pre- and postsurgical. Data analyzed in this thesis were part of the CARDIOVIB study, which also looked at vibration exercise as a measure to counteract the effects of bedrest. Results from that part of the study are reported in another thesis (96). Figure 11 outlines the study process for the whole study. For the present thesis only data emerging from the measurements pre- and post-intervention and from groups B (head-up tilt) and C (control) was relevant.

The first measurement was performed pre-surgery at the time of the patients´ admission to the hospital, usually 24 hours pre-surgery. The second measurement took place 24-48 hours after surgery, at the time of first mobilization in the ICU and before any intervention was performed. After the post-surgical measurement, the patients´ treatment followed one of the three different paths determined by their group assignment. After 7 days of group specific treatment patients were measured again to collect data on possible impacts of their respective intervention. The fourth and final measurement was planned to be conducted as a follow up three months after hospital discharge.

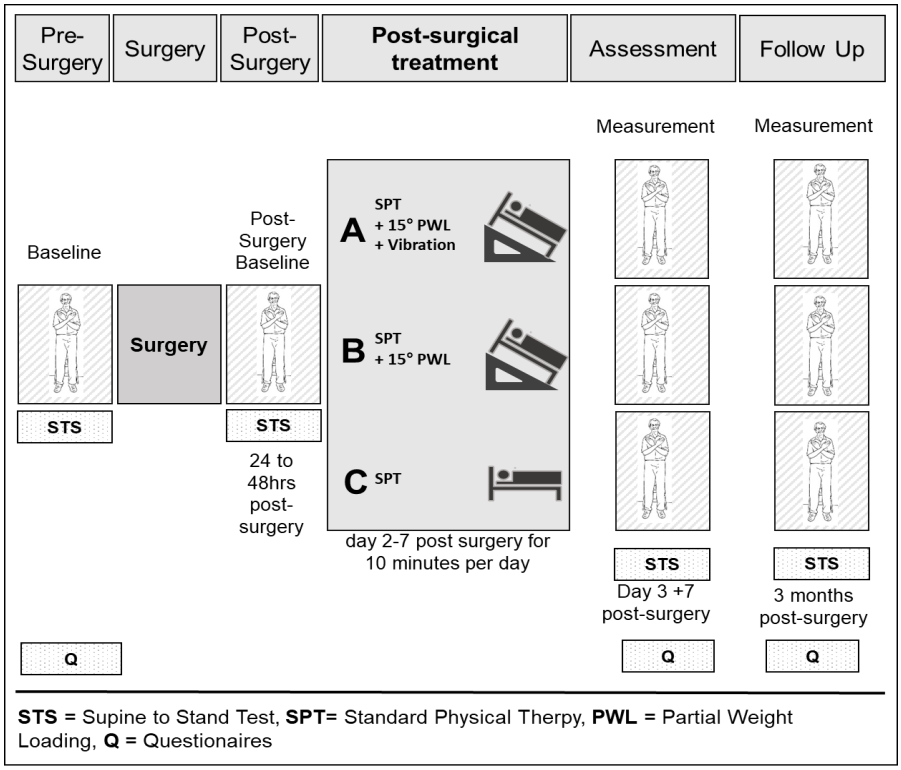

Figure 11: schematic depiction of the study protocol for the CARDIOVIB study, of which this thesis is a part of (Source: study protocol)

3.2.4.1 Supine-To-Stand Test

To evaluate data of cardiovascular adaptation to postural changes, measurements were conducted while patients performed a Supine-To-Stand-Test (STS-Test). The procedure consisted of three stages and was followed during each measurement. Measuring devices were installed and data were recorded continuously during the whole process.

First, baseline values were collected while patients were lying on their back in a horizontal position for five minutes (supine). The second stage consisted of five minutes of standing in an upright position to collect data on adaptation processes upon standing up. For the upright position it was important that patients were standing still with their feet placed 10 cm apart on a sway sensor plate, hands folded to their sides with their head directed straight ahead without moving (stand). With patients being impaired under postsurgical conditions it was expected that not all patients would be able to complete this period. In case of discontinuance of the standing phase, the successfully passed time was documented and emerging data were counted as valid. The third stage of the STS-Test consisted of a recovery phase and horizontal recumbency for five minutes (supine). Since standing up on the first or second day after surgery was challenging for patients and took longer than in healthy individuals, the transition phase from supine to standing up was affected by many artifacts and thus was not included in the statistical analyses. For statistical processing, measurements were assigned to distinct epochs during the STS-Test (see Figure 12). Each epoch comprised 10 seconds of the test. Epoch 1 provided baseline values before mobilizing the patient. Epochs 2, 3 and 4 represent the first 30 seconds after taking an upright position. Epochs 5, 6 and 7 show the first 30 seconds of the recovery phase with the patient lying horizontally again. Epoch 8 represents the last 10 seconds of the STS-Test and thus the final recovery phase.

