

# **Diplomarbeit**

## **Effects of Resistive Vibration Exercise on Physiological Responses**

eingereicht von

**Alexander Holzhausen**

zur Erlangung des akademischen Grades

**Doktor der gesamten Heilkunde**

**(Dr. med. univ.)**

an der

**Medizinischen Universität Graz**

ausgeführt am

**Lehrstuhl für Physiologie**

unter der Anleitung von

**Assoz. Prof. Priv. Doz. Dr. med. Dr. med. univ. MMedSci PhD. Nandu**

**Goswami**

und

**Mag. Dr.rer.nat. Karin Schmid-Zalaudek**

Wien 26.08.2021

*Eidesstattliche Erklärung*

*Ich erkläre ehrenwörtlich, dass ich die vorliegende Arbeit selbstständig und ohne fremde Hilfe verfasst habe, andere als die angegebenen Quellen nicht verwendet habe und die den benutzten Quellen wörtlich oder inhaltlich entnommenen Stellen als solche kenntlich gemacht habe.*

*Wien, am 26.08.2021*

*Alexander Holzhausen eh.*

## I. Acknowledgment

I would like to thank all the patients who participated in this study, without them we would not have been able to conduct this research. A big thank you goes to my supervisors Assoz. Prof. Priv.-Doz. Dr.med.univ. MMedSci PhD.Nandu Goswami and to Mag. Dr.rer.nat. Karin Schmid-Zalaudek and to the whole team of physiology and cardiac surgery.

## Table of Content

<b>I. ACKNOWLEDGMENT .....</b>	<b>3</b>
<b>II. GLOSSARY AND ABBREVIATIONS.....</b>	<b>6</b>
<b>III. LIST OF FIGURES.....</b>	<b>7</b>
<b>IV. LIST OF TABLES .....</b>	<b>8</b>
<b>V. ZUSAMMENFASSUNG.....</b>	<b>9</b>
<b>VI. ABSTRACT.....</b>	<b>10</b>
<b>1 INTRODUCTION.....</b>	<b>11</b>
<b>1.1 IMMOBILITY .....</b>	<b>11</b>
1.1.1 DEFINITION OF IMMOBILITY .....	11
1.1.2 CONSEQUENCES OF IMMOBILITY .....	12
<b>1.2 REGULATION OF THE CARDIOVASCULAR SYSTEM.....</b>	<b>13</b>
1.2.1 BARORECEPTORS .....	13
<b>1.3 ORTHOSTATIC INTOLERANCE .....</b>	<b>14</b>
<b>1.4 ORTHOSTATIC SYNCOPE .....</b>	<b>15</b>
<b>1.5 THE CARDIO-POSTURAL MODEL .....</b>	<b>16</b>
<b>1.6 WHOLE BODY VIBRATION.....</b>	<b>17</b>
1.6.1 POSITIVE EFFECTS OF WHOLE BODY VIBRATION .....	17
1.6.2 NEGATIVE EFFECTS OF VIBRATION .....	17
1.6.3 SAFETY OF WHOLE-BODY VIBRATION THERAPY IN INTENSIVE CARE PATIENTS.....	17
<b>2 AIMS AND OBJECTIVES .....</b>	<b>18</b>
<b>2.1 AIM .....</b>	<b>18</b>
<b>2.2 OBJECTIVES.....</b>	<b>18</b>
<b>2.3 HYPOTHESIS .....</b>	<b>19</b>
<b>3 METHODS .....</b>	<b>19</b>
<b>3.1 ETHICAL APPROVAL.....</b>	<b>19</b>
<b>3.2 STUDY PROTOCOL .....</b>	<b>19</b>
3.2.1 PATIENT GROUPS .....	20
3.2.2 SIT-TO-STAND TEST (S-T-S TEST) .....	21
<b>3.3 SUBJECT INCLUSION AND EXCLUSION CRITERIA.....</b>	<b>22</b>
3.3.1 INCLUSION CRITERIA.....	22
3.3.2 EXCLUSION CRITERIA .....	22
3.3.3 DROPOUTS .....	23
<b>3.4 RANDOMIZATION.....</b>	<b>23</b>
<b>3.5 STATISTICS .....</b>	<b>23</b>
3.5.1 MAIN TARGET VARIABLE.....	23
3.5.2 NULL HYPOTHESIS.....	24

3.5.3	ALTERNATIVE HYPOTHESIS.....	24
3.5.4	NUMBER OF PATIENTS - SAMPLE SIZE.....	24
3.5.5	PLANNED STATISTICAL PROCEDURES.....	25
<b>3.6</b>	<b>STUDY DESIGN.....</b>	<b>25</b>
<b>3.7</b>	<b>DEVICES USED FOR MEASUREMENTS.....</b>	<b>25</b>
3.7.1	TASK FORCE MONITOR.....	25
3.7.2	BAGNOLI 8-CHANNEL EMG SYSTEM.....	26
3.7.3	NEAR-INFRARED SPECTROSCOPY (NIRS).....	26
3.7.4	DWL MULTIFLOW.....	26
3.7.5	ACS – ACCUSWAY BALANCE AND SWAY PLATFORM.....	27
3.7.6	BLOOD SAMPLES.....	27
<b>3.8</b>	<b>DEVICES USED FOR THE INTERVENTION.....</b>	<b>28</b>
3.8.1	GALILEO.....	28
<b>3.9</b>	<b>DOCUMENTATION.....</b>	<b>29</b>
<b>3.10</b>	<b>LITERATURE RESEARCH.....</b>	<b>29</b>
<b>4</b>	<b><u>RESULTS.....</u></b>	<b><u>30</u></b>
<b>4.1</b>	<b>PATIENTS.....</b>	<b>30</b>
<b>4.2</b>	<b>POST-OPERATIVE 48 HOURS.....</b>	<b>30</b>
4.2.1	GROUP A (RESISTIVE VIBRATION INTERVENTION).....	31
4.2.2	GROUP C (STANDARD PHYSIOTHERAPY).....	32
<b>4.3</b>	<b>POST-OPERATIVE 7 DAYS.....</b>	<b>34</b>
4.3.1	GROUP A (RESISTIVE VIBRATION INTERVENTION).....	34
4.3.2	GROUP C (STANDARD PHYSIOTHERAPY).....	36
<b>4.4</b>	<b>COMPARISON OF GROUP A AND C.....</b>	<b>38</b>
4.4.1	POST-OPERATIVE 48H.....	38
4.4.2	POST-OPERATIVE 7 DAYS – COMPARISON OF INTERVENTION.....	42
<b>5</b>	<b><u>DISCUSSION.....</u></b>	<b><u>46</u></b>
<b>5.1</b>	<b>INTERPRETATION.....</b>	<b>46</b>
<b>5.2</b>	<b>CONCLUSION.....</b>	<b>48</b>
<b>5.3</b>	<b>LIMITATIONS.....</b>	<b>48</b>
<b>6</b>	<b><u>REFERENCES.....</u></b>	<b><u>49</u></b>

## II. Glossary and Abbreviations

ANS: autonomic nervous system

BDNF: Brain-derived neurotrophic factor

CC: Cardiovascular Control

CO: Cardiac Output

COPD: Chronic obstructive pulmonary disease

dBp: diastolic Blood Pressure

EMG: Electromyography

HR: Heart Rate

Hz: hertz

ICU: intensive care unit

LKH: Landeskrankenhaus

MAP: Mean Arterial Pressure

MHz: megahertz

mmHg: millimetremillimeter of mercury

NIRS:; near-infrared spectroscopy

PC: Postural Control

PO: post-operative

RV: Resistive Vibration

S-T-S test: sit to stand test

sBP: systolic Blood Pressure

SPT: standard physio therapy

STS: supine to stand test

SV: Stroke Volume

TCD: Transcranial Doppler Sonography

TFM: task force monitor

TPR: total peripheral resistance

### III. List of Figures

Figure 1: Control mechanism for short-term regulation of MAP; The primary drop in arterial pressure, which was assumed here to be the result of blood loss, sets in motion a chain of regulatory processes that lead to sympathetic activation via the pressoreceptors and thus to increased cardiac activity and vascular constriction (20).....	13
Figure 2: Orthostatic cardiovascular reaction (26) .....	15
Figure 3: Cardio-postural interactions: Illustration of the cardio-postural components associated with mechanisms that prevent falls: Left—cardiovascular component of the regulation of blood pressure (blood volume, heart rate and vascular resistance); Right—sensory motor input components related to postural control; Center—cardio-postural integration: hypothesized as baroreflex activation of skeletal muscle pump (32).....	16
Figure 4: Illustration of the study protocol.....	20
Figure 5: Epochs from different phases of the S-T-S test included into the analyses. Trans. = Transition from supine to stand, 1-10 = epochs, each 10 sec.	25
Figure 6: Task Force Monitor® (TFM) for measuring haemodynamic parameters. ....	26
Figure 7: DWL Multiflow.....	27
Figure 8: AccuSway Balance and Sway Platform .....	27
Figure 9: Candidate connected to all examination equipment and ready for measurement.....	28
Figure 10: Galileo Training Device (Vibration plate) .....	29
Figure 11: HR of Group A and C - 48h post OP with mean HR during different epochs .....	39
Figure 12: sBP of Group A and C - 48h post OP with mean sBP during different epochs .....	40
Figure 13: SV of Group A and C - 48h post OP with mean SV during different epochs .....	42
Figure 14: HR of Group A and Group C during S-T-S Test 7d post-operative (after intervention) with mean HR during different epochs .....	43
Figure 15: change in sBP during S-T-S test of Group A and C - 7d post OP; blue line: Group A (Intervention) red line: Group C (no intervention) with mean sBP during different epochs .....	44
Figure 16: change in SV during S-T-S test of Group A and C - 7d post OP; blue line: Group A (Intervention) red line: Group C (no intervention) with mean SV during different epochs .....	45

## IV. List of Tables

Table 1: Dropouts and missing data of different parameters (HR, sBP, SV) in group A and C .....	23
Table 2: HR of Group A - 48h post OP .....	31
Table 3: sBP of Group A - 48h post OP .....	31
Table 4: SV of Group A - 48h post OP .....	32
Table 5: HR of Group C - 48h post OP .....	32
Table 6: sBP of Group C - 48h post OP .....	33
Table 7: SV of Group C - 48h post OP .....	33
Table 8: HR of Group A - 7d post OP .....	34
Table 9: sBP of Group A - 7d post OP .....	35
Table 10: SV of Group A - 7d post OP .....	35
Table 11: HR of Group C - 7d post OP .....	36
Table 12: sBP of Group C - 7d post OP .....	36
Table 13: SV of Group C - 7d post OP .....	37
Table 14: mean HR during the S-T-S test 48h post-operative in Group A and Group C .....	39
Table 15: : mean sBP during the S-T-S test 48h post-operative in Group A and Group C .....	40
Table 16: mean SV during the S-T-S test 48h post-operative in Group A and Group C .....	42
Table 17: mean HR during the S-T-S test 7d post-operative in Group A (after the intervention) and Group C (no intervention) .....	43
Table 18: mean sBP during the S-T-S test 7d post-operative in Group A (after the intervention) and Group C (no intervention) .....	44
Table 19: mean SV during the S-T-S test 7d post-operative in Group A (after the intervention) and Group C (no intervention) .....	45

## V. Zusammenfassung

### **Hintergrund**

Patientinnen und Patienten sind häufig krankheitsbedingt immobil, dies kann zu Muskelschwund, Knochenschwund und einer Schwächung des Herzkreislaufsystems führen und sich als insuffiziente Kreislaufadaptierung bei Veränderung der Körperposition äußern. Um diesem Problem entgegenzuwirken, testet diese Studie die Auswirkung einer täglichen Übung mit einer Vibrationsplatte auf das Herzkreislaufsystem von herzoperierten Patienten und Patientinnen.

### **Methodik**

19 Patientinnen und Patienten wurden in 2 Gruppen aufgeteilt. Die eine Gruppe erhielt postoperativ die standard Physiotherapie und die andere Gruppe erhielt die standard Physiotherapie und eine zusätzlich Intervention mit einer Vibrationsplatte. Es wurden kardiovaskuläre Parameter von beiden Gruppen postoperativ ohne Intervention gemessen und 7 Tage postoperativ mit Interventionen gemessen.

### **Ergebnisse**

Es konnten keine signifikanten kardiovaskulären Unterschiede zwischen den beiden Gruppen gefunden werden. Jedoch gab es in der Interventionsgruppe die Tendenz zu einer höheren Herzfrequenz bei Lagewechsel und in der Kontrollgruppe eine Tendenz zu einem höheren Schlagvolumen bei Lagewechsel.

### **Schlussfolgerung**

Die Ergebnisse zeigen keine signifikanten Veränderungen der kardiovaskulären Parameter auf einen Lagewechsel. Doch aufgrund der geringen Anzahl der untersuchten Patienten und Patientinnen, wäre eine weitere wissenschaftliche Untersuchung dieser Thematik relevant.

## VI. Abstract

### **Background**

Patients have extended bed rest due to illness, which can lead to muscle loss, bone loss and cardiovascular decompensation and resulting in insufficient adaptation during change in posture. To counteract this problem, this study evaluates the effect of daily exercise using a vibration plate to engage the cardiovascular system of patients who have undergone cardiac surgery and are facing prolonged bed rest and inactivity.

### **Methodology**

19 patients were divided into 2 groups. One group received standard physiotherapy, post-operative, and the other group received standard physiotherapy and an additional intervention using a vibration plate. Cardiovascular parameters of both groups were measured post-operative without intervention and 7 days post-operative with intervention.

### **Results**

There were no significant cardiovascular differences were found between the two groups. However, there was a tendency for a higher heart rate during position change in the intervention group and a tendency for a higher stroke volume during position change in the control group.

### **Conclusion**

The results show no significant changes in cardiovascular parameters in response to change in position. However, due to the small number of patients examined, further scientific investigation would be useful.

# 1 Introduction

After heart surgery, or any other major operation, patients can be bedridden for long periods of time. This can result in muscle loss (1), bone loss (2,3) and cardiovascular decompensation (4). These common problems after prolonged time in bed can contribute or result in negative outcomes for a patient's recovery.

Immobility and orthostatic intolerance and particularly challenging and mutually influencing factors that can contribute negatively to a patient's recovery, these will be discussed further in this thesis. This thesis will look at one possible solution to improve outcomes through early mobilization.

This diploma thesis will compare two different types of interventions on patients who have undergone heart surgery. This thesis explores the classic (standard physiotherapeutic) mobilization methods used at hospitals and combines these with an additional intervention called resistive vibration (RV).

The aim of this study was to find out if cardiovascular response to posture change can be improved by an additional intervention called resistive vibration.

## 1.1 Immobility

### 1.1.1 Definition of Immobility

Immobility is described as a partial or total restriction of a patient's freedom of movement due to physical or psychological illnesses. This is a common problem for bedridden patients, ICU patients, post-operative (PO) patients, elderly people, geriatric patients and even astronauts.

Early mobilization of heart surgery patients, usually 48 hours post-operative, in an intensive care unit is a common procedure and an important step for a patient's positive recovery. Initial steps include sitting on the bed edge and if successful is followed by a patient attempting to stand. This often comes with dizziness, a sudden decrease in mean arterial pressure (MAP) (5), which patients often recognize as weakness. If patients are too weak for mobilization it can inhibit recovery.

### 1.1.2 Consequences of Immobility

Patients spend more than 80% of their hospitalization in bed (6) which can result in acquired muscle weakness (7), higher morbidity, mortality and poorer long-term prognosis (8), and are common consequences for long term immobility.

About 0.85-1.5% of all health care costs are related to falls during immobility and orthostatic intolerance (9).

Immobility also has an impact on metabolic processes. Murine studies have shown, that chronic immobility reduces brain-derived neurotrophic factor (BDNF) concentration in the hippocampus (10–13) and that immobility leads to metabolic alterations in both the young and old (14). Immobility also triggers oxidative stress and inflammation, which can cause muscle atrophy (15). Furthermore, immobility can lead to bone loss (2,3), cardiac atrophy (4), decreased muscle thickness (1), cognitive changes (16), cortical inhibition (17), decreases of gray matter volume in the bilateral frontal lobes, temporal poles, parahippocampal gyrus, insula and right hippocampus (18).

One approach to counteract immobility is to improve mobilization after surgery and to enhance the patient's orthostatic blood pressure regulation and improve patients mobilization process and timelines to returning home.. However, in order to pursue these goals, the basic principles of the cardiovascular system must be considered and understood.

## 1.2 Regulation of the Cardiovascular System

The main task of the cardiovascular system is to keep arterial blood pressure constant in order to ensure adequate blood flow to various organs.

Baroreceptors and arterial chemoreceptors sense changes in blood pressure within a few seconds and deliver immediate information to the autonomic nervous system (ANS) in order to adapt cardiac output (CO) and heart rate (HR) (19).

### 1.2.1 Baroreceptors

In the case of rapid and short-term (seconds to minutes) regulatory processes, neurogenic regulation via circulatory reflexes dominate. These function according to the principle of a control loop with a negative feedback slope. The presso (or baro) receptors play a particularly important role and are located in the high-pressure system in the area of the carotid sinus, near the dividing points of the common carotid arteries, and at the aortic arch, which is why they are also called sinoaortic pressoreceptors. There are located as free nerve endings in the tunica media and tunica adventitia and are excited depending on the vessel dilatation (20). Figure 1 provides an overview of the above-mentioned short-term regulation of mean arterial pressure (MAP).

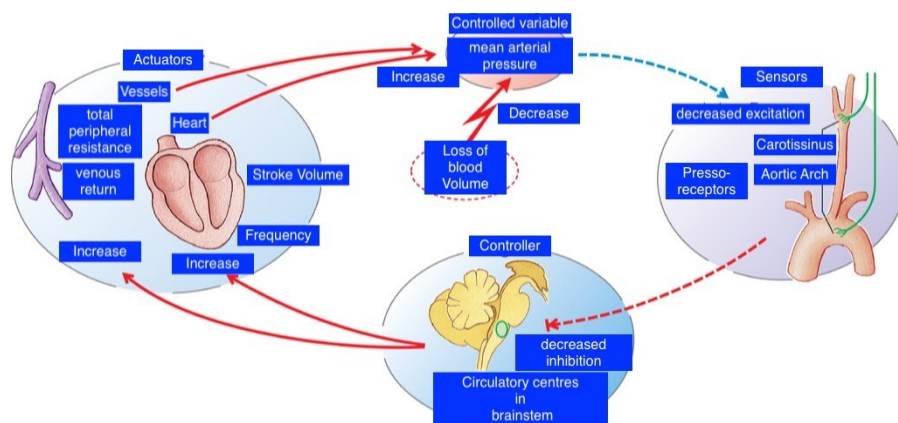


Figure 1: Control mechanism for short-term regulation of MAP; The primary drop in arterial pressure, which was assumed here to be the result of blood loss, sets in motion a chain of regulatory processes that lead to sympathetic activation via the pressoreceptors and thus to increased cardiac activity and vascular constriction (20).

Baroreceptors can detect changes in volume, pressure and frequency and send them via afferent nerve fibres to the central nervous system, which then adjusts the cardiovascular system by modifying the efferent nerve fibres of the autonomic nervous system. However, the system of short-term blood pressure regulation can be disturbed by various factors. Under physiological conditions, receptors regulate

heart rate and peripheral resistance on a rapid "beat-to-beat" basis. In heart failure, there is a dysfunction of the baroreceptors. When the baroreceptor is stressed, vasoconstriction occurs in control subjects, which is absent in heart failure patients. Therefore, the baroreceptor's sensitivity is decreased in heart failure. Ultimately, the loss of sensitivity of the baroreceptors results in an increase of sympathetic activity and a general activation of sympathetic efferents and a decrease in parasympathetic activity (22). Elderly people and bedridden patients may be particularly vulnerable for orthostatic intolerance.

### 1.3 Orthostatic Intolerance

Orthostatic Intolerance describes an insufficient blood pressure adaptation to posture changes. Orthostatic intolerance is defined by a systolic blood pressure (sBP) drop of  $>20\text{mmHg}$  or a diastolic drop of  $>10\text{mmHg}$  within 3 minutes after posture change. Normally, change in posture should result in sympathetic vasoconstriction, but in orthostatic intolerant patients this mechanism is insufficient, even the compensatory heart rate increase may not occur (23). Some patients complain about dizziness or even loss of consciousness when standing up. These conditions are being elicited due to an insufficient orthostatic blood pressure regulation. Clinical symptoms can include: nausea, visual disturbances (24) and a sudden decrease in mean arterial pressure (MAP) (5).

Figure 2 shows an overview of the cardio-vascular changes during a change in posture. By getting into an upright posture, about 300ml of blood rushes into the venous system and the splanchnic system. As a result, venous return to the heart is no longer sufficient and leads to a decrease in CO of approximately 20%. In response to this decrease in CO, the sympathetic system is activated and the parasympathetic system (vagus nerve) is inhibited. This counter mechanism has a positive inotropic and chronotropic effect on the heart and leads to constriction of the peripheral arterioles. This results in CO increase and total peripheral resistance (TPR) increase and leads to an increase in HF. Therefore, blood pressure remains approximately the same, despite the change in position (25).

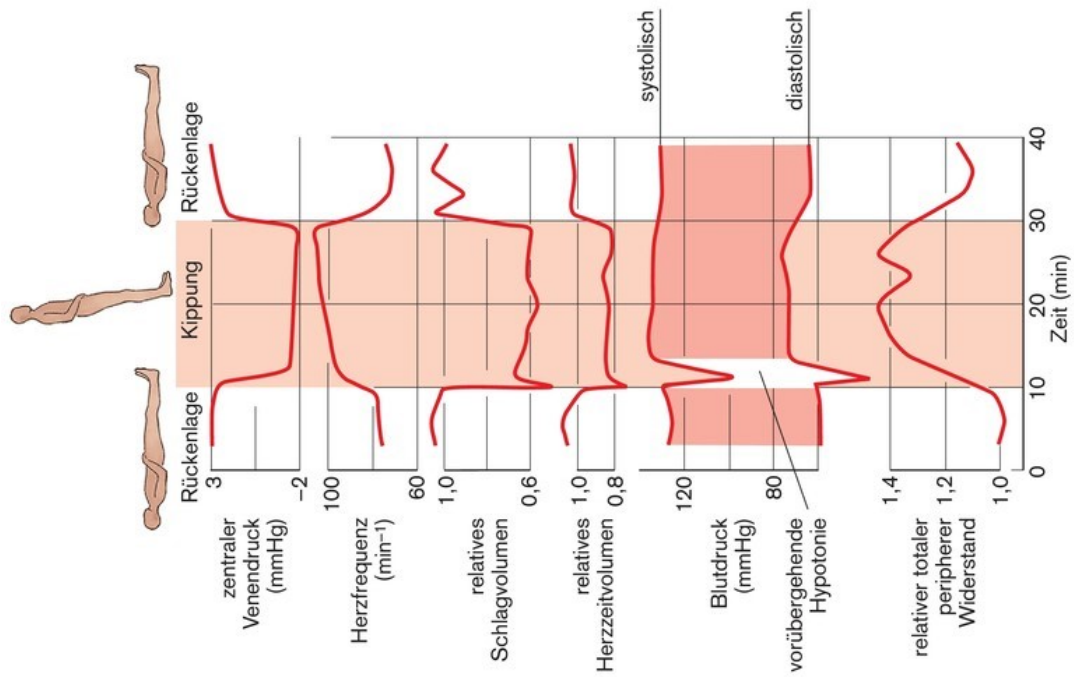


Figure 2: Orthostatic cardiovascular reaction (26)

If these mechanisms are not sufficient orthostatic hypotension can occur and patients may even syncope.

#### 1.4 Orthostatic Syncope

Orthostatic syncope can occur when changing from lying or sitting to standing: The venous blood pools in the lower half of the body, which is accompanied by a drop in blood pressure (hypotension). Normally, the autonomic nervous system counteracts the drop in blood pressure. However, a disturbed circulatory regulation can lead to reduced blood flow to the brain and syncope (27). Another way to support the cardiovascular system and to prevent possible syncope during change of position, is to increase the activity of calf muscles.

## 1.5 The Cardio-Postural Model

Studies have shown a connection between calf muscle activation and posture change (28) and an increase of calf muscle activation leads to an increased HR while passive standing (29). The calf muscle activation was measured with an electromyography (EMG), which was also used in this study. These results suggest that the muscle pump is being used to provide enough blood to the heart to compensate posture and blood pressure changes. For a better understanding of the interaction between the cardiovascular control (CC) and the postural control (PC), the Cardio-Postural Model was developed (30). This Model (Figure 3) combines the Cardiovascular Control with the Postural Control to achieve a better overview about the physiological response on posture and blood pressure changes. Postural control describes the ability of the body to adapt to gravity and body position changes. This is based on central-nerval, sensoric processing of the vestibular organ, the visual system, the proprioceptors and the exteroceptors (31).