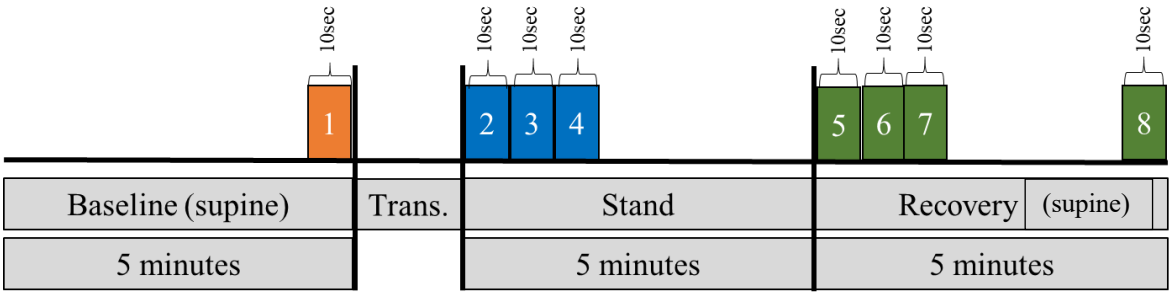

Figure 12: Illustration of Time Epochs during the STS-Test (Source: study protocol)

3.2.5 Documentation

Data were stored pseudo-anonymized and encrypted. Patients' identities were encrypted via case numbers allowing relevant background information to be connected to individuals without revealing their identity to the reader.

3.2.6 Measuring Device

3.2.6.1 Task Force Monitor (TFM)

The Task Force Monitor (TFM, CNSystems, Graz, Austria) was used to measure a variety of hemodynamic parameters. It included oscillometric and plethysmographic measurement of BP, electrocardiographic HR analysis and measurement of thoracic impedance delivering parameters such as stroke volume, cardiac output and total peripheral resistance. Heart rate variability allowed to draw conclusions on vegetative nerval balance.

For the present thesis the relevant parameters were HR, MAP and TPRI. These parameters were calculated by the TFM based on the data it measured and were put out in the units of beats per minute (BPM) for HR, mmHg for MAP and dyne*s*m^2/cm^5 for TPRI·

3.3 Statistics

3.3.1 Main Target Variables

Main target variable of the present thesis was the cardio-postural control defined by hemodynamic parameters, in particular MAP, HR and TPRI.

3.3.2 Null Hypothesis

Exposing patients to 15 ° head up tilt positioning for 10 minutes per day in addition to the standard physiotherapeutic treatment has no relevant effects on postoperative cardiovascular parameters contributing to cardio-postural control.

3.3.3 Alternative Hypothesis

Exposing patients daily to 15 ° head up tilt position in addition to standard physiotherapeutic treatment has measurable effects on orthostatic cardiovascular control compared to standard treatment. In accordance with the mechanisms described in paragraph 1.1 it would be assumed that patients in the intervention group would show improved hemodynamic adaptation to postural change.

3.3.4 Sample Size and Informative Value

Planned sample size in this pilot study was 10 individuals per group, adding up to 20 participants in total. With this study being a pilot study, at the time of designing the protocol it was not yet possible to determine a number of cases needed to generate valid data.

3.3.5 Statistical Analysis

Statistical analyses included descriptive statistics and comparative statistical analyses of parameters within and between the two groups of interest. Data were explored regarding their distribution and outliers, largely deviating from the respective group mean, were excluded. Comparisons between the groups were intended to be analyzed by repeated measures ANOVA, however due to the low sample size, univariate two-way ANOVAs were performed to compare the groups regarding single epochs during the STS-Test. All data were analyzed using IBM SPSS Statistics 28.