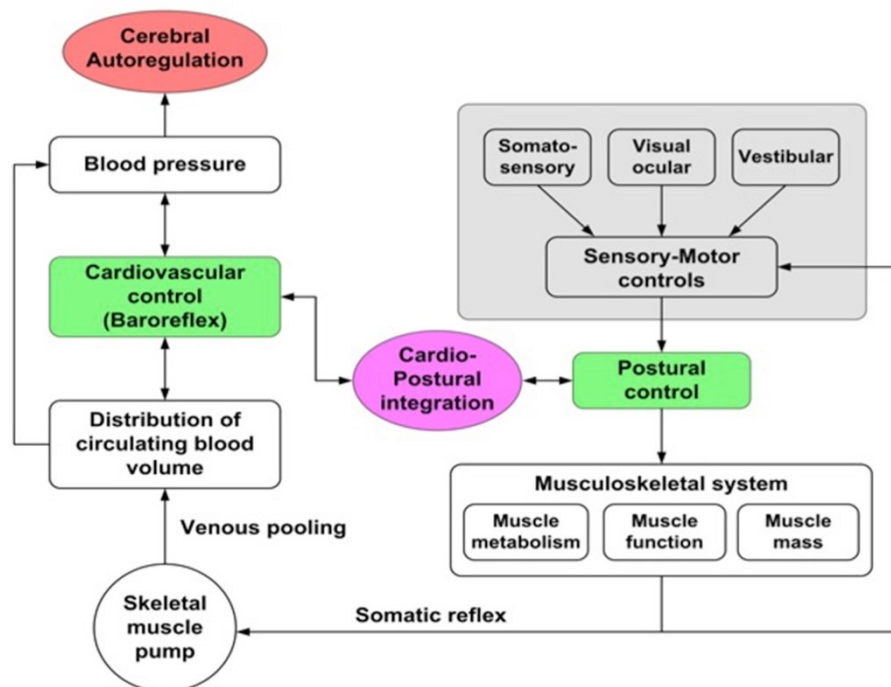


Figure 3: Cardio-postural interactions: Illustration of the cardio-postural components associated with mechanisms that prevent falls: Left—cardiovascular component of the regulation of blood pressure (blood volume, heart rate and vascular resistance); Right—sensory motor input components related to postural control; Center—cardio-postural integration: hypothesized as baroreflex activation of skeletal muscle pump (32)

## 1.6 Whole Body Vibration

The hypothesis we put forward to strengthen the cardiovascular system, especially in bedridden patients, was through exercise with a vibration plate. In this process, patients stand on a vibration plate with their full weight. The vibration of the plate causes the whole body to vibrate, hence the name “Whole Body Vibration”. This topic has already been investigated in a number of studies and the results are presented in the following chapter.

### 1.6.1 Positive Effects of Whole Body Vibration

Studies have shown, that exercising on a vibration plate leads to an improvement of leg muscle strength (33,34), bone mineral density (33,35), back pain (36,37), health-related quality of life and decreased fall risk (38,39). However, regular, chronic exposure of whole body vibration can also have some negative effects.

### 1.6.2 Negative Effects of Vibration

Known negative effects of chronic whole-body vibration are disorders of the skeletal system, digestive system, reproductive system, visual system and vestibular system (39–43). For example, operators of off-road vehicles, tractors, helicopters and armored vehicles are frequently exposed to high-magnitude vibration for prolonged durations. The resulting vibration of the spinal column is believed to cause intervertebral disc displacement, spinal vertebrae degeneration, and osteo-arthritis (44–46). Vibration transmitted through the spinal column to the head may induce hearing loss, visual impairment, vestibular damage, and can even induce brain hemorrhaging at very high vibration magnitudes (39,44,47–49). Due to the negative effects of repetitive whole body vibration, it is questionable whether this exercise can be safely used in the clinical setting in an intensive care unit.

### 1.6.3 Safety of whole-body vibration therapy in intensive care patients

The study by Wollersheim and colleagues showed that there were no clinically relevant changes in vital signs or hemodynamic parameters in intubated intensive care patients after a 15 minute whole body vibration in supine position (50).

## 2 Aims and Objectives

### 2.1 Aim

The aim of this study was to explore how the cardio-postural control of bedridden patients, post heart surgery, could be affected by the intervention of resistive vibration which uses a training device called Galileo, applying vibration to the foot sole in combination of a transition of 15 degrees (see Figure 4).

### 2.2 Objectives

The postural control is a central concern of surgical intensive care medicine and physiotherapy. From the patient's point of view, there is insecurity when standing, resulting in avoidance behavior. Postural control while sitting, in contrast to standing, is often not a problem. This is explained by the different cognition, and different sensory and motor functions when sitting compared to standing. The key to quick postural control is not fully understood. Influencing factors include the antigravity muscles of the knee, hip and trunk extensors. If these are insufficient, a protective step is taken to support the phases of steady-state, the anticipatory mechanisms and the reactive measures.

In geriatric patients, vibration can be used to treat elderly, fragile and fall-prone patients in order to effectively counteract the loss of mobility and the resulting muscles, and thus indirectly, bone loss (51). Several studies have shown that this is a safe method to decrease fall risk (52), improve walking ability (53), muscle strength, gait, balance and quality of life in older people (54).

The Galileo device has been used successfully in patients with back pain to increase muscle strength (55) which changes blood flow in the leg (56), muscle oxygenation and blood volume (57). Studies have shown that whole body vibration is safe to use in patients with dialysis (58), chronic obstructive pulmonary disease (COPD) (59), lung transplantation (60), multiple sclerosis (61), and cerebral palsy (62).

## 2.3 Hypothesis

The postoperative application of vibration (Galileo) and / or the change of position at 15 ° leads to a changed cardio-postural control compared to the standard mobilization.

## 3 Methods

This study was carried out at the heart surgery unit of the University Hospital, Graz (LKH), Austria. It was organized by the Division of Physiology and the Clinical Department of Heart Surgery at the Medical University, Graz.

In the study we tried to gather as much information about the cardiovascular system as possible using a variety of different devices. We measured different cardiovascular parameters during a sit to stand test (S-T-S test) pre-operative as well as 48 hours after the surgery. This provided information on the impact of the operation. After the second sit-to-stand test we started with the new intervention for one full week. Patients were randomly assigned to one of three different types of interventions (see 3.2.1.). At 7 days and 3 month post-operative the S-T-S test was repeated.

The present thesis will be focusing on the comparison of resistive vibration (Group A) and standard physiotherapy (Group C), comparing differences in hemodynamic parameters before and after the intervention/control condition.

### 3.1 Ethical Approval

Ethical approval was obtained from the Ethics Committee of the Medical University of Graz, Austria (EK: 31-343 ex 18/19). The study was conducted according to the principals of the Declaration of Helsinki (2013). Prior to study inclusion, written informed consent was obtained from each patient.

### 3.2 Study Protocol

The S-T-S test can often be challenging for patients due to post-operative weakness. Therefore, we started the test in a half supine position. This test was carried out 24 hours before surgery and on the 2<sup>nd</sup> and 7<sup>th</sup> day as well as 3 months post-operative keeping the measurement times constant. As post-operative

treatment, group A (intervention group 1) received a daily vibration unit of 10 minutes (at an angle of 15 degrees and with 25 Hz) from the 2nd day post-operative onwards. Group B (intervention group 2) was also tilted to 15 degrees for 10 minutes per day from day 2 post-operative onwards, but without vibration. The control group (C) received only the usual standard physiotherapy that all patients (also those in groups A and B) receive as part of clinical routine (see Figure 4).

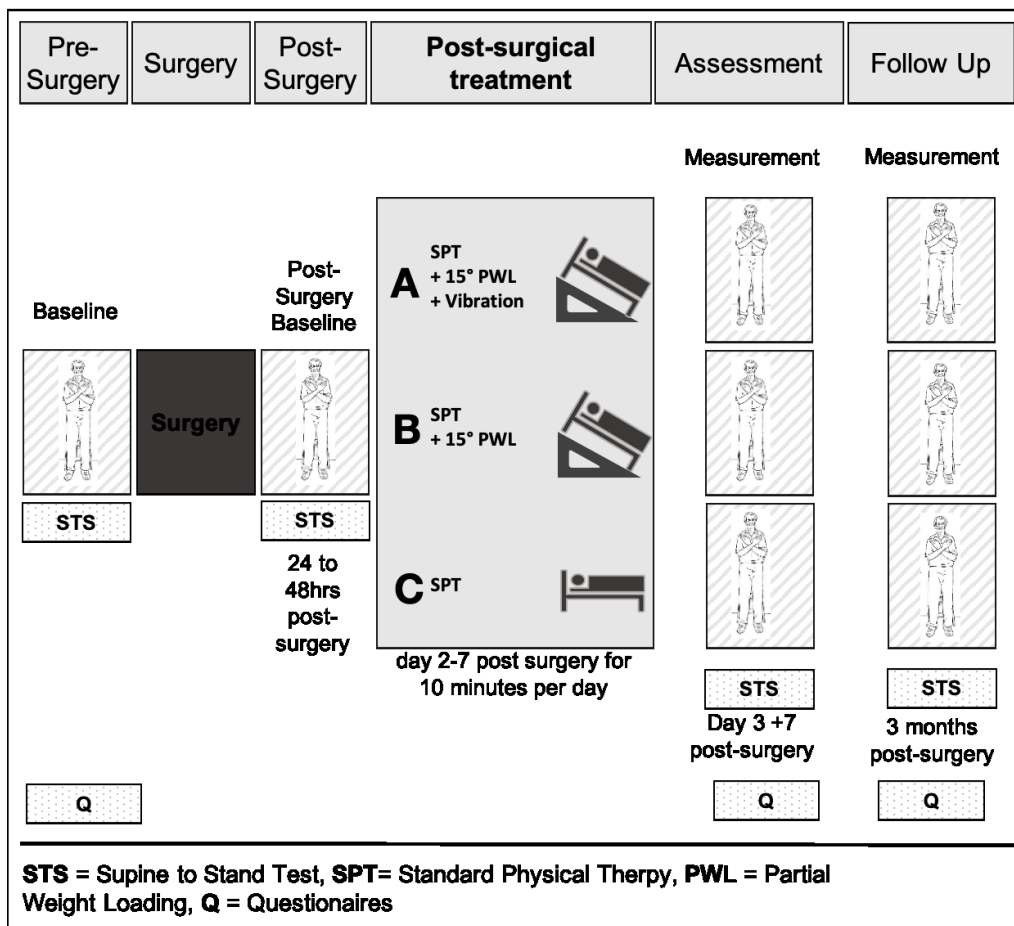


Figure 4: Illustration of the study protocol

### 3.2.1 Patient groups

The patients were randomized split in one of the following three groups.

#### 3.2.1.1 Group A: Intervention Group 1 (10 Patients)

In this intervention group, the patients received standard physiotherapy after the second post-operative day and additionally daily vibration with the Galileo training plate. The patients were in an 15° inclined bed position so they were standing on

the Galileo plate with their own feet and a small amount of their own weight. They were vibrated at 25 Hz for 10 minutes.

#### 3.2.1.2 Group B: Intervention Group 2 (10 Patients)

This intervention group received standard physiotherapy after the second post-operative day and the added tilted bed position but to 15° without vibration. This intervention group was necessary to see if a possible effect was triggered by the tilt only.

#### 3.2.1.3 Group C: Intervention Group 3 (10 Patients)

This control group underwent standard physiotherapy after operation which was provided by the clinic. During the extended standard physiotherapy the patients are moved to sit transverse in bed and touch the ground with their feet. Additionally they receive breathing therapy for 15 minutes. If it is possible the patients are encouraged to stand up. This is followed by a daily standup test and an active cardiovascular gymnastic. About 4-5 days post operation the patients are encouraged to walk around.

#### 3.2.2 Sit-to-Stand Test (S-T-S test)

The Sit-to-Stand test is a standard method for examining cardiac postural changes in patients.

The S-T-S test includes three parts: (i.) resting phase, where the patient has to sit quietly for 5 minutes, (ii.) followed by standing up for 5 minutes and a (iii.) recovery phase, where the patients return to a seated position for 5 minutes. If patients are not fit enough to stand for five minutes after the second postoperative day, the standing is shortened and adapted to the patient's fitness.

The standard standing position was retained for all patients. They had to stand quietly, hands at the side of the body, with eyes open, fixing a point on the opposite wall. The feet had to be parallel and in this case not on the floor but on the pressure plate at 10 cm apart.

If the patient was unable to stand for five minutes, the standing test was stopped, the patient was to sit down again and the duration of the standing test was documented. During the S-T-S test hemodynamic parameters were measured by the task force monitor (TFM©, CNSystems) using electrodes positioned at the thorax and continuous blood pressure by a finger plethysmograph. Cerebral blood flow was measured by Doppler sonography and blood flow of the calf muscles by two near-infrared spectroscopy (NIRS) electrodes. Additionally, we positioned an EMG for muscle measurement at the calf muscles.

### 3.3 Subject Inclusion and Exclusion Criteria

#### 3.3.1 Inclusion Criteria

- 65 to 85 years old patients undergoing conventional aortic valve replacement surgery or an elective coronary artery bypass surgery.

#### 3.3.2 Exclusion Criteria

- Euroscore II > 8
- Patients with possible operative delirium at the second day
- Patients who still needed to be ventilated after two days post-operative
- Patients who required higher dose of catecholamines on the second day post-operative (norepinephrine over 0.05-0.1 micrograms / kg body weight, suprenen over 0.05-0.1 micrograms / kg body weight, Dobutrex over 5 micrograms / kg body weight)
- Existing thrombosis: Existing thrombosis of the leg veins was excluded by preoperative sonography of the leg veins in the study group. This examination is not performed in everyday cardiac surgery, although the superficial leg veins are removed as part of coronary artery bypass surgery, which would be obsolete in the case of deep leg vein thrombosis. In long-term practice, no case has occurred where leg vein thrombosis would not have been clinically and preoperatively recognized. If the leg vein thrombosis was positive, the patient was excluded from the study.
- Dropouts

### 3.3.3 Dropouts

During the study, probationary withdrawals occurred for various reasons. Originally, 10 persons per group, 30 in total, were planned. Due to artefacts, missing data or poor quality of data, some measurements could not be taken into statistical consideration and led to drop outs of patient data.

In group A with 11 patients, 48 h post-operative, only the data of 9 patients could be statistically evaluated for the measured values HR, sBP, SV; the rest could not be taken into account due to artefacts, missing data or poor data quality. 7d post-operative, only 7 patients could be used for sBP and only 6 patients for HR and SV.

In group C with 8 patients, 48 h post-operative, only the data of 4 patients could be statistically evaluated for the measured values HR, sBP, SV, the rest could not be taken into account due to artefacts, missing data or poor data quality. 7d post-operative, only 4 patients could be used for SV and only 5 patients for HR and sBP.

**Dropouts and Missing Data**

Parameter	Group	Original	48h post	7d post
HR	A	11	9	6
	C	8	4	5
sBP	A	11	9	7
	C	8	4	5
SV	A	11	9	6
	C	8	4	4

Table 1: Dropouts and missing data of different parameters (HR, sBP, SV) in group A and C

## 3.4 Randomization

Randomization was carried out using an online tool (randomizer.at)

## 3.5 Statistics

### 3.5.1 Main target variable

Cardio-postural control (= hemodynamic parameters)

### 3.5.2 Null hypothesis

There are no differences in the post-operative orthostatic regulation on the application of a vibration plate (Galileo) used for early mobilization with a 15 degree inclination compared to standard physiotherapy alone.

### 3.5.3 Alternative hypothesis

There is a difference in the post-operative orthostatic regulation depending on the application of a vibration plate (Galileo) used for early mobilization and change in position to 15 degrees inclination compared to standard physiotherapy.

### 3.5.4 Number of patients - sample size

Since this is a pilot study, a detailed calculation of the number of cases is not possible at this stage. In this pilot study, 10 patients per group were required (a total of 30 patients) in order to be able to calculate a sample size number for further studies.

### 3.5.5 Planned statistical procedures

Analysis of variance for repeated measurements, applying group as between subjects factor and the selected epochs as the repeated measures factor. From the continuously recorded hemodynamic parameters the following epochs were selected for the analyses: epoch 1 (last 10sec of rest), epochs 2, 3, 4 (each 10 sec. during stand) and epochs 5, 6, 7, 8 (each representing 10 sec.) during recovery (see Figure 5). The transition from lying/sitting in bed to standing was not analyzed due to the number of artifacts and increased variation of timing between the patients

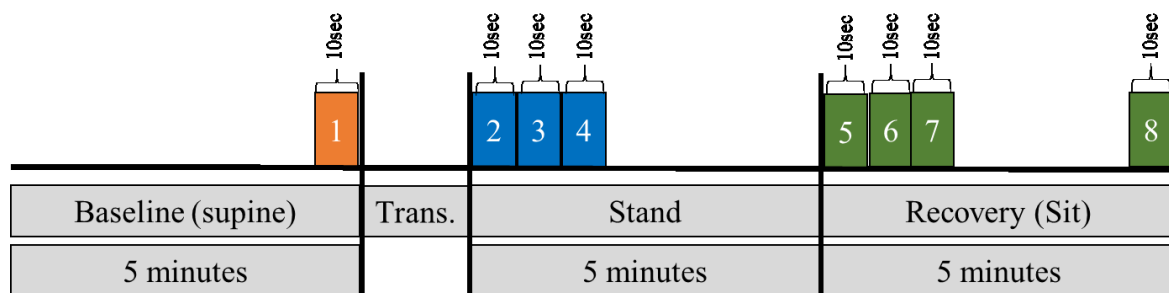


Figure 5: Epochs from different phases of the S-T-S test included into the analyses. Trans. = Transition from supine to stand, 1-10 = epochs, each 10 sec.

## 3.6 Study Design

Prospective, interventional randomized clinical trial to prove the effectiveness of resistive vibration intervention on cardio-postural

### 3.7 Devices used for measurements

To gain as much information as possible, we measured hemodynamic parameters, brain blood flow, muscle blood flow, electric muscle activity and movements while standing.

#### 3.7.1 Task Force Monitor

Along with the standard monitoring provided by the ICU at the hospital, a task force monitor (TFM) was used to measure blood pressure, heart frequency and the thoracic impedance. The task force monitor measures blood pressure by oscillometric measurement of the upper arm and by a plethysmograph on the finger. The thoracic impedance provides information about stroke volume, (SV) cardiac output and total peripheral resistance (TPR).

The heart frequency is being measured by a standard three channel ECG. Systolic and diastolic blood pressure are calculated by the task force monitor.

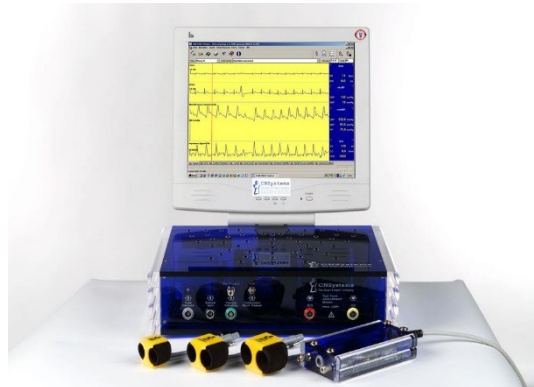


Figure 6: Task Force Monitor® (TFM) for measuring haemodynamic parameters.

### 3.7.2 Bagnoli 8-Channel EMG System

The Bagnoli 8-Channel EMG System measures transdermal signals. One electrode per leg was attached to the lower leg over the gastrocnemius muscle and soleus muscle. The postural movements were calculated with the data provided by the EMG system combined with the pressure plate (and reported elsewhere).

### 3.7.3 Near-infrared spectroscopy (NIRS)

The NIRS was positioned on one calf and fixed with tape. The NIRS was used to measure changes in the artery vasoconstriction and venous congestion in the legs caused by standing up. The oxygenation monitor is measuring the blood volume and the oxygenation level of the muscle.

### 3.7.4 DWL Multiflow

Blood and cerebral blood flow in the limbs would change while patients are standing up therefore, we used the standard transcranial Doppler sonography. A 2 MHz Doppler-Sensor was positioned right over the cerebri media artery and fixed by a headset. Beat to beat data of the systolic, diastolic and average blood speed were sent to the task force monitor to analyze the cerebral auto regulation. This would also identify spontaneously appearing fluctuations in blood pressure and cerebral blood flow.



Figure 7: DWL Multiflow

Available from: <https://www.dwl.de/produkte/mdt/>

### 3.7.5 ACS – AccuSway Balance and Sway Platform

The AccuSway Balance and Sway Platform is being used to measure the postural movements based on the body's center of gravity. Body shift and changes were recorded. To describe the postural movement, global parameters like length and range of fluctuations were used.



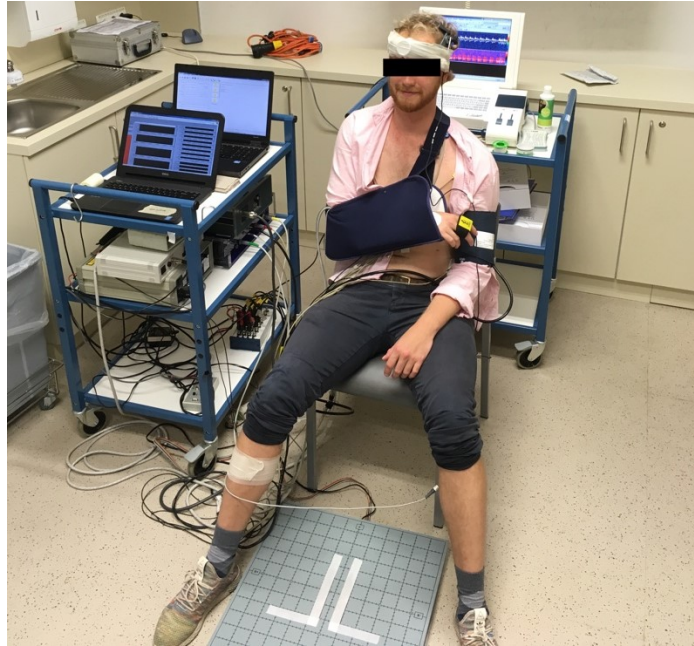
Figure 8: AccuSway Balance and Sway Platform

Available from:

<https://amti.biz/select%20product%20PDFs/Biomechanics%20force%20platforms/AccuSway%20brochure.pdf>

### 3.7.6 Blood samples

There were no blood samples collected during the individual measurement appointments. However, there were regular blood samples taken at the clinic. These samples were not included in the study. There were no additional bloods drawn from the patients.



*Figure 9: Candidate connected to all examination equipment and ready for measurement*

## 3.8 Devices used for the intervention

### 3.8.1 Galileo

Galileo is a training device made by a German company, which imitates a walking motion by vibration. By alternating left and right movements, the body is being forced to compensate the vibration through rhythmic muscle contractions. Those contractions are not made on purpose, but by a reflex called the stretch reflex. Through this reflex, leg muscles, abdomen muscles and back muscles are being stimulated. By using a frequency of 25 hearts there were 25 contraction periods per second as a compensation. This corresponds to about 9000 steps over three minutes. This device is mainly used for geriatric patients to counteract immobility and the resulting muscle loss and bone loss. But not only in geriatric medicine Galileo is being used, also in space medicine. For example, astronauts on the ISS are using a similar device to counteract their bone and muscle loss due lack of gravity.



Figure 10: Galileo Training Device (Vibration plate)

### 3.8.1.1 Stretch Reflex

The best known stretch reflex is the patellar tendon reflex. Through passive muscle stretching a signal is transported through the afferent nerves into the spinal cord, where the signal is redirected to the efferent nerves in the muscle and a muscle contraction is triggered. The stretch reflex is the fastest spinal reflex.

## 3.9 Documentation

The patient names are pseudo-anonymized by sequential case numbers. The group assignment was randomized. The collection of personal data for identification and measurements took place at the University Clinic for Surgery, Clinical Department for Cardiac Surgery, LKH Graz. After completing the study, this data will be deleted, while de-identified data with case numbers remain at the Department of Physiology.

## 3.10 Literature Research

For literature research, PubMed® online access of the Medical University of Graz was used with following keywords: "resistive vibration", "cardio postural", "vibration intervention".

## 4 Results

For the present diploma thesis only cardiovascular parameters, in particular heart rate (HR), systolic blood pressure (sBP) and stroke volume (SV), were included. These measured parameters will be shown further down this thesis.

The following tables "**Descriptive Statistics**" show the mean values of the measured parameters (HR, sBP, SV) from group A (with intervention) and C (without intervention) at different epochs during the sit to stand test (see 3.5.5.).

- 48h post-operative measured values: baseline\_post, stand\_post, recovery\_post
- 7d post-operative measured values: baseline\_7d, stand\_7d, recovery\_7d

### 4.1 Patients

In total 27 patients were enrolled in the study, 6 female, 21 male. Of those 19 patients completed the study at all three time points (pre-, post, 7d-post)

Their average age was 69.63 years, average height of 170.37 cm and average weight of 78,68 kg.

Group A: 11 Patients, 3 female, 8 male, average age 70,64 years

Group C: 8 Patients, 2 female, 6 male, average age 68,25 years

### 4.2 Post-operative 48 hours

48 hours post-operatively, the patients were connected to the task force monitor and measured during the first attempt to stand. Up to this point no attempt of mobilization or any intervention had been made. From the total duration of the S-T-S test 8 epochs were selected for the analyses.