4 Results

This Chapter will depict results and statistical analyses of the cardiovascular parameters HR, MAP and TPRI. The tables shown in paragraph 4.2. describe medians and standard deviations for MAP, HR and TPRI at the different time epochs during the STS-Test and statistical analyses between the intervention group and control group 24-48 hours after surgery and on the 7th post-surgical day.

4.1 Patients

In total 27 patients were enrolled and participated in the measurements of this pilot study. The study sample consisted of 6 female and 21 male individuals.
Descriptive statistics of the patients anthropometric data are summarized in Table 2.

	Age in years		Weight in kg		Height in cm	
	Mean	SD	Mean	SD	Mean	SD
Intervention Group (n=8, 1 female)	68,50	6,57	87,19	16,46	178,13	7,12
Control Group (n=8, 2 female)	68,25	7,48	78,44	10,59	169,44	9,47
Total (n=16)	68,38	6,80	81,20	14,11	172,67	9,18

Table 2: descriptive statistic for anthropometric patient data by group

4.2 Statistics

To evaluate the effects of the intervention (PWL) on cardiovascular adaptation, the two groups were compared by repeated measures ANOVA, applying epochs (see Figure 13) as the repeated measures factor and group (Intervention vs. Control) as the between-subjects factor. Comparisons included group differences 24-48 hours post-surgery as well as 7 days post-surgery. Due to the low sample size of reliable data post-surgery, each epoch of the 7 days post-surgery data was also compared between the groups and contrasted as change between baseline and stand/recovery.

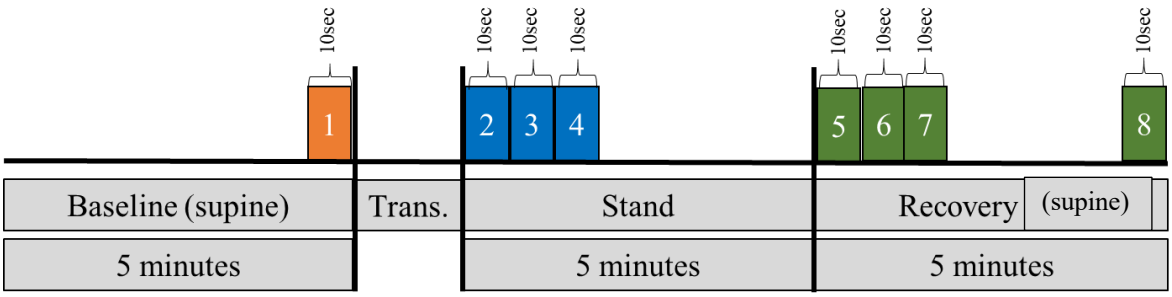

Figure 13: Epochs and the times they represent during the STS-Test (Source: study protocol)

4.2.1 Pre-Intervention Measurement

The first measurement shown took place between 24 h and 48 h post-surgery, depending on the physical condition of the patient. No interventions had been performed by that time and the measurements were conducted along with first mobilization attempts in the ICU of the Department of Cardiac Surgery.

4.2.1.1 HR

Comparison of the heart rate during the STS test pre-interventional revealed significant changes between the epochs ($F_{(3.3, 26)}$=4.742, p<.001, ε=.47, η^2= .377), but no significant differences between the groups (see Table 3). HR increased during the epochs of standing and returned to baseline during recovery in both groups.

The following table shows the results for the parameter HR in the unit of bpm prior to any intervention.

Descriptive Statistics HR in bpm pre-intervention

	Intervention Group (n=6)		Control Group (n=4)	
	Mean	SD	Mean	SD
Baseline	83	4,05	82	10,88
Stand 1	84	11,18	98	13,64
Stand 2	89	7,56	98	15,24
Stand 3	88	9,33	98	15,52
Recovery 1	84	4,60	89	14,79
Recovery 2	86	7,72	88	14,87
Recovery 3	85	5,51	89	14,47
Recovery 4	82	1,88	85	11,77

Table 3: descriptive statistics - HR in bpm - pre-intervention

4.2.1.2 MAP

Due to loss of data in several epochs, each epoch was contrasted to the baseline by 2-way ANOVA separately, applying group as the between-subjects factor. Significant group x epoch effects were found for stand 1 ($F_{(1, 7)}$=7.350, p=.030, η^2= .512), a tendency for stand 2 ($F_{(1, 7)}$=4.823, p=.064, η^2= .408) and stand 3 ($F_{(1, 7)}$=5.233, p=.056, η^2= .428), where there was also a main effect for group ($F_{(1, 7)}$=9.867, p=.016, η^2= .585) indicating higher MAP in the control group (see Table 4).

The following table shows the results for the parameter MAP in the unit of mmHg prior to any intervention.

Descriptive Statistics MAP in mmHg pre-intervention

	Intervention Group			Control Group		
	N	Mean	SD	N	Mean	SD
Baseline	3	78	13,44	3	77	10,30
Stand 1	5	72	23,28	4	118	27,44
Stand 2	5	79	22,51	4	118	25,36
Stand 3	5	*65	24,90	4	111	20,83
Recovery 1	5	97	43,82	6	76	10,69
Recovery 2	5	94	31,54	6	79	8,72
Recovery 3	5	94	26,62	6	81	12,49
Recovery 4	4	79	9,11	5	78	11,02

Table 4: descriptive statistics - MAP in mmHg - pre-intervention – due to compromised data in several epochs, each epoch was contrasted to the baseline by 2-way ANOVA separately. Sample numbers varied, depending on the amount of missing data and are shown in an extra column for each epoch.

4.2.1.3 TPRI

Data from the pre-intervention measurement showed no significant differences between the groups regarding TPRI.

The following table shows the results for the parameter TPRI in dyne*s*m^2/cm^5 prior to any intervention.

Descriptive Statistics TPRI in dyne*s*m^2/cm^5 pre-intervention

	Intervention Group (n=3)		Control Group (n=3)	
	Mean	SD	Mean	SD
Baseline	2808,07	920,05	2065,77	762,87
Stand 1	2652,03	336,88	3131,23	1344,86
Stand 2	2848,93	741,68	3666,40	1059,06
Stand 3	2393,27	535,89	3276,97	775,88
Recovery 1	2736,87	889,55	2357,23	611,32
Recovery 2	2961,73	1165,76	2509,73	399,57
Recovery 3	2452,50	305,56	2458,57	987,81
Recovery 4	3091,50	1415,79	2846,63	825,03

*Table 5: descriptive statistics - TPRI in dyne*s*m2/cm5 - pre-intervention*

4.2.2 Post Intervention Measurement

The second measurement was conducted on the 7th day post-surgical after interventions and/or standard physical therapy had been performed daily in the course of treatment. With effects of the intervention adding up day by day with each execution, possible impacts can be expected to show more clearly after a number of days of treatment.

4.2.2.1 HR

After seven days of intervention, aside the main effect for epochs ($F_{(1.8, 12.3)}$=17.75, p<.001, ε=.25, η^2= .717), a significant main effect was also found for group ($F_{(1, 7)}$=6.76, p<.035, η^2= .49) indicating a higher heart rate in patients of the intervention group compared to the control group (see Figure 10, Table 6).

The HR change from baseline to epochs during stand and recovery revealed no significant group effects, though a tendency for stand 3 (interaction: $F_{(1, 8)}$=3.605, p=.094, η^2= .311) towards a larger HR increase in patients of the intervention group and higher HR during recovery 4 (interaction: $F_{(1, 8)}$=4.67, p=.067, η^2= .40).

The table below shows the results for the parameter HR in bpm after the intervention was carried out daily for one week.

Descriptive Statistics HR in bpm post-intervention

	Intervention Group (n=5)		Control Group (n=4)	
	Mean	SD	Mean	SD
Baseline	74	7,67	72	7,19
Stand 1	92	6,52	82	2,82
Stand 2	91	7,07	81	2,11
Stand 3	89*	6,67	83	7,42
Recovery 1	84	7,80	75	2,88
Recovery 2	84	7,52	71	1,37
Recovery 3	83	7,51	73	3,49
Recovery 4	77	6,08	69	3,48

Table 6: descriptive statistics - HR in bpm - post-intervention

Graphical comparison:

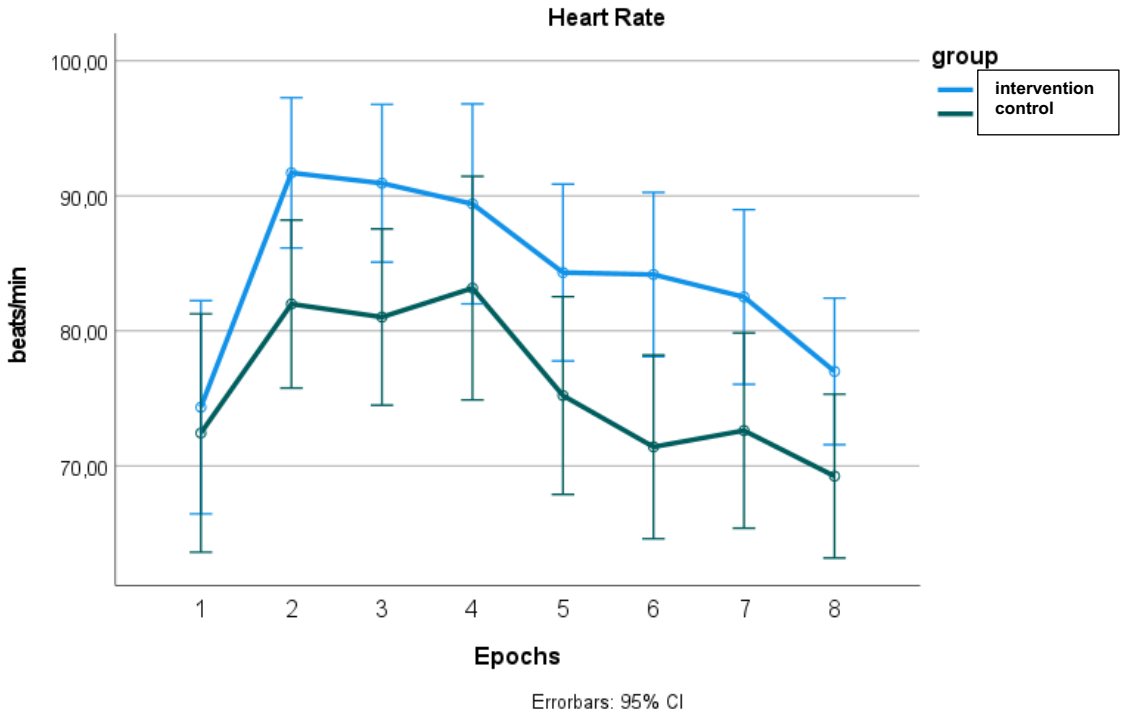

Figure 14: graphic depiction of results - HR in BPM - post-intervention

4.2.2.2 MAP

Regarding MAP no significant differences between the groups were found after 7 days of intervention. Comparison of the single epochs contrasted to baseline and group by a two-way ANOVA, however, revealed a tendency towards lower MAP at the end of the recovery in the intervention group ($F_{(1, 7)}$=4.156, p=.081, η^2=.37).

The table below shows the results for the parameter MAP in mmHg after seven days of intervention.

Descriptive Statistics MAP in mmHg post-intervention

	Intervention Group			Control Group		
	N	Mean	SD	N	Mean	SD
Baseline	4	85	6,57	3	100	1,05
Stand 1	4	105	37,37	5	98	19,53
Stand 2	4	96	27,45	5	96	28,09
Stand 3	4	96	25,89	4	103	11,45
Recovery 1	5	92	9,03	5	87	16,15
Recovery 2	5	93	13,45	5	87	16,26
Recovery 3	5	90	10,75	5	89	18,61
Recovery 4	4	69	13,76	5	92	18,61

Table 7: descriptive statistics - MAP in mmHg - post-intervention – due to compromised data in several epochs, each epoch was contrasted to the baseline by 2-way ANOVA separately. Sample numbers varied, depending on the amount of missing data, and are shown in an extra column for each epoch.

Graphical comparison:

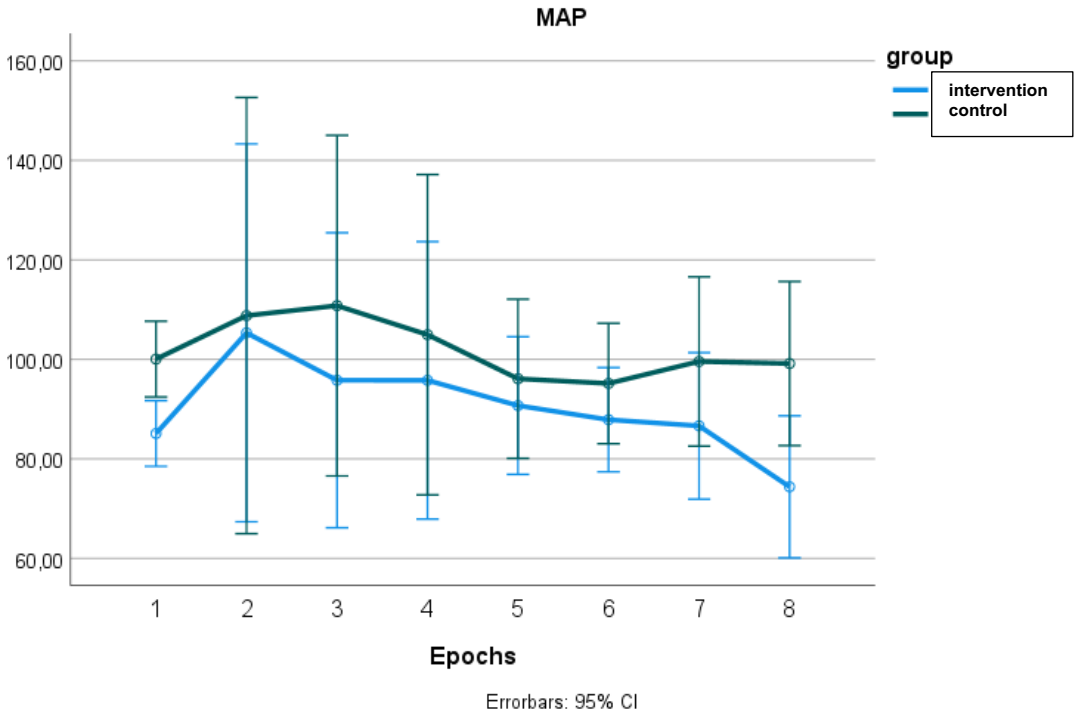

Figure 15: graphic depiction of results - MAP in mmHg - post-intervention

4.2.2.3 TPRI

Due to the low sample size for TPRI only comparisons of single epochs were performed. Aside a main effect ($F_{(1,7)}$=7.393, p=.030, η^2=.51) indicating a significant decrease of TPRI at the beginning of the recovery compared to baseline, a significant interaction for group was found at the end of recovery ($F_{(1,7)}$=6.059, p=.043, η^2=.0464) indicating lower TPRI in the intervention group.

The table below shows the results for the parameter TPRI after seven days of intervention (intervention group) or standard physiotherapy (control group).

Descriptive Statistics TPRI in dyne*s*m^2/cm^5 post-intervention

	Intervention Group (n=4)		Control Group (n=2)	
	Mean	SD	Mean	SD
Baseline	2906,05	436,27	3196,85	560,52
Stand 1	2677,94	2019,47	1760,50	563,28
Stand 2	2504,73	1441,75	2694,50	122,33
Stand 3	2340,55	1003,46	2672,35	218,71
Recovery 1	2650,52	481,50	2042,30	336,30
Recovery 2	2780,13	397,42	2396,25	173,88
Recovery 3	2795,48	542,81	3217,30	641,63
Recovery 4	2679,65	606,95	3301,40	380,42

*Table 8: descriptive statistics - TPRI in dyne*s*m^2/cm^5 - post-intervention*

Graphical comparison:

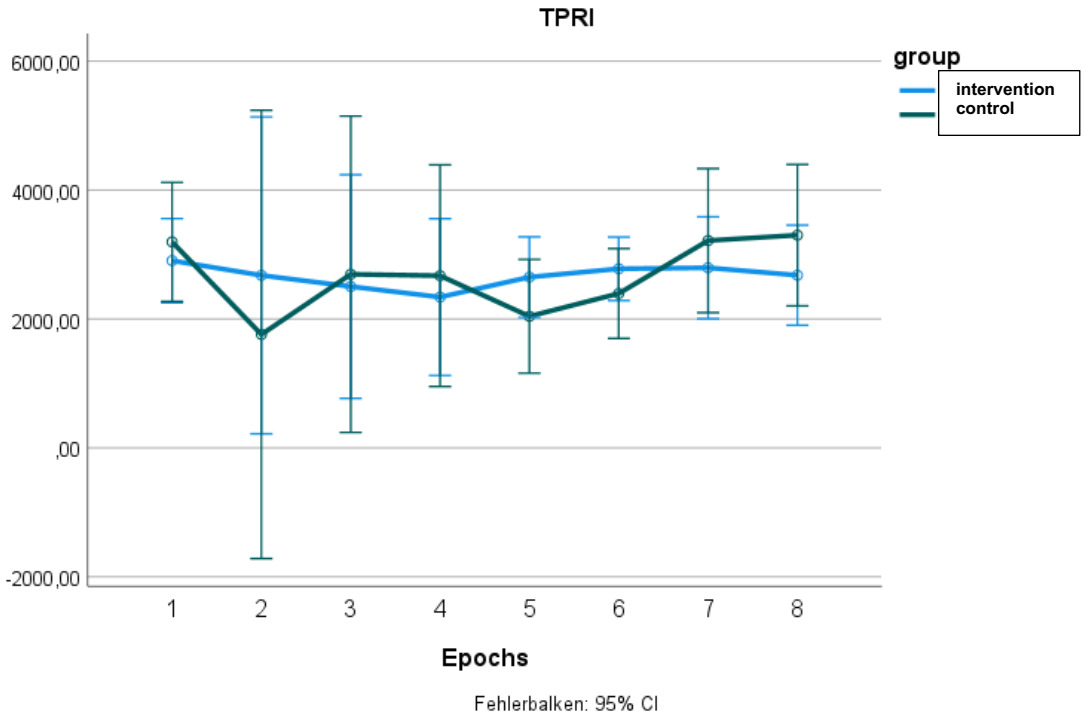

*Figure 16: graphic depiction of results - TPRI in dyne*s*m^2/cm^5 - post-intervention*

5 Discussion

Data emerging from the pre-intervention measurement by large reflected physiological cardiovascular adaptation during the STS-Test. HR increased upon standing up and redeveloped during the recovery phase. MAP and TPRI values showed no decreases, giving no indications for the occurrence of OH or excessive fluid pooling in the lower extremities upon standing up. A significant difference between the two groups could be seen concerning MAP upon standing up (p=.016) before the intervention. This could possibly be attributed to different durations of the transition phase between recumbency and standing up and consequent differences in adaptation mechanism activation. Data showed lower HR adaptability to postural changes in this measurement than in the following. Changes in vascular tone, reflected by TPRI, where low. This could be attributed to impairments resulting from the stresses of the surgery.

The post-intervention measurement showed the same general trends. Adaptability to postural change though was more pronounced at the time of the second measurement. This could reflect progressing convalescence and improved general cardiovascular condition after seven days of rehabilitation. No signs of OH could be detected in neither of the two measurements.

Effects of the intervention

Since the aim of this research was to explore effects of the intervention on the cardio-vascular performance, the following shows the focus of interest in this thesis. Statistical analysis of data recorded after seven days of group specific treatment revealed a significant main effect (p<.035), showing a higher **HR** in the intervention group upon standing up. In addition, a tendency for stand 3 (interaction: p=.094) towards a larger HR increase in patients of the intervention group and higher HR during recovery 4 (interaction: p=.067) was shown. This suggests improved cardio-postural control in the intervention group. Patients in the intervention group received more orthostatic loading during their treatment than patients in the control group. This improved leg perfusion, induced higher VR, and consequently led to higher CO and cardiac training. Thereby, tilt-treatment countered deconditioning effects of bedrest on the cardiac function and furthermore improved patients´ adaptability to orthostatic challenge.

For the parameter **TPRI** a significant group effect in terms of lower TPRI in the intervention group was shown at the end of the recovery phase (p=.043). This indicates more effective recovery from orthostatic challenge in the intervention group. The head-up tilting presumably countered deconditioning of the baroreceptor reflex which remained more sensitive to increased BP in the upper body region after lying down again and thereby mediated a higher decrease in TPRI in the intervention group. The delay between lying down and the decrease in TPRI can be explained by the fact, that the baroreflex initially compensates via HR and subsequently via vascular tone.

Regarding **MAP,** analysis of group effects revealed no significant difference between the two groups. No significant decrease in MAP occurred after standing up during the STS-Test. Hence, no signs of OH could be detected.