The following tables show the results of HR, sBP and SV of Group A and C at different time points, 48 hours post-operative. The first measure point "HR\_baseline\_post" shows the last 10 seconds of the resting phase (patient lying/sitting in bed). "HR\_stand\_post" shows the epochs during standing and "HR\_recovery" shows the epochs while the patient is resting after the stand again. These values were measured before any intervention in order to compare them 7 days later, after a daily intervention, to explore the null hypothesis.

#### 4.2.1 Group A (Resistive Vibration Intervention)

Groupe A included 11 Patients (7 male, 4 female). Average age 70,64 years, average height of 170,81 cm and average weight of 78,86 kg.

##### 4.2.1.1 Heart Rate (HR)

The following table describes the measurement results of the HR of Group A, at the different measure points 48 hours post-operative.

**Descriptive Statistics (HR) (Group A) 48h post OP**

	N	Minimum	Maximum	Mean	SD
HR_baseline_post	9	78,17	97,95	86,58	7,25
HR_stand1_post	9	77,58	113,79	93,81	9,73
HR_stand2_post	9	75,73	112,19	92,60	10,02
HR_stand3_post	9	76,87	112,78	92,73	10,78
HR_recovery1_post	9	76,80	104,55	89,51	8,12
HR_recovery2_post	9	70,77	103,16	88,45	10,63
HR_recovery3_post	9	73,07	102,34	85,67	9,90
HR_recovery4_post	9	67,97	92,86	82,98	8,20

Table 2: HR of Group A - 48h post OP

##### 4.2.1.2 Systolic Blood Pressure (sBP)

The following table describes the measurement results of the sBP of Group A at the different measure points, 48 hours post-operative.

**Descriptive Statistics (sBP) (Group A) 48h post OP**

	N	Minimum	Maximum	Mean	SD
sBP_baseline_post	9	73	145	115	20,32
sBP_stand1_post	9	86	150	116	25,08
sBP_stand2_post	9	86	158	118	25,61
sBP_stand3_post	9	87	140	114	21,81
sBP_recovery1_post	9	86	143	115	20,69
sBP_recovery2_post	9	85	144	116	23,70
sBP_recovery3_post	9	86	148	117	24,72
sBP_recovery4_post	9	88	146	119	20,21

Table 3: sBP of Group A - 48h post OP

#### 4.2.1.3 Stroke Volume (SV)

The following table describes the measurement results of the SV of Group A at different measure points, 48 hours post-operative.

**Descriptive Statistics (SV) (Group A) 48h post OP**

	N	Minimum	Maximum	Mean	SD
SV_baseline_post	9	42,94	65,91	52,10	7,71
SV_stand1_post	9	39,70	68,84	56,12	9,13
SV_stand2_post	9	41,19	66,91	53,30	9,13
SV_stand3_post	9	43,08	66,62	53,00	7,03
SV_recovery1_post	9	42,99	69,51	53,71	8,96
SV_recovery2_post	9	42,06	87,37	56,19	14,27
SV_recovery3_post	9	44,05	94,37	57,99	15,77
SV_recovery4_post	9	42,03	65,48	51,06	7,66

Table 4: SV of Group A - 48h post OP

#### 4.2.2 Group C (standard physiotherapy)

Group C included 8 Patients (6 male, 2 female) with an average age of 68.25 years, average height of 169.75 cm and average weight of 78.43 kg.

##### 4.2.2.1 Heart Rate (HR)

The following table describes the measurement results of the heart rate of Group C at the different measure points 48 hours post-operative.

**Descriptive Statistics (HR) (Group C) 48h post OP**

	N	Minimum	Maximum	Mean	SD
HR_baseline_post	4	66,34	90,94	82,11	10,88
HR_stand1_post	4	79,35	110,27	98,31	13,64
HR_stand2_post	4	78,32	111,98	97,71	15,24
HR_stand3_post	4	77,20	110,12	97,95	15,52
HR_recovery1_post	4	76,26	109,10	89,02	14,79
HR_recovery2_post	4	76,41	108,37	88,38	14,87
HR_recovery3_post	4	75,58	108,46	88,99	14,47
HR_recovery4_post	4	67,06	91,01	84,70	11,77

Table 5: HR of Group C - 48h post OP

#### 4.2.2.2 Systolic Blood Pressure (sBP)

The following table describes the measurement results of the sBP of Group C at the different measure points, 48 hours post-operative.

**Descriptive Statistics (sBP) (Group C) 48h post OP**

	N	Minimum	Maximum	Mean	SD
sBP_baseline_post	4	96	131	111	16,51
sBP_stand1_post	4	76	176	132	41,99
sBP_stand2_post	4	84	174	132	37,14
sBP_stand3_post	4	73	164	120	37,26
sBP_recovery1_post	4	101	115	107	6,53
sBP_recovery2_post	4	96	121	110	10,13
sBP_recovery3_post	4	99	139	115	17,56
sBP_recovery4_post	4	86	107	97	11,07

Table 6: sBP of Group C - 48h post OP

#### 4.2.2.3 Stroke Volume (SV)

The following table describes the measurement results of the SV of Group C at the different measure points, 48 hours post-operative.

**Descriptive Statistics (SV) (Group C) 48h post OP**

	N	Minimum	Maximum	Mean	SD
SV_baseline_post	4	37,07	116,14	65,66	35,34
SV_stand1_post	4	37,59	90,76	63,99	26,86
SV_stand2_post	4	37,78	74,11	55,93	15,23
SV_stand3_post	4	38,81	76,29	53,88	16,89
SV_recovery1_post	4	45,04	79,39	68,95	16,05
SV_recovery2_post	4	43,43	91,49	57,45	22,83
SV_recovery3_post	4	40,89	91,04	74,01	22,86
SV_recovery4_post	4	37,07	75,30	47,76	18,43

Table 7: SV of Group C - 48h post OP

### 4.3 Post-Operative 7 days

The following tables describe the measurement results of HR, sBP and SV of Group A and C different epochs, 7 days post-operative.

#### 4.3.1 Group A (Resistive Vibration Intervention)

##### 4.3.1.1 Heart Rate (HR)

The following table describes the measurement results of the HR of Group A at the different measure points, 7 days post-operative.

**Descriptive Statistics (HR) (Group A) 7d post OP**

	<b>N</b>	<b>Minimum</b>	<b>Maximum</b>	<b>Mean</b>	<b>SD</b>
HR_baseline_7d	6	73,02	99,65	84,40	9,11
HR_stand1_7d	6	75,53	116,64	100,50	16,22
HR_stand2_7d	6	74,66	116,98	99,66	16,37
HR_stand3_7d	6	76,70	112,21	94,78	13,36
HR_recovery1_7d	6	73,25	114,64	94,71	16,65
HR_recovery2_7d	6	72,83	122,21	95,30	19,52
HR_recovery3_7d	6	78,31	113,71	91,84	15,33
HR_recovery4_7d	6	71,75	114,75	88,99	15,17

*Table 8: HR of Group A - 7d post OP*

#### 4.3.1.2 Systolic Blood Pressure (sBP)

The following table describes the measurement results of the sBP of Group A at the different measure points, 7 days post-operative.

**Descriptive Statistics (sBP) (Group A) 7d post OP**

	N	Minimum	Maximum	Mean	SD
sBP_baseline_7d	7	93	151	116	19,70
sBP_stand1_7d	7	103	160	137	22,07
sBP_stand2_7d	7	100	189	146	27,99
sBP_stand3_7d	7	86	188	142	32,29
sBP_recovery1_7d	7	91	141	121	17,03
sBP_recovery2_7d	7	96	139	118	16,40
sBP_recovery3_7d	7	90	147	122	18,96
sBP_recovery4_7d	7	101	131	120	9,83

Table 9: sBP of Group A - 7d post OP

#### 4.3.1.3 Stroke Volume (SV)

The following table describes the measurement results of the SV of Group A at the different measure Dpoints, 7 days post-operative.

**Descriptive Statistics (SV) (Group A) 7d post OP**

	N	Minimum	Maximum	Mean	SD
SV_baseline_7d	6	37,25	53,49	46,23	5,66
SV_stand1_7d	6	54,53	116,73	71,20	22,98
SV_stand2_7d	6	47,64	69,20	57,37	7,58
SV_stand3_7d	6	47,91	72,12	59,28	9,41
SV_recovery1_7d	6	48,24	64,67	55,64	6,51
SV_recovery2_7d	6	38,58	55,82	49,18	6,83
SV_recovery3_7d	6	38,49	55,38	48,18	5,63
SV_recovery4_7d	6	33,65	59,99	46,14	8,36

Table 10: SV of Group A - 7d post OP

#### 4.3.2 Group C (standard physiotherapy)

##### 4.3.2.1 Heart Rate (HR)

The following table describes the measurement results of HR of Group C at the different measure points, 7 days post-operative.

**Descriptive Statistics (HR) (Group C) 7d post OP**

	N	Minimum	Maximum	Mean	SD
HR_baseline_7d	5	66,25	82,82	74,50	7,75
HR_stand1_7d	5	78,84	94,59	84,51	6,14
HR_stand2_7d	5	78,21	96,13	84,05	7,00
HR_stand3_7d	5	76,18	97,65	86,06	9,12
HR_recovery1_7d	5	72,56	87,46	77,66	6,02
HR_recovery2_7d	5	69,60	86,91	74,51	7,03
HR_recovery3_7d	5	69,02	86,70	75,44	6,98
HR_recovery4_7d	5	65,94	85,44	72,48	7,85

Table 11: HR of Group C - 7d post OP

##### 4.3.2.2 Systolic Blood Pressure (sBP)

The following table describes the measurement results of sBP of Group C at the different measure points, 7 days post-operative.

**Descriptive Statistics (sBP) (Group C) 7d post OP**

	N	Minimum	Maximum	Mean	SD
sBP_baseline_7d	5	93	143	124	18,78
sBP_stand1_7d	5	75	154	124	29,48
sBP_stand2_7d	5	51	152	119	40,48
sBP_stand3_7d	5	39	148	112	43,03
sBP_recovery1_7d	5	81	146	119	25,07
sBP_recovery2_7d	5	82	139	118	22,53
sBP_recovery3_7d	5	86	147	123	24,54
sBP_recovery4_7d	5	96	148	126	22,27

Table 12: sBP of Group C - 7d post OP

#### 4.3.2.3 Stroke Volume (SV)

The following table describes the measurement results of SV of Group C at the different measure points 7 days post-operative.

**Descriptive Statistics (SV) (Group C) 7d post OP**

	<b>N</b>	<b>Minimum</b>	<b>Maximum</b>	<b>Mean</b>	<b>SD</b>
SV_baseline_7d	4	44,30	78,10	62,14	14,27
SV_stand1_7d	4	41,99	148,09	88,32	45,15
SV_stand2_7d	4	43,28	83,29	66,74	18,07
SV_stand3_7d	4	43,94	82,65	65,09	16,09
SV_recovery1_7d	4	41,82	98,77	76,90	25,99
SV_recovery2_7d	4	50,13	88,16	71,44	16,87
SV_recovery3_7d	4	46,72	83,30	62,98	15,36
SV_recovery4_7d	4	39,02	77,68	60,88	16,27

*Table 13: SV of Group C - 7d post OP*

## 4.4 Comparison of Group A and C

The following figures show the analyzed parameters (HR, sBP, SV) of group A and C, both 48h post-operative and 7d post-operative. Since the measured data were not all normally distributed, in chapter 4.4.1, analyses were run for log-transformed data to prove the results.

### 4.4.1 Post-operative 48h

#### 4.4.1.1 Heart Rate (HR)

Comparison of group A and C 48h after heart surgery and before onset of the intervention revealed the following differences in HR:

**Epoch:** Results of the repeated measures ANOVA with a Greenhouse-Geisser correction, comparing HR during the epochs between the two groups, indicated a significant main effect for epoch ( $F_{(2.52, 27.69)} = 6.86, p < .002, \eta^2 = .38$ ), reflecting the physiological adaptation during change of posture.

**Epoch x Group:** No significant interaction between epochs x group was found ( $F_{(2.52, 27.69)} = .82, p = 0.48$ ).

**Group:** Also no significant interaction in intervention group (group A) was observed ( $F_{(1, 11)} = .06, p = 0.81$ ).

The following figure shows the measured HR of group A and C 48h post-operative at the different points of time. No intervention was applied before this measurement. This is the first standing attempt post-operative. The taskforce monitor measured an increase in HR in both groups during standing period. The HR decreased again in both groups during the recovery phase.