In summary the results show that head-up tilt positioning is a safe and effective measure to counteract deconditioning effects of bedrest in a clinical setting. Patients received more orthostatic loading because of the intervention and compensation mechanisms to orthostatic challenge could be engaged successfully. Therefore, cardiovascular deconditioning was less present in the intervention group and patients showed improved cardio-postural control upon standing up during the STS-Test as well as improved recovery from orthostatic challenge in the recovery phase of the Test.

Studies in the context of geriatrics, fall prevention and microgravitational environments have looked at different measures to counteract deconditioning effects of bedrest confinement. Greenleaf et al. investigated effects of isotonic or isokinetic exercise on orthostatic responses upon head down bedrest, though were not able to identify significant benefits of either treatment (97). In 2010, Shibata et al. looked at supine cycling and volume loading to address cardiovascular deconditioning upon bedrest and were able to identify positive effects (16). Lower body negative pressure combined with exercise showed effective against bedrest deconditioning in research conducted by Watenpaugh et al. in 2000 (98). Physical exercise in various forms has been identified as a potent way to address OI because of its positive effects on the cardiovascular system (46).

The above described countermeasures to bedrest deconditioning, show a high level of demand in time, financial, technical or personnel resources. In addition to illness-

related factors, bed rest also results from structural deficits in health care and therefore, countermeasures should be made as easy as possible. No machines are needed to implement head-up tilting in everyday hospital routine, since most beds already are tiltable. Physical exercise can be very demanding for sick people and a rigorous exercise regime is not practicable for all patients, especially under post-surgical conditions. Head-up tilt positioning presents a very gentle way of engaging cardio-postural adaptation mechanisms and can therefore be used on a wider range of patients. Administering pharmaceutical products to counteract bedrest (e.g., volume loading) is a more invasive measure compared to head-up tilting and thus offers more room for adverse side effects.

The bottom line is that head elevation is effective in terms of cost, personnel, and time compared to other cardiovascular deconditioning countermeasures that have been studied. In addition, it is also an effective and gentle measure with a wide range of applicability that can benefit patients in many clinical situations, even at the ICU.

5.1 Limitations

During the conduct of this study limiting factors came up and complicated the realization of the project.

Due to low sample numbers (one female patient in the intervention group) it was not possible to take gender differences into consideration when performing statistical analysis. Since it is known that women and men differ in BP regulation, further research should aim at a balanced gender ratio.

To improve the informative value, sample sizes in both groups should be higher than in this pilot study.

Furthermore, ten minutes per day of standardized positioning can be overshadowed by other factors as e.g. patients regaining mobility and walking around with progressing recovery. Longer duration of head up tilt positioning (several times per day), especially during the beginning of recovery after surgery, could amplify it´s effects and make them more presentable.

Implementing the study in everyday hospital life proved to be difficult. Nursing staff´s working routine and department structure sometimes made it difficult to find time slots to perform focused and undisturbed measurements. Measurements during the first mobilization in the ICU were especially difficult. For future projects

communication with hospital staff should be improved and nursing staff should be involved from the very beginning to understand the aim and benefits of the interventions.

Another possible adversity consisted in the duration of the transition phase between lying flat and standing up. Some patients showed better post-operative fitness and where able to stand up quicker. Others had to sit on the edge of the bed for longer time, before assuming an upright position. Cardio-postural compensation mechanisms where thereby possibly activated differently from patient to patient, which could have had effects on the outcome. In future research, a more standardized execution could be beneficial.

Performing the intervention of 15 ° Head Up Tilt left room for improvement because adjustability of hospital beds varied. Different types of beds where used in the different hospital units where interventions were performed. In order to guarantee a standardized implementation of interventions and improve data quality all used beds should be equally adjustable.

5.2 Conclusion and future directions

15° head up tilt positioning for 10 minutes a day additionally to standard physiotherapeutic treatment showed significant improvement of the patients´ orthostatic cardiovascular control. The study displayed a safe way to engage cardio-postural adaptation mechanisms during recovery and thereby counteracted the deconditioning effects of bedrest.

Future research should address these findings and aim to increase the duration, frequency and intensity of the intervention. On the one hand, this means that the duration of head elevation should be increased and/or performed more often. On the other hand, the angle of inclination should be increased and passive stance should be approximated. In this way, orthostatic loading during the rehabilitation process could be increased and cardio-postural adaptation mechanisms could be engaged to a greater extent. Thereby the cardio postural reactions could be trained more effectively and even better results could be achieved.

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