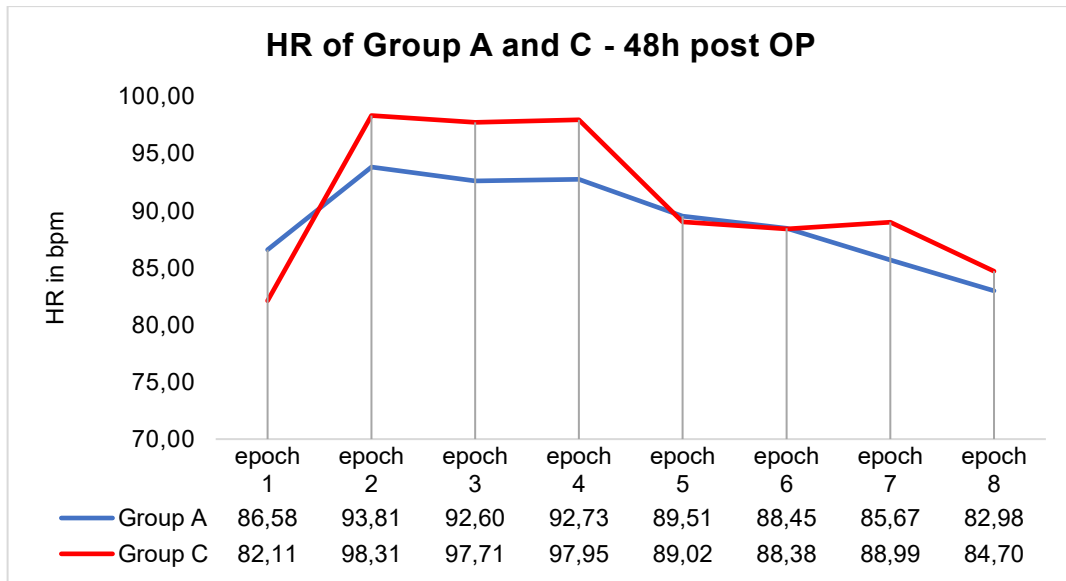


Figure 11: HR of Group A and C - 48h post OP with mean HR during different epochs

HR Group A and C 48h post OP

	epoch 1	epoch 2	epoch 3	epoch 4	epoch 5	epoch 6	epoch 7	epoch 8
Group A	86,58	93,81	92,60	92,73	89,51	88,45	85,67	82,98
Group C	82,11	98,31	97,71	97,95	89,02	88,38	88,99	84,70

Table 14: mean HR during the S-T-S test 48h post-operative in Group A and Group C

#### 4.4.1.2 Systolic Blood Pressure (sBP)

Comparison of group A and C 48h after heart surgery and before onset of the intervention revealed the following differences in sBP;

**Epoch:** Results of the repeated measures ANOVA with a Greenhouse-Geisser correction, comparing sBP during the epochs between the two groups, indicated no significant main effect for epoch ( $F_{(1.93, 21.23)} = 1.59, p = .229, \eta^2 = .13$ ), reflecting a non-physiological adaptation of Group A during change of posture.

**Epoch x Group:** No significant interaction between epochs x group was found ( $F_{(1.93, 21.23)} = 1.89, p = .177$ ).

- **Group:** Also no significant interaction in intervention group (group A) was observed ( $F_{(1, 11)} = .06, p = .896$ ).

The following figure shows the measured sBP of group A and C 48h post-operative at different points of time. No intervention was applied before this measurement. This is the first standing attempt post-operative. The taskforce monitor measured an increase in sBP in both groups during standing period. The sBP decreased again in both groups during the recovery phase.

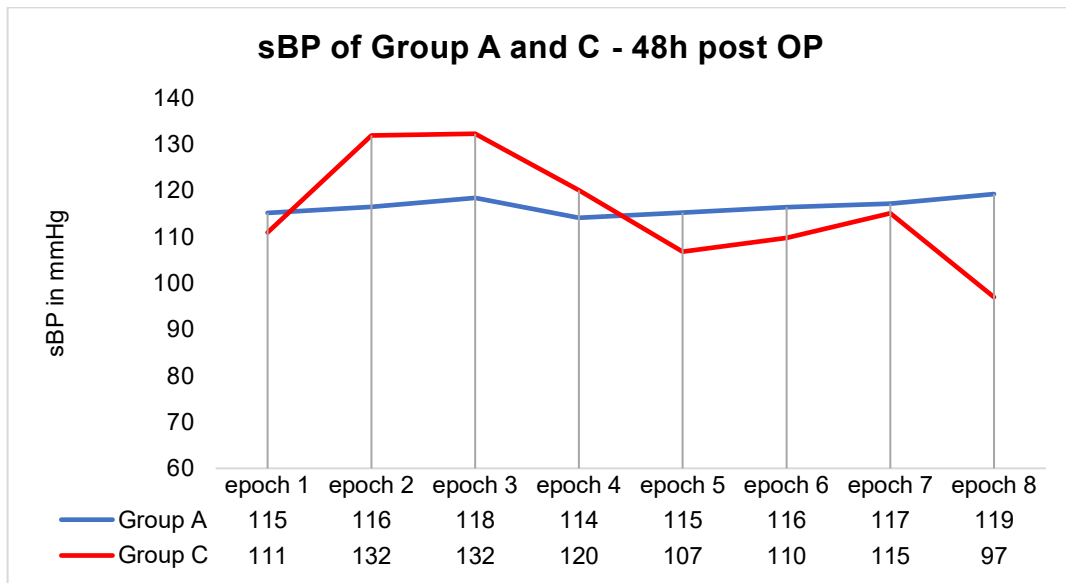


Figure 12: sBP of Group A and C - 48h post OP with mean sBP during different epochs

	epoch 1	epoch 2	epoch 3	epoch 4	epoch 5	epoch 6	epoch 7	epoch 8
Group A	115	116	118	114	115	116	117	119
Group C	111	132	132	120	107	110	115	97

Table 15: : mean sBP during the S-T-S test 48h post-operative in Group A and Group C

#### 4.4.1.3 Stroke Volume (SV)

Comparison of group A and C 48h after heart surgery and before onset of the intervention revealed the following differences in SV;

- **Epoch:** Results of the repeated measures ANOVA with a Greenhouse-Geisser correction, comparing SV during the epochs between the two groups, indicated no significant main effect for epoch ( $F_{(1.86, 20.50)} = 1.59$ ,  $p = 2.30$ ,  $\eta^2 = .13$ ), reflecting a non-physiological adaptation during change of posture.
- **Epoch x Group:** No significant interaction between epochs x group was found ( $F_{(1.86, 20.50)} = 1.17$ ,  $p = .326$ ).
- **Group:** Also no significant interaction in intervention group (group A) was observed ( $F_{(1, 11)} = .52$ ,  $p = 0.488$ ).

The following figure compares the measured SV of group A and C 48h post-operative at different points. No intervention was applied before this measurement. This is the first standing attempt post-operative. The taskforce monitor measured a decrease in SV in both groups during standing. The SV decreased again in both groups during the recovery phase. The decrease of Group C was less significant than the decrease of Group A.

### SV of Group A and C - 48h post OP

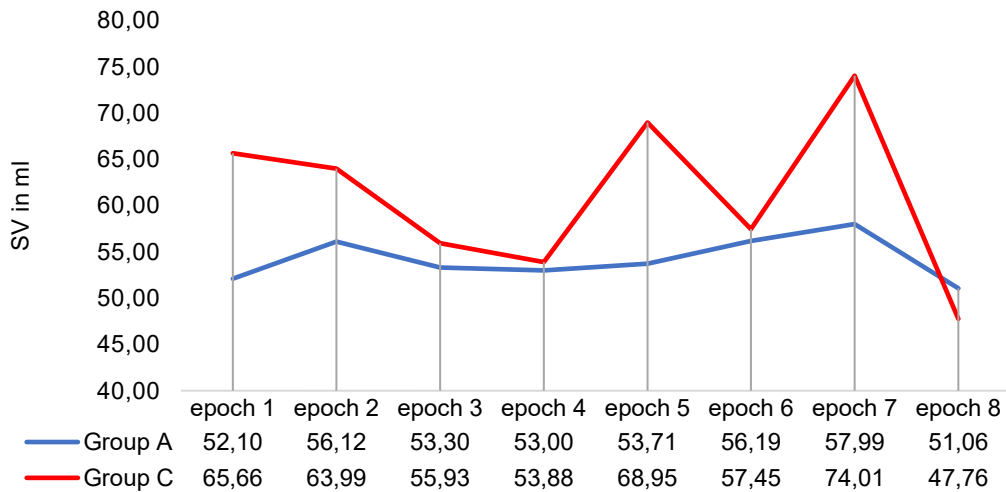


Figure 13: SV of Group A and C - 48h post OP with mean SV during different epochs

### SV Group A and C 48h post OP

	epoch 1	epoch 2	epoch 3	epoch 4	epoch 5	epoch 6	epoch 7	epoch 8
Group A	52,10	56,12	53,30	53,00	53,71	56,19	57,99	51,06
Group C	65,66	63,99	55,93	53,88	68,95	57,45	74,01	47,76

Table 16: mean SV during the S-T-S test 48h post-operative in Group A and Group C

#### 4.4.2 Post-operative 7 days – Comparison of Intervention

##### 4.4.2.1 Heart Rate (HR)

Comparison of group A and C 7d after heart surgery and after intervention was applied revealed the following differences in HR;

- Epoch:** Results of the repeated measures ANOVA with a Greenhouse-Geisser correction, comparing HR during the epochs between the two groups, indicated a significant main effect for epoch ( $F_{(2.7, 24.5)} = 10.89$ ,  $p < .001$ ,  $\eta^2 = .55$ ), reflecting the physiological adaptation during change of posture.
- Epoch x Group:** No significant interaction between epochs x group was found ( $F_{(2.72, 24.51)} = 1.71$ ,  $p = 0.16$ ).
- Group:** Furthermore, a tendency towards higher HR in the intervention group (group A) was observed ( $F_{(1, 9)} = 4.62$ ,  $p = .060$ ,  $\eta^2 = .34$ ).

Figure 14 shows the change of HR during rest, stand and recovery of group A (blue line) and C (red line) 7d post-operative and post intervention. Post-hoc tests indicated a faster increase of HR in patients of the intervention group and a larger decrease in the control group at the beginning of the recovery (epoch 4).

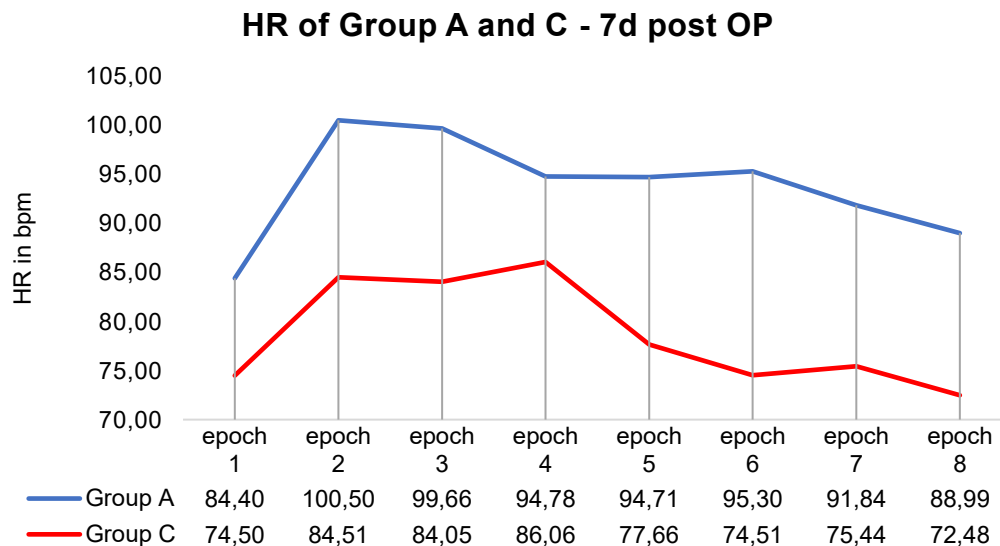


Figure 14: HR of Group A and Group C during S-T-S Test 7d post-operative (after intervention) with mean HR during different epochs

**HR Group A and C 7d post OP**

	epoch 1	epoch 2	epoch 3	epoch 4	epoch 5	epoch 6	epoch 7	epoch 8
<b>Group A</b>	84,40	100,50	99,66	94,78	94,71	95,30	91,84	88,99
<b>Group C</b>	74,50	84,51	84,05	86,06	77,66	74,51	75,44	72,48

Table 17: mean HR during the S-T-S test 7d post-operative in Group A (after the intervention) and Group C (no intervention)

#### 4.4.2.2 Systolic Blood Pressure (sBP)

Comparison of group A and C 7d after heart surgery and after intervention was applied revealed the following differences in sBP;

- **Epoch:** Comparison of the sBP during the S-T-S test between the groups revealed no statistically significant effect for the repeated measures factor epoch after sphericity correction with a Greenhouse-Geisser correction of the data ( $F_{(1.7, 17.0)} = 2.35, p=.132, \eta^2= .19$ ).

- **Epoch x Group:** However, a significant interaction between group x epochs was found ( $F_{(1.7, 17.0)} = 4.43, p < .033, \eta^2 = .31$ ), which was due to a large increase of sBP during standing in the intervention group (Figure 15).
- **Group:** Also no significant main effect for group, meaning that intervention group had no significant difference ( $F_{(1, 10)} = .29, p = .600, \eta^2 = .03$ ).

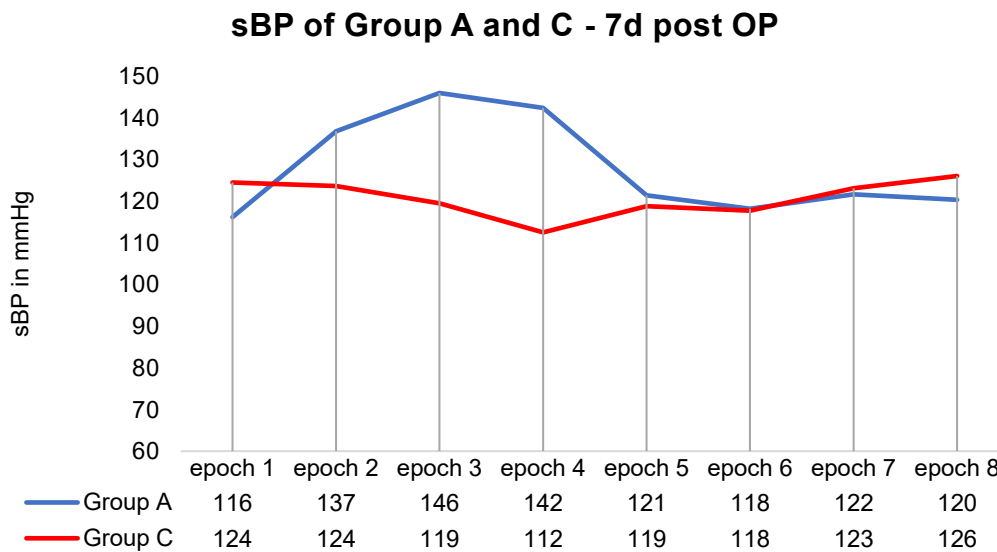


Figure 15: change in sBP during S-T-S test of Group A and C - 7d post OP; blue line: Group A (Intervention) red line: Group C (no intervention) with mean sBP during different epochs

**sBP Group A and C 7d post OP**

	epoch 1	epoch 2	epoch 3	epoch 4	epoch 5	epoch 6	epoch 7	epoch 8
<b>Group A</b>	116	137	146	142	121	118	122	120
<b>Group C</b>	124	124	119	112	119	118	123	126

Table 18: mean sBP during the S-T-S test 7d post-operative in Group A (after the intervention) and Group C (no intervention)

#### 4.4.2.3 Stroke Volume (SV)

Comparison of group A and C 7d after heart surgery and intervention was applied revealing the following differences in SV;

- **Epoch:** Results of the repeated measures ANOVA with a Greenhouse-Geisser correction, comparing SV during the epochs between the two groups, indicated a significant main effect for epoch ( $F_{(1.3, 10.2)} = 4.79, p = .046, \eta^2 = .37$ ).

- **Epoch x Group:** No significant interaction between group x epochs were found ( $F_{(1,28, 10,25)} = 0.50, p = 0.54$ ).
- **Group:** However the main effect for group showed only a tendency ( $F_{(1, 8)} = 3.854, p = .085, \eta^2 = .33$ ) towards a higher SV in the control group.

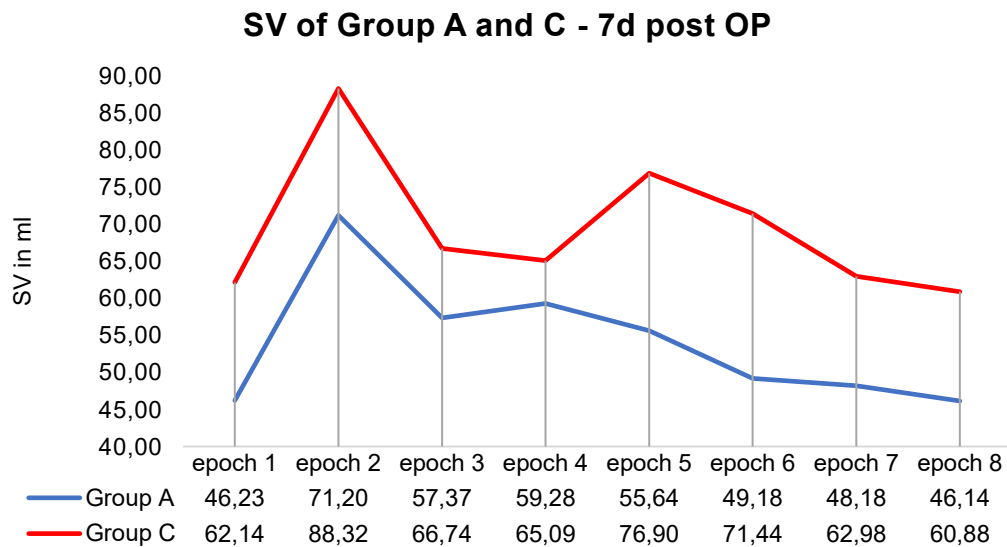


Figure 16: change in SV during S-T-S test of Group A and C - 7d post OP; blue line: Group A (Intervention) red line: Group C (no intervention) with mean SV during different epochs

**SV Group A and C 7d post OP**

	epoch 1	epoch 2	epoch 3	epoch 4	epoch 5	epoch 6	epoch 7	epoch 8
<b>Group A</b>	46,23	71,20	57,37	59,28	55,64	49,18	48,18	46,14
<b>Group C</b>	62,14	88,32	66,74	65,09	76,90	71,44	62,98	60,88

Table 19: mean SV during the S-T-S test 7d post-operative in Group A (after the intervention) and Group C (no intervention)

## 5 Discussion

### 5.1 Interpretation

When standing up, the circulation has to adapt to the changed hydrostatic pressure conditions in the vessels due to gravity. Changing positions causes more blood to enter the low-pressure system of the veins and the SV of the heart to fall, arterial pressoreceptors are then less excited and lead to a disinhibition of the sympathetic tone. This increase in sympathetic tone leads to an increase in cardiac frequency, total peripheral resistance and systolic blood pressure (26). These changes were observed in all patients 48 h post-operative and were understood to be a physiological reaction to the change in posture.

The same physiological changes could be observed 7 days post-operative in both groups, group A (intervention group) and group C (control group). These changes were also understood to be a physiological reaction to the change of posture.

**Epochs:** The epochs of systolic blood pressure and stroke volume of the two groups 48 h after surgery were not significant in comparison to each other. This was due to group A, who were unable to adapt physiologically to the change of position. Only the heart rate could be physiologically adapted to the change of position in both groups. The lack of adaptation can be explained by the severity of the operation and the first attempt to stand up or due to an already known insufficient adaptation to posture change. At this point, the cardiovascular system was overtaxed and could not adapt sufficiently.

In contrast, 7 days after the operation, a significant increase in the parameters HR and SV and adaptation to the change of position were observed in both groups and can be understood as a physiological reaction. Only in the case of sBP, due to the lack of adaptation in group C, was no significance observed in the epochs.

**Group:** 48h after surgery without any intervention, no significant differences in HR, SBP and SV were found between group A and C. However, at 7d post-operative, a tendency towards a higher HR was observed in group A with a change of position. This difference could be explained by the regular implementation of resistive vibration intervention. The vibration and tilting of the bed could have trained the

cardiovascular system of the patients in group A to adapt better to changes in position by adjusting the heart rate.

In group C, a tendency towards increased SV was observed 7 days post-operative. However, it should not be ignored that group C already had a higher stroke volume than group A 48h post-operative.

Furthermore, no significant change in sBP were observed between the two groups 7d post-operatively. It can be assumed that the intervention has no effect on systolic blood pressure adaptation during change in position.

**Epoch x Group:** In almost all parameters, both 48h post-operative and 7d post-operative, no significant values were found in the epoch x group; only in the sBP 7d post-operative where a significant value was observed. This is due to the opposite behaviour of group C. This can probably be explained by the fact that the adaptation of the sBP of group C is not as sufficient as in group A.

Interestingly, there were no significant differences between group A (intervention group) and group C (control group) 7 days post-operative. A faster adaptation of the cardiovascular system to the posture change of group A (intervention group), which received a daily intervention with Galileo, was to be expected.

With the evaluation of the collected data, therefore, no significant post-operative improvement can be shown by the described intervention. However, it should be noted that the number of patients (19) is most likely too small to make a clear statement. Further tests with a larger number of patients would be necessary to obtain a statistically deeper insight into the intervention effect.

## 5.2 Conclusion

The results show no significant improvement in cardiovascular response to a change of posture post-operative after intervention. The aims were therefore not achieved and the hypothesis was disproved.

## 5.3 Limitations

Numerous limitations interfered with this study and made it difficult to measure different cardiovascular parameters.

**Malfunctions:** The main limitations of this Thesis were the recurring failures and malfunctions of various devices described in the methods, especially the “DWL Multiflow” repeatedly went on strike. This led to regular delays in measurements and collecting data.

**Hospital Staff:** Another limitation was the nursing staff in the hospital, who often resisted the measurements of the patients. In future, the nursing staff should be incorporated into the study to ensure a stable workflow.

**Hospital Beds:** An additional limitation were different hospital beds. Not all of them could be tilted 15 degrees. Therefore, the daily intervention could not be always carried out in the same way, which could have a negative impact on significance an outputs. For future studies, only standardized hospital beds should be used.

**S-T-S test:** This could not always be performed accurately due to weakness of the patients. Often patients were in a supine position completely lying or sitting in bed.

**Measurement time:** The measurement times of patients could not always be carried out at same time.

**Number of Patients:** The number of patients was another limitation of this thesis. Due to the small number of patients tested and the repeated withdrawal of patients the data set was continuously reduced and weakened the statistical normal distribution and significance.

## 6 References

1. Pišot R, Narici M V., Šimunič B, De Boer M, Seynnes O, Jurdana M, et al. Whole muscle contractile parameters and thickness loss during 35-day bed rest. *European Journal of Applied Physiology*. 2008;104(2):409–14.
2. Leblanc AD, Schneider VS, Evans HJ, Engelbretson DA, Krebs JM. Bone mineral loss and recovery after 17 weeks of bed rest. *Journal of Bone and Mineral Research*. 1990;5(8):843–50.
3. Rittweger J, Simunic B, Bilancio G, Gaspare De Santo N, Cirillo M, Biolo G, et al. Bone loss in the lower leg during 35 days of bed rest is predominantly from the cortical compartment. *Bone*. 2009;44(4):612–8.
4. Perhonen MA, Franco F, Lane LD, Buckey JC, Blomqvist CG, Zerwekh JE, et al. Cardiac atrophy after bed rest and spaceflight. *Journal of Applied Physiology*. 2001;91(2):645–53.
5. Grasser EK, Goswami N, Hinghofer-Szalkay H. Presyncopal cardiac contractility and autonomic activity in young healthy males. *Physiological Research*. 2009;
6. Pedersen MM, Bodilsen AC, Petersen J, Beyer N, Andersen O, Lawson-Smith L, et al. Twenty-four-hour mobility during acute hospitalization in older medical patients. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*. 2013;
7. Ali NA, O'Brien JM, Hoffmann SP, Phillips G, Garland A, Finley JCW, et al. Acquired weakness, handgrip strength, and mortality in critically ill patients. *American Journal of Respiratory and Critical Care Medicine*. 2008;
8. Hermans G, Van Mechelen H, Clerckx B, Vanhullebusch T, Mesotten D, Wilmer A, et al. Acute outcomes and 1-year mortality of intensive care unit-acquired weakness: A cohort study and propensity-matched analysis. *American Journal of Respiratory and Critical Care Medicine*. 2014;
9. Heinrich S, Rapp K, Rissmann U, Becker C, König HH. Cost of falls in old age: A systematic review. *Osteoporosis International*. 2010.
10. Rasmusson AM, Shi L, Duman R. Downregulation of BDNF mRNA in the hippocampal dentate gyrus after re-exposure to cues previously associated with footshock. *Neuropsychopharmacology*. 2002;
11. Roceri M, Hendriks W, Racagni G, Ellenbroek BA, Riva MA. Early maternal deprivation reduces the expression of BDNF and NMDA receptor subunits in rat hippocampus. *Molecular Psychiatry*. 2002;
12. Smith MA, Makino S, Kvetnansky R, Post RM. Stress and glucocorticoids affect the expression of brain-derived neurotrophic factor and neurotrophin-3 mRNAs in the hippocampus. *Journal of Neuroscience*. 1995;15(3 I):1768–77.
13. Vaidya VA, Marek GJ, Aghajanian GK, Duman RS. 5-HT(2A) receptor-mediated regulation of brain-derived neurotrophic factor mRNA in the hippocampus and the neocortex. *Journal of Neuroscience*. 1997;17(8):2785–95.
14. Pišot R, Marusic U, Biolo G, Mazzucco S, Lazzar S, Grassi B, et al. Greater loss in muscle mass and function but smaller metabolic alterations in older compared with younger men following 2 wk of bed rest and recovery. *Journal of Applied Physiology*. 2016;120(8):922–9.
15. Agostini F, Mazzucco S, Biolo G, Biolo G, Medica C, Cattinara O, et al. METABOLIC ADAPTATION TO INACTIVE LIFESTYLE : FROM MUSCLE ATROPHY TO CARDIOVASCULAR RISK. 2010;47–60.
16. Lipnicki DM, Gunga HC. Physical inactivity and cognitive functioning: Results from bed rest studies. *European Journal of Applied Physiology*. 2009;105(1):27–35.

17. Marušič U, Meeusen R, Pišot R, Kavcic V. The brain in micro- and hypergravity: The effects of changing gravity on the brain electrocortical activity. *European Journal of Sport Science*. 2014;14(8):813–22.
18. Li K, Guo X, Jin Z, Ouyang X, Zeng Y, Feng J, et al. Effect of simulated microgravity on human brain gray matter and white matter - Evidence from MRI. *PLoS ONE*. 2015;10(8):1–10.
19. Brandes R, Lang F, Schmidt RF, GmbH S-V. *Physiologie des Menschen : mit Pathophysiologie*. 2020.
20. Ehmke H. Regulation des arteriellen Blutdrucks. In: Pape H-C, Kurtz A, Silbernagl S, editors. 9., vollst. Georg Thieme Verlag KG; 2019. Available from: [https://eref.thieme.de/ebooks/cs\\_10278468#/ebook\\_cs\\_10278468\\_\\_AAE1339F\\_D35F\\_4617\\_807F\\_EEF8A255B252\\_BT](https://eref.thieme.de/ebooks/cs_10278468#/ebook_cs_10278468__AAE1339F_D35F_4617_807F_EEF8A255B252_BT) - Physiologie
21. Ehmke H. Kreislaufregulation. In: Pape H-C, Kurtz A, Silbernagl S, editors. 9., vollst. Georg Thieme Verlag; 2019.
22. Böhm M. Barorezeptorenreflexe. In: Blum HE, Müller-Wieland D, editors. 11., unver. Georg Thieme Verlag; 2020. Available from: [https://eref.thieme.de/ebooks/cs\\_11584564#/ebook\\_cs\\_11584564\\_SL87426775\\_BT](https://eref.thieme.de/ebooks/cs_11584564#/ebook_cs_11584564_SL87426775_BT) - Klinische Pathophysiologie
23. Radtke A. Orthostatische Hypotonie. In: Dietel M, Suttorp N, Zeitz M, editors. 18. Auflag. ABW Verlag; 2012. Available from: [https://eref.thieme.de/cockpits/0/0/cosym0788/4-788\\_BT](https://eref.thieme.de/cockpits/0/0/cosym0788/4-788_BT) - Harrisons Innere Medizin
24. Grasser EK, Goswami N, Rössler A, Vrecko K, Hinghofer-Szalkay H. Hemodynamic and neurohormonal responses to extreme orthostatic stress in physically fit young adults. *Acta Astronautica*. 2009;
25. Maack C, Böhm M. Orthostasesyndrom. In: Blum HE, Müller-Wieland D, editors. 11., unver. Georg Thieme Verlag; 2020. Available from: [https://eref.thieme.de/ebooks/cs\\_11584564#/ebook\\_cs\\_11584564\\_SL87428193\\_BT](https://eref.thieme.de/ebooks/cs_11584564#/ebook_cs_11584564_SL87428193_BT) - Klinische Pathophysiologie
26. Ehmke H. Kreislauffunktion unter Belastung. In: Pape H-C, Kurtz A, Silbernagl S, editors. 9., vollst. Georg Thieme Verlag; 2019. Available from: [https://eref.thieme.de/ebooks/cs\\_10278468#/ebook\\_cs\\_10278468\\_cs2201\\_BT](https://eref.thieme.de/ebooks/cs_10278468#/ebook_cs_10278468_cs2201_BT) - Physiologie
27. Mattle H, Fischer U. Orthostatische Synkope. In: Mattle H, Fischer U, editors. 5., überar. Georg Thieme Verlag KG; 2021.
28. Blaber AP, Landrock CK, Souvestre PA. Cardio-postural deconditioning: A model for post-flight orthostatic intolerance. *Respiratory Physiology and Neurobiology*. 2009;169(SUPPL.):21–5.
29. Garg A, Xu D, Laurin A, Blaber AP. Physiological interdependence of the cardiovascular and postural control systems under orthostatic stress. *American Journal of Physiology - Heart and Circulatory Physiology*. 2014;307(2):259–64.
30. Goswami N, Blaber AP, Hinghofer-Szalkay H, Montani JP. Orthostatic intolerance in older persons: Etiology and countermeasures. *Frontiers in Physiology*. 2017.
31. Dichgans J, Diener HC. The Contribution of Vestibulo-spinal Mechanisms to the Maintenance of Human Upright Posture. *Acta Oto-Laryngologica*. 1989 Jan 1;107(5–6):338–45.
32. Goswami N, Blaber AP, Hinghofer-Szalkay H, Montani JP. Orthostatic intolerance in older persons: Etiology and countermeasures [Internet]. Vol. 8, *Frontiers in Physiology*. Frontiers Media S.A.; 2017 [cited 2020 Aug 15]. p. 803. Available from: [www.frontiersin.org](http://www.frontiersin.org)

33. Verschueren SMP, Roelants M, Delecluse C, Swinnen S, Vanderschueren D, Boonen S. Effect of 6-month whole body vibration training on hip density, muscle strength, and postural control in postmenopausal women: A randomized controlled pilot study. *Journal of Bone and Mineral Research*. 2004;
34. Roelants M, Delecluse C, Goris M, Verschueren S. Effects of 24 Weeks of Whole Body Vibration Training on Body Composition and Muscle Strength in Untrained Females. *International Journal of Sports Medicine*. 2004;
35. Rubin C, Turner AS, Bain S, Mallinckrodt C, McLeod K. Low mechanical signals strengthen long bones. *Nature*. 2001;
36. Iwamoto J, Takeda T, Sato Y, Uzawa M. Effect of whole-body vibration exercise on lumbar bone mineral density, bone turnover, and chronic back pain in postmenopausal osteoporotic women treated with alendronate. *Aging Clinical and Experimental Research*. 2005.
37. Rittweger J, Just K, Kautzsch K, Reeg P, Felsenberg D. Treatment of chronic lower back pain with lumbar extension and whole-body vibration exercise: A randomized controlled trial. *Spine*. 2002;
38. Bruyere O, Wuidart MA, Di Palma E, Gourlay M, Ethgen O, Richy F, et al. Controlled whole body vibration to decrease fall risk and improve health-related quality of life of nursing home residents. *Archives of Physical Medicine and Rehabilitation*. 2005;
39. Abercromby AFJ, Amonette WE, Layne CS, McFarlin BK, Hinman MR, Paloski WH. Vibration exposure and biodynamic responses during whole-body vibration training. *Medicine and Science in Sports and Exercise*. 2007;39(10):1794–800.
40. Bovenzi M. Health effects of mechanical vibration. In: *Giornale Italiano di Medicina del Lavoro ed Ergonomia*. 2005.
41. Griffin MJ, Erdreich J. *Handbook of Human Vibration*. The Journal of the Acoustical Society of America. 1991;
42. Lings S, Leboeuf-Yde C. Whole-body vibration and low back pain: A systematic, critical review of the epidemiological literature 1992-1999. *International Archives of Occupational and Environmental Health*. 2000.
43. Seidel H. Selected health risks caused by long-term, whole-body vibration. *American Journal of Industrial Medicine*. 1993;
44. Griffin MJ, Erdreich J. *Handbook of Human Vibration*. The Journal of the Acoustical Society of America. 1991;
45. Lings S, Leboeuf-Yde C. Whole-body vibration and low back pain: A systematic, critical review of the epidemiological literature 1992-1999. *International Archives of Occupational and Environmental Health*. 2000.
46. Seidel H. Selected health risks caused by long-term, whole-body vibration. *American Journal of Industrial Medicine*. 1993;
47. Bochnia M, Morgenroth K, Dziewiszek W, Kassner J. Experimental vibratory damage of the inner ear. *European Archives of Oto-Rhino-Laryngology*. 2005;
48. Draeger J, Dupuis H. MECHANISCHE FAKTOREN BEI DER AUSLOSUNG DER AMOTIO RETINAE. *Klinische Monatsblätter für Augenheilkunde*. 1975;
49. Ishitake T, Ando H, Miyazaki Y, Matoba F. Changes of Visual Performance Induced by Exposure to Whole-body Vibration. *Kurume Medical Journal*. 1998;
50. Wollersheim T, Haas K, Wolf S, Mai K, Spies C, Steinhagen-Thiessen E, et al. Whole-body vibration to prevent intensive care unit-acquired weakness: Safety, feasibility, and metabolic response. *Critical Care [Internet]*. 2017;21(1):1–10. Available from: <http://dx.doi.org/10.1186/s13054-016-1576-y>

51. Gómez-Cabello A, González-Agüero A, Morales S, Ara I, Casajús JA, Vicente-Rodríguez G. Effects of a short-term whole body vibration intervention on bone mass and structure in elderly people. *Journal of Science and Medicine in Sport*. 2014;
52. Bruyere O, Wuidart MA, Di Palma E, Gourlay M, Ethgen O, Richey F, et al. Controlled whole body vibration to decrease fall risk and improve health-related quality of life of nursing home residents. *Archives of Physical Medicine and Rehabilitation*. 2005;86(2):303–7.
53. Kawanabe K, Kawashima A, Sashimoto I, Takeda T, Sato Y, Iwamoto J. Effect of whole-body vibration exercise and muscle strengthening, balance, and walking exercises on walking ability in the elderly. *Keio Journal of Medicine*. 2007;56(1):28–33.
54. Kawanabe K, Kawashima A, Sashimoto I, Takeda T, Sato Y, Iwamoto J. Effect of whole-body vibration exercise and muscle strengthening, balance, and walking exercises on walking ability in the elderly. *Keio Journal of Medicine*. 2007;
55. Rittweger J, Just K, Kautzsch K, Reeg P, Felsenberg D. Treatment of chronic lower back pain with lumbar extension and whole-body vibration exercise: A randomized controlled trial. *Spine*. 2002;27(17):1829–34.
56. Perchthaler D, Hauser S, Heitkamp HC, Hein T, Grau S. Acute effects of whole-body vibration on trunk and neck muscle activity in consideration of different vibration loads. *Journal of Sports Science and Medicine*. 2014;
57. Kerschman-Schindl K, Grampp S, Henk C, Resch H, Preisinger E, Fialka-Moser V, et al. Whole-body vibration exercise leads to alterations in muscle blood volume. *Clinical Physiology*. 2001;
58. Seefried L, Genest F, Luksche N, Schneider M, Fazeli G, Brandl M, et al. Efficacy and safety of whole body vibration in maintenance hemodialysis patients - A pilot study. *Journal of Musculoskeletal Neuronal Interactions*. 2017;
59. Greulich T, Nell C, Koepke J, Fechtel J, Franke M, Schmeck B, et al. Benefits of whole body vibration training in patients hospitalised for COPD exacerbations - a randomized clinical trial. *BMC Pulmonary Medicine*. 2014;14(1):1–9.
60. Gloeckl R, Heinzelmann I, Seeberg S, Damisch T, Hitzl W, Kenn K. Effects of complementary whole-body vibration training in patients after lung transplantation: A randomized, controlled trial. *Journal of Heart and Lung Transplantation* [Internet]. 2015;34(11):1455–61. Available from: <http://dx.doi.org/10.1016/j.healun.2015.07.002>
61. Mason RR, Cochrane DJ, Denny GJ, Firth EC, Stannard SR. Is 8 weeks of side-alternating whole-body vibration a safe and acceptable modality to improve functional performance in multiple sclerosis? *Disability and Rehabilitation*. 2012;
62. Stark C, Herkenrath P, Hollmann H, Waltz S, Becker I, Hoebing L, et al. Early vibration assisted physiotherapy in toddlers with cerebral palsy – a randomized controlled pilot trial. *Journal of Musculoskeletal Neuronal Interactions*. 2016;16(3):183–92